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Role of Light Physical Activity Towards Stress in The Elderly in Nursing Home

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Abstract

Introduction: It was reported that one in five adults and four out of five adolescents around the world did not do enough physical activity, especially the elderly tend not to do physical activity that is classified as active. Less physical activity can inhibit the release of ACTH and decrease cortisol secretion so that it can cause stress. Although it has been reported about the relationship between physical activity and stress levels at the age of 23-54 years, there has not been much research on the relationship in the elderly. Many elderly people aged over 60 years, especially those living in nursing homes experience stress due to lack of physical activity. Thus, further research is needed regarding the relationship between light physical activity and stress levels in the elderly at the Nursing Home.

Methods: It was an unpaired categorical comparative analytic study. Elderly respondents at the Nursing Home aged 60-74 years will fill out the PASE questionnaire to assess physical activity and the PSS-10 to assess stress levels. The data obtained will be processed using Microsoft Excel and analyzed with the Pearson Chi-Square test using the SPSS-25 program.

Result: Of the 40 respondents, 30 did light physical activity and 10 did heavy physical activity. It was also found that 14 experienced mild stress and 26 experienced severe stress. The results from Pearson Chi-Square show p-value <0.001 and OR = 16.000.
Conclusions: The results of this study states that there is a significant relationship between light physical activity and stress levels in the elderly aged 60-74 years who live in nursing homes.

Introduction

The "WHO Global action plan on physical activity and health 2018-2030: More active people for a healthier world" was launched in 2018 which said one in five adults and four out of five adolescents around the world do not do enough physical activity.[1] In Latin America and the Caribbean is a region that has a population with less physical activity. Meanwhile, Uganda and Mozambique have residents with the highest physical activity. Only 6 percent of adults in this country are not physically active.[2]

Physical activity is a movements produced by skeletal muscles that result in an increase in energy expenditure that is more than at rest.[3] Physical activity is divided into 3 categories, that is mild, moderate and severe physical activity. Physical activity can be measured with the

Physical Activity Scale for Elderly (PASE) questionnaire which is specifically for the elderly with mild physical activity into 3 categories, namely mild with a score of 0-16, moderate with a score of 17-21 and severe with a score of 22-36.[4] Doing physical activity can affect stress levels, due to an increase in beta-endorphins produced in the hypothalamus pituitary adrenal (HPA) which will then be stimulated when the stressor induces the production of Corticotropin Releasing Hormone (CRH) causing the release of Adrenocorticotropic (ACTH) and increasing the secretion of epinephrine. So when beta-endorphins increase it will reduce stress levels.[5,6]

Stress can be obtained from external factor, such as the environment, work, and other aspects, and can also be internal, that is self. Stress levels can be measured using the Perceived Stress Scale (PSS-10) questionnaire into 3 categories, namely mild with a score of 1-13, moderate with a score of 14-26 and severe.[8] Stress is a state where homeostasis feels threatened which is triggered by certain environmental conditions which are a source of problems (stressors) which are then countered by physiological responses to maintain body balance (eustasis). Hypothalamic pituitary adrenal (HPA) and Autonomic Nervous System (ANS) are components of the stress system that will mediate neuroendocrine responses.[9] Stress will be perceived differently by each individual, so the resulting response is also different. The process of perception is influenced by mental factors and individual experiences in living life, so that perceptions will be different at the age of children, adolescents, adults and the elderly.[10] According to the World Health Organization (WHO) elderly (elderly) are people aged 60 years or more, who are categorized into 4 categories, namely middle aged 45-59 years, elderly 60-74 years, old 75-90 years, and very old 90 over.[11] In this study, respondents with the criteria of elderly aged 60-74 years at the Nursing Home will be used. In addition, there is also an age division according to the Indonesian Ministry of Health, which is divided into 9 categories, starting from toddlers 0-5 years, children 6-11 years, early adolescents 12-16 years, late adolescents 17-25 years, early adults 26-35 years, late adults 36-45 years, early elderly 46-55 years, late elderly 56-65 years and seniors over 65 years.[12] The Central Statistics Agency reported that last December 2021, there were 29.3 million elderly people, equivalent to 10.82% of the total population in Indonesia.[13] Some of the elderly population, especially those living in nursing homes only do light physical activity with a lifestyle that is not classified as active and spends a lot of time in bed.[14,15]

It was reported in 2019 by Hery Setiawan et al, that there was a significant relationship between the average physical activity and the level of stress carried out by hospital employees aged 23-54 years. The study used the International Physical Activity (IPAQ) questionnaire to measure the average physical activity of respondents without age restrictions[16]. Thus, it is still necessary to examine the relationship between light physical activity using a special questionnaire for the elderly, namely the Physical Activity Scale for Elderly (PASE) and stress levels in the elderly at nursing homes.

Material And Methods

Materials needed for conducting this research were consent forms for respondents, a Physical Activity Scale for Elderly (PASE) questionnaire to assess physical activity, and a Perceived Stress Scale-10 (PSS-10) questionnaire to assess stress levels. The study design in this study was an unpaired categorical comparative analytic study. The sampling method used was purposive sampling technique, with the target population being the elderly aged 60-74, while the reachable population was the elderly aged 60-74 living in the Bina Bhakti Serpong Nursing Home. The research sample was 40 elderly people who met the inclusion criteria, namely aged 60-74 years, communicative, did not consume psychotropic drugs, had no history of stress illness and were willing to fill out an informed consent form.

Method of Research: Forty elderly people who met the inclusion criteria were given an Informed Consent sheet as a sign of their willingness to participate in the study. All samples were given a PASE questionnaire to measure their physical activity as light, moderate or heavy physical activity; and the PSS-10 questionnaire to obtain mild, moderate or severe stress levels.The independent variable in this study was physical activity which was measured using the Physical Activity Scale for Elderly (PASE), the dependent variable was stress level which was measured using the Perceived Stress Scale (PSS-10) while the confounding variables included family and genetic background. Data in the form of physical activity and stress levels will be processed using Microsoft Excel 365 and analyzed using the Pearson Chi-Square test on the Statistical Package for the Social Sciences -25 (SPSS-25) with an accuracy of 95% ($p < 0.05$).

Result

Data on Elderly Characteristics in Nursing Homes

This research was conducted on the elderly who resided at the Bina Bhakti Werdha Nursing Home, totaling 67 people consisting of 27 men and 40 women with an age range of 56 - 84 years. However, according to the inclusion criteria, namely residents aged 60-74 there were only 40 people. Characteristic data of all residents in the Bina Bhakti Werdha Nursing Home can be seen in the table below:

Table 1. Baseline Characteristics

Characteristic		N=67	Percent-age (%)
Age (years)	45-59	1	1,5%
	60-74	40	59,7%
	75-90	21	31,3%
	90 Over	5	7,5%
Gender	Male	27	40,3%
	Female	40	59,7%

Physical Activity Data

The physical activity questionnaire was conducted through interviews with 67 elderly people, but only 53 respondents could be interviewed. Of the 53 respondents, 13 were excluded due to certain medical conditions so that the number of respondents who could collect data was only 40 people. Of the 40 who met the inclusion criteria, there were 30 people with light physical activity, 7 people with moderate physical activity and 3 people with heavy physical activity, see the table below:

Table 2. Physical Activity Data

Physical Activity	Frequency (n)	Percentage (%)
Light	30	75%
Moderate	7	17,5%
Heavy	3	7,5%
Total	40	100%

Stress Level Data

A total of 53 elderly people at the Bina Bhakti Serpong Nursing Home were interviewed to fill out the Perceived Stress Scale questionnaire (PSS-10) to see their level of stress, but only 40 met the inclusion criteria.[25] The stress level in this study was divided into 3 groups, that is mild stress with a score of 0-13, moderate stress with a score of 14-26 and severe stress with a score of 26-40. Of the 40 respondents, there were 14 respondents who experienced mild stress, 11 respondents experienced moderate stress and 26 respondents experienced severe stress. The results of the analysis of the respondent's stress level can be seen in the table below:

Table 3. Stress Level Data

Stress Level	Frequency (n)	Percentage (%)
Mild	14	35%
Moderate	11	27,5%
Severe	15	37,5%
Total	40	100%

Analysis of the Relationship Between Physical Activity and Stress Levels

The 40 respondents who met the inclusion criteria were divided into 2 groups, namely group I which consisted of 30 respondents who had light physical activity and group II which consisted of 10 respondents who did heavy physical activities. From group I, there were 30 respondents who had light physical activity, there were 24 respondents who had moderate-severe levels of stress and 6 respondents who had mild stress. From group II, 10 respondents who did strenuous physical activity, there were 2 respondents with high levels of stress and 8 respondents with mild stress. The data were analyzed using the Pearson Chi-square test with a 95% degree of confidence which can be seen in the table below:

Table 4. The Relationship Between Physical Activity And Stress Levels

Variablel	Stress Level		*Odd Ratio (95% CI)*	*P- value*
	Yes	No		
Light Physical Activity	24	6	*16.000 (2.674-95.754)*	*<0.001*
Heavy Physical Activity	2	8		

Discussion

From **Table 1** regarding data on the characteristics of the elderly at the Nursing Home above, it is found that more than half of the elderly at the Bhina Bakti Nursing Home are aged 60-74 years, namely 40 respondents (59.7%) and there are more elderly women than men with a male ratio 32.5% (n=27) and women 67.5% (n=13). In another social institution, namely the Tresna Werdha Jombang Social Institution, there were 38 respondents (67.9%) aged 60-74 with a male ratio of 39.3% (n=22) and 60.7% female (n=34).[17] The characteristics of the elderly in these two institutions are the same where there are more women than men. The difference in the number of female and male residents is thought to be due to the higher life expectancy for women than for men, where the life expectancy for women is 72 years and men is 69 years.[18] Life expectancy in women is high because women have two X chromosomes which provide redundancies to compensate for mutations, while men only have one X chromosome.[19] In addition, female hormones also provide more responsive immunity to maintain homeostasis and reduce stress more than men. In males, besides having only one X chromosome, there are other factors such as behavioral factors where males tend to carry out risky and dangerous behaviors compared to females.[20]

From **Table 2**, data on elderly people at the Bhina Bhakti Werdha Nursing Home above found that 30 elderly people with an age range of 69-74 years did light physical activity and 10 elderly people aged 60-68 years did heavy physical activity. The results of this study showed that out of 40 respondents, 75% did light physical activity and only 25% did heavy physical activity. This supports previous research, which reported that there were more people who did light physical activity than those who did heavy physical activity where there were 39 people who did light physical activity (69.9%) and 17 people who did heavy physical activity (30.4%).[17,21] So there are similarities from the two studies above. Inactivity for not doing physical activity is thought to be due to the age factor, where there is a decrease in muscle mass, a decrease in muscle pH and muscles become stiffer so that as you get older the decrease in physical activity also decreases.[22] The elderly also experience problems with balance due to decreased peripheral vision, decreased ability to detect information about their surroundings (spatial) so that this condition can be a risk of falling in the elderly.[23] In addition to the age factor, the decrease in physical activity in the elderly is also thought to be due to a lack of support from the social environment.[24]

From **Table 3** regarding the stress level data above, the elderly who live in the Bhina Bakti Nursing Home starting from the age of 70 experience levels of severe

stress with a total of 15 respondents, then the elderly aged 65-70 experience moderate stress with a total of 11 respondents and the elderly aged 60 -65 experienced mild stress levels with a total of 14 respondents. This supports previous research at the Tresna Werdha Social Service Center, which reported that respondents who experienced high levels of stress were more than respondents who experienced mild levels of stress where there were 20 respondents (55.6%) who experienced high stress and 16 respondents (44,4%) who experienced mild stress.[26] So there are similarities from the two studies above. This is presumably because a decrease in physical activity can cause physiological changes such as cardiovascular, neurological, reproductive and endocrine disorders, so that when there are physiological changes the sympathetic nervous system will inhibit hypothalamic activation resulting in inhibition of ACTH which increases cortisol secretion and causes stress.[5]

In **Table 4**, it was found that respondents who did not carry out light physical activity showed a higher level of stress. Meanwhile, respondents who did strenuous physical activity showed lower levels of stress. Using the Pearson Chi-Square test, the relationship between light physical activity and stress level was significant with a p-value <0.001, and odds ratio (OR) = 16.000. These results indicate that respondents who did not carry out strenuous physical activity had a 16 times greater chance of severe stress.

In a previous report conducted on Alam Sutera hospital employees aged 23-54 years, it showed a significant relationship between physical activity and stress levels.[16] In another study conducted on Surabaya State University students aged 17-23 years, there was no significant relationship between physical activity and stress levels.[27] In research conducted on previous research at the Budi Luhur Yogyakarta PSTW Center, it was found that 75% of people who had high levels of stress were due to a lack of support from their families. From the research report, it was found that there is an equation for risk factors for family problems that can cause stress in the elderly.[28]

Research on elderly aged 60-74 years shows the significance of the relationship between physical activity and stress levels. This difference is thought to be due to the difference in age of the respondents. Where as the age of the respondents increases, physical activity becomes the main factor for maintaining mental, psychological and social productivity.[29] Physical activity will activate the sympathetic nervous system and then inhibit the hypothalamus, so that adenocorticotropic (ACTH) is inhibited and causes a decrease in cortisol secretion which results in stress. Physical activity can also improve cognitive function in the elderly by increasing blood flow to the brain to form brain neurotransmitters, thereby reducing setbacks in dealing with stressors that lead to stress such as loss of physical abilities.[30] The age range for the elderly at the Bina Bhakti Werdha Nursing Home is 56-84 years and over, who are vulnerable to psychological and neurological disorders that can affect stress levels.[22]

Conclusion

The results of this study are in accordance with the hypothesis which states that there is a significant relationship between physical activity and stress levels in the elderly aged 60-74 years living at the Bina Bhakti Werdha Nursing Home. The odds ratio of 16,000 shows that elderly people aged 60-74 who do not do physical activity have a 16-fold risk of experiencing stress.

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Association Between Body Mass Index and Low Back Pain Among Students at The Faculty of Medicine, Pelita Harapan University

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Abstract

Background: Low back pain (LBP) is the most common musculoskeletal complaint and the largest contributor to the burden of disability in the world. One of the risk factors for LBP is having higher body mass index (BMI). Although the relationship between BMI and LBP in the age group susceptible to LBP has been widely studied, the relationship in the young adult age group is still under-researched. Meanwhile, several studies report that lifestyle changes that occur during the COVID-19 pandemic might lead to an increasing number of overweight-obese sufferers, including in the young adult age group. Given the context, this research aims to determine the relationship between BMI and LBP in UPH Medical Faculty (FK UPH) students during the COVID-19 pandemic.

Method: A cross-sectional method of unpaired categorical comparative analytical study design was conducted with a population of 414 medical students. Data were collected by an online survey of BMI measurement and Nordic Musculoskeletal Questionnaire. Statistical analysis was done using SPSS Statistics with Chi-squared or Fischer's exact method.

Result: The study involved a sample of 372 people with 188 people (50.5%) being LBP sufferers. Most of the sample belong to the category of BMI < 23 kg/m2, which is 215 people (57.8%).

Conclusion: The result from this research concludes that there is no significant relationship between BMI and LBP in FK UPH students during the COVID-19 pandemic (P = 0.420); significant relationships were found between LBP with gender (P = <0.001) and smoking habit (P = 0.022).

Introduction

Low back pain (LBP) is the most common musculoskeletal complaint in the world with a prevalence reaching 568 million people, reported by *Global Burden of Disease, Injuries, and Risk Factor Study 2019* (GBD 2019). The same study reported LBP as the main cause of disability since 1990.[1] LBP is the leading cause of activity limitation and absenteeism from work, which results in a large medical and economic burden.[2] LBP is also the most common concomitant condition in patients with neuropathic pain in Indonesia based on a study by the *Indonesian Neurological Association*.[3]

Overweight and obesity are risk factors for LBP.[4,5] One cross-sectional study showed the percentage of LBP sufferers increased with an increase in body mass index (BMI) as follows: 47.5% were underweight and normal; 51.8% overweight group; 52.6% of the obese I group; 55.4% for the obese II group; and 72.8% in theobese III group.[6] Another cross-sectional study also found an increased prevalence of persistent LBP in the group with high BMI rates and low levels of physical activity.[7]

The relationship between BMI and LBP in the vulnerable age group for LBP (30-50 years old) has been extensively studied in previous studies, but the relationship between the two in the young adult age group (18-24 years old) is still under-researched. GBD 2019 reports that the 25-49 years old age group bears the most burden of disability from LBP, however the burden of disability in the 10-24 years old age group is currently experiencing a significant increase.[8]

Poor sleep quality, snacking after dinner, irregular eating patterns, eating in response to stress and decreased physical activity are suspected to cause the increasing number of overweight and obese sufferers during the COVID-19 pandemic.[9] This phenomenon also occurs in the young adults, where 32% of university students who participated in a research conducted in Saudi Arabia experienced weight gain during the pandemic lock-down.[10]

Material And Methods

A *cross-sectional* study was conducted on-line using *Google Form* within the range of Faculty of Medicine, Pelita Harapan University from January 2022 to May 2022. It was an unpaired categorical comparative analytical study, that aims to determine the relationship between BMI groups and prevalence of LBP using *Nordic Musculoskeletal Questionnaire.* The obtained data would be tabulated using *Microsoft Excel* 2019, then analyzed with *Chi-squared* method using SPSS *Statistics*.

The criteria of inclusion in this study were pre-clinical students of the Faculty of Medicine in Pelita Harapan University, aged between 18-24 years old, and had given approval of *informed consent* to participate in the study. Respondents with a history of LBP precipitating diseases and/or a history of low back injuries were excluded from this study.

Result

Of the 414 respondents who participated in this study, there were 372 respondents who met the criteria as the research sample. The results of the Nordic Musculoskeletal Questionnaire showed that 188 (50.54%) people had LBP, while 184 (49.46%) people did not. Categorized BMI based on the Asia-Pacific standard showed that the largest sample distribution was in the normal weight category with 161 (43.28%) people and the smallest in the underweight category with 54 (14.52%) people. A more comprehensive presentation of sample characteristics can be seen in Table 1 as presented below.

Table 1. Sample Characteristics

Characteristics	Frequency (n=372)
Gender	
Male	112 (30,1%)
Female	260 (69,9%)
Low Back Pain	
Yes	188 (50,5%)
No	184 (49,5%)
Body Mass Index (Asia-Pacific Classification)	
Underweight	54 (14,5%)
Normal weight	161 (43,3%)
Overweight	68 (18,3%)
Obese	89 (23,9%)
Smoking Habit	
Yes	26 (7,0%)
No	346 (93,0%)
Level of Physical Activity	
Inactive	338 (90,9%)
Minimally active	34 (9,1%)
HEPA active	0 (0%)
Sitting Duration per Day	
<6 hours	179 (48,1%)
≥6 hours	193 (51,9%)

Table 2 shows the results of statistical tests to determine the existence of a significant relationship (P > 0.05) between BMI and LBP in respondents.

Tabel 2. Association Between Low Back Pain and Body Mass Index

Body Mass Index	Low Back Pain		Total	OR (95% CI)	P-value
	Yes	No			
IMT<23	113 (52,6)	102 (47,4)	215	0,826 (0,547-1,246)	0,420
IMT ≥23	75 (47,8)	82 (52,2)	157		
Total	188 (50,5)	184 (49,5)	372		

Table 3 shows the results of statistical tests to determine the existence of a significant relationship (*P* > 0.05) between gender and LBP in respondents.

Tabel 3. Association between low back pain and gender

Gender	Low Back Pain		Total	OR (95% CI)	P-value
	Yes	No			
Male	41 (36,6)	71 (63,4)	112	2,253 (1,428-3,554)	<0,001
Female	147 (56,5)	113 (43,5)	260		
Total	188 (50,5)	184 (49,5)	372		

Table 4 shows the results of statistical tests to determine the existence of a significant relationship (*P* > 0.05) between smoking habit and LBP in respondents.

Tabel 4. Association between low back pain and smoking habit

Smoking habit	Low Back Pain		Total	OR (95% CI)	P-value
	Yes	No			
Yes	7 (26,9)	19 (73,1)	26	0,336 (0,138-0,819)	0,022
No	181 (52,3)	165 (47,7)	346		
Total	188 (50,5)	184 (49,5)	372		

Table 5 shows the results of statistical tests to determine the existence of a significant relationship (*P* > 0.05) between level of physical activity and LBP in respondents.

Tabel 5. Association between low back pain and level of physical activity

Level of physical activity	Low Back Pain		Total	OR (95% CI)	P-value
	Yes	No			
MET < 600	170 (50,3)	168 (49,7)	338	1,112 (0,549-2,253)	0,909
MET ≥ 600	18 (52,9)	16 (47,1)	34		
Total	188 (50,5)	184 (49,5)	372		

Table 6 shows the results of statistical tests to determine the existence of a significant relationship (*P* > 0.05) between sitting duration per day and LBP in respondents.

Tabel 5. Association between low back pain and sitting duration per day

Sitting duration per day	Low Back Pain		Total	OR (95% CI)	P-value
	Yes	No			
< 6 hours	85 (47,5)	94 (52,5)	179	1,266 (0,842-1,902)	0,303
≥ 6 hours	103 (53,4)	90 (46,6)	193		
Total	188 (50,5)	184 (49,5)	372		

Discussion

In this study, no significant relationship was found between BMI and LBP (P = 0.420). Previous studies have obtained mixed results regarding the relationship between the two variables. A study by Alhowimel et al. obtained similar results in finding no significant association between BMI and LBP.[11] Another study by Koley et al. only found a significant association between LBP and height and weight separately, but no significant association with BMI.[12] Moreover, Hershkovich et al. found in their study that high BMI and height were significantly associated with the occurrence of LBP in adolescents in Israel.[13] These conflicting results are thought to occur due to various biophysical, psychological, social, genetic, and other comorbid factors that influence each other in the occurrence of LBP.[4,14–16]

Higher BMI is thought to be related to the occurrence of LBP by means of additional mechanical load to be supported by the spine, activation of proinflammatory pathways that cause systemic inflammation, degeneration of the intervertebral discs and vertebral endplate structures, and the emergence of comorbidities that affect perfusion to the spinal structures.[17,18] Higher BMI can also have a psychological effect on increasing the risk of LBP by forming a bad self-perception, especially in women.[6,19,20]

In this study, a significant association was found between the occurrence of LBP and gender (P = <0.001) and smoking habits (P = 0.022). The study by Alnojeidi et al. does not only found similar results, but also found that the prevalence of LBP was significantly higher in women than men.[21] Women have shown to have a lower threshold for pain perception and are more likely to report LBP to health professionals. Other psychological factors, hormonal changes and menstruation disturbances might also play a role in higher LBP occurrences in women.[12,15]

A significant relationship between smoking habit and LBP was also found in the study by Green et al. The nicotine in

cigarettes might trigger systemic inflammation and overstimulate the central nervous system which can lead to amplification and changes in the threshold for perception of pain.[22] Smoking can also trigger vasoconstriction which causes decreased perfusion and malnutrition in spinal structures.[23]

In this study, a significant relationship was not found between the occurrence of LBP and the level of physical activity (P = 0.909) and duration of sitting (P = 0.303). A study by Sitthipornvorakul et al. found no clear relationship between the level of physical activity and LBP.[24] The relationship between the two variables was depicted to form a U-curve where recurrent LBP tends to occur in the low physical activity level group and chronic LBP in the group with high physical activity level.[25,26]

Study by Lis et al. found that sitting duration can significantly increase the risk of developing LBP when accompanied by exposure to whole body vibration.[16] Prolonged sitting duration is thought to increase pressure and inhibit nutrient supply to the intervertebral discs, as well as reduce joint mobility and muscle strength in the lumbar area.[27,28]

Conclusion

In this study, no significant relationship was found between BMI and LBP in pre-clinical students of the Faculty of Medicine in Pelita Harapan University during the COVID-19 pandemic (P=0.420). However, a significant relationship was found between LBP and gender (P=<0.001); and smoking habits (P=0.022).

It is suggested for future research to increase the number of samples and expand the range of sampling and to directly measure BMI of the respondents. An increase in BMI and the occurrence of LBP are health problems that are multi-factorial, therefore living a healthy lifestyle is suggested to prevent these conditions in the future.

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The Role of Classical Music Therapy on Dysmenorrhea Pain and Anxiety in Pelita Harapan University Medical Students

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Abstract

Introduction: Dysmenorrhea is menstrual pain that often occurs in young women. The pain felt in every women can be different from one another. Anxiety experienced by each women can also worsen the menstrual pain. Efforts to treat dysmenorrhea can be in the form of non-pharmacological therapy, one of which is music therapy.

Aim: This study uses an experimental method with random allocation to divide 122 respondents who are medical students of Pelita Harapan University into a control group and an intervention group.
Methodology: The intervention group has been given anexperiment of random allocationin the form of classical music therapy for 20 minutes on the first day of the respondent getting menstruation. As for the control group given 40Hz sound for 20 minutes. The data analyzed using chi-square and wilcoxon test.

Results: The results of the study found that the average menstrual pain in the control group before the intervention was 6.11 and after the intervention was 6.07. Meanwhile, in the intervention group, the average menstrual pain before being given classical music therapy was 6.46 and after the intervention was 3.39.

Conclusion: So that classical music therapy is effective for reducing anxiety by 0.77 and the menstrual pain scale is 3.07 in the group given classical music therapy with P value <0.001.

Introduction

Dysmenorrhea is defined as difficult menstrual flow characterized by abdominal pain.[1,2] Symptoms of dysmenorrhea can begin several hours before and/or several hours after the start of menstruation.[1] Dysmenorrhea in general is the most common gynecological disease reported by women.[3] According to WHO, the number of dysmenorrhea in the world is very large, on average more than 50% of women in every country experience dysmenorrhea. In Indonesia, the incidence of dysmenorrhea is quite large, around 60-70% of women experience dysmenorrhea.[4] The level of dysmenorrhea pain can vary which has an impact on disruption of daily activities such as school attendance. Previous research conducted by Gunawan in 4 junior high schools in Jakarta in 2002 showed that 76.6% of female students were absent from school because of menstrual pain.[5]

Pain that will be felt during menstruation arises because of uterine muscle contractions and vasoconstriction of the blood supply to the endometrium. Pain that arises will activate the sympathetic nervous system to stimulate the adrenal medulla to release epinephrine and norepinephrine to produce a stress response. This physiological response will increase anxiety, muscle tension and facial perception.[6] Treatment of dysmenorrhea can be overcome, one of which is non-pharmacological therapy, namely music therapy. Non-pharmacological therapy can be recommended because it has few side effects, does not cost money and is easy to do.[7]

Music therapy can release sensory stimuli that can cause the release of endorphins. Endorphins are produced by the brain and function as natural sedatives that work by blocking the transmission of painful stimuli. 5,8 The psychological effect of music therapy is relaxation which can reduce heart rate, respiratory rate, metabolism, improve physical signs, reduce stress hormones and stabilize vital signs.[9] Previous studies have reported that different musical characteristics are processed differently in the brain so that different musical characteristics may have different effects.[10] Previous research in Colombia on classical music therapy for dysmenorrheal pain found that the treatment group music pain score on average was lower (p=0.0006) than the control group.[7] Although previous research has been conducted, the effectiveness of classical music therapy on anxiety in dysmenorrheal pain has not been yet discussed. The experimental research involving music conducted between the intervention and control groups necessitates the implementation of randomization to ensure the reduction of research bias. This step is crucial to enhance the validity and reliability of the study findings. This practice aligns with the principles of rigorous scientific inquiry and contributes to the overall robustness of the research outcomes.

Objective

This study aims to determine the effectiveness of classical music therapy in reducing anxiety and dysmenorrhea pain in Medical Students of Pelita Harapan University.

Material And Methods

Design

This research was randomized clinical trial with experimental study design

Respondents

The sample in this research are 2018-2020 medical students of Pelita Harapan University with the inclusion criteria for this study are people who experienced dysmenorrhea. They agreed to participate in this research when they were given google form which has informed consent. Respondents who met the exclusion criteria such as: deafness that had been diagnosed by a doctor, doing acupressure, massage, diet and heat compression, were not included in this study. With the classification of research variables in the form of independent variables, it was classical music therapy, and the dependent variable was anxiety and dysmenorrhea pain, as well as cofounding variables was use of pain medication and anti-anxiety medication, age at first menstruation <10 years and >16 years, irregular menstrual cycle, menstrual cycle duration <21 days and >35 days, and menstrual duration >7 days.

Method of Collecting The Data

This research data were collected using convenience sampling method from 2018-2020 medical students of Pelita Harapan University who experience dysmenorrhea on the first day of menstruation. The menstrual pain would be assessed by Numeric Rating Scale (NRS) which has a pain scale from 0-10 while for anxiety assessed by Zung Self-Rating

Anxiety Scale (SAS) questionnaire which contains 20 questions.

Method of Collecting The Data

Data obtained were processed and analyzed using Microsoft Excel and Statistical Package for the Social Sciences (SPSS) 23.0 by chi-square and Mann Whitney U analysis.

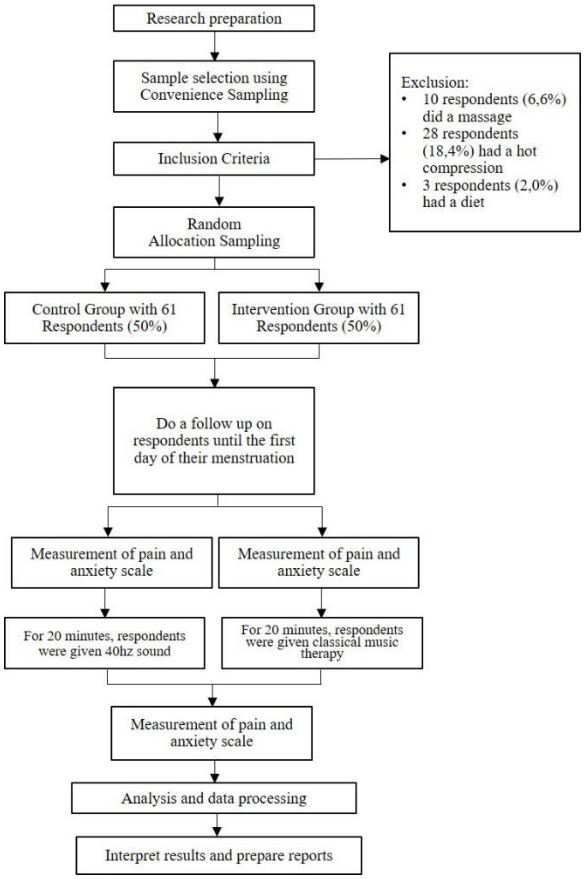

Figure 1. Ways of working and data collection technique

Result

The number of samples included in this study were 122 respondents. Data on respondent's age, age of first menstruation, regular or irregular menstrual cycle, duration of menstrual cycle, duration of menstruation, number of sanitary napkins used in a day, blood clots, and use of pain medication were recorded and shown in the table of overall research respondent characteristic (Table 1). The sample of this study was 100% women with an average sample age of 19.37 ± 1.069 years. The youngest age in this study was 17 years old and the oldest was 24 years old and the most respondents were at the age of 11-12 years, namely 59 (48.4%) respondents. Furthermore, 122 respondents were divided into two groups, namely 61 respondents (50%) as the control group and 61 respondents (50%) as the intervention group (Table 2).

Table 1. Overall Research Respondent Characteristics

Characteristic	Total (n=122)	
	n (%)	Mean ± SD
Age (years)		
17	1 (8)	
18	26 (21.3)	
19	36 (29.5)	19.37 ± 1.069
20	51 (41.8)	
21	6 (4.9)	
24	2 (1.6)	
Age of first menstruation (years)		
<10	6 (4.9)	
11-12	59 (48.4)	12.03 ± 1.366
13-14	48 (39.3)	
15-16	7 (5.7)	
>16	2 (1.6)	
Regular menstrual cycle		
Yes	87 (71.3)	
No	35 (28.7)	
Menstrual cycle duration (days)		
<21	13 (10.7)	
21-35	89 (73)	
>35	20 (16.4)	
Menstrual duration (days)		
≤7	99 (81.1)	
> 7	23 (18.9)	
Number of pads in a day		
1-2x	22 (18)	
2-3x	52 (42.6)	
3-4x	42 (34.4)	
≥4x	6 (4.9)	
Blood clots		
Yes	62 (50.8)	
No	60 (49.2)	
Use of pain medication		
Yes	11 (9)	
No	111 (91)	

Table 2. Research Respondents Characteristics by Type of Group

Characteristic	Group, n (%)		P Value
	Intervention (n=61)	Control (n=61)	
Age (years), median (min/max)	19 (18/21)	20 (17/24)	0.519
Age of first menstruation (years)			
<10	4 (66.7)	2 (33.3)	0.236
11-12	28 (47.5)	31 (52.5)	
13-14	27 (56.3)	21 (43.8)	
15-16	1 (14.3)	6 (85.7)	
>16	1 (50)	1 (50)	
Regular menstrual cycle			
Yes	45 (51.7)	42 (48.3)	0.689
No	16 (45.7)	19 (54.3)	
Menstrual cycle duration (days)			
<21	7 (53.8)	6 (46.2)	0.340
21-35	47 (52.8)	42 (47.2)	
>35	7 (35)	13 (65)	
Menstrual duration (days)			
≤7	51 (51.5)	48 (48.5)	0.643
> 7	10 (43.5)	13 (56.5)	
Number of pads in a day			
1-2x	7 (31.8)	15 (68.2)	0.003
2-3x	32 (61.5)	20 (38.5)	
3-4x	22 (52.4)	20 (47.6)	
≥4x	0	6 (100)	
Blood clots			
Yes	31 (50)	31 (50)	1.000
No	30 (50)	30 (50)	
Use of pain medication			
Yes	7 (63.6)	4 (36.4)	0.527
No	54 (48.6)	57 (51.4)	

In this study, menstrual pain was assessed using the Numeric Rating Scale with a pain scale of 0-10. On the first day of menstruation, each respondent assessed for menstrual pain before the intervention and after the intervention, both the control group and the group given classical music therapy. The intervention group will be given classical music therapy for 20 minutes, while the control group will not be given classical music but only given 40Hz sound instead.

In this research, Anxiety was assessed using the Zung Self-Rating Anxiety Scale (SAS) questionnaire. Anxiety was also measured before and after the intervention in both groups on the first day of the respondent getting menstruation. The level of anxiety will be divided into 4 groups, namely normal, mild-moderate, severe and extreme. From the results of the anxiety data obtained, in the control group and the intervention group, more respondents experienced mild anxiety-moderate. However, after being given classical music therapy for 20 minutes in the intervention group, the anxiety decreased by 9.9% of respondents to 24 respondents who experienced mild-moderate anxiety. Meanwhile, in the control group that was given a voice of 40hz reduced by 1 respondent to become 29 respondents who experienced mild-moderate anxiety.

Table 3. Comparison of anxiety levels in the control group

Anxiety Level (Range 20-80)	Control, n (%)		*Δ Delta Anxiety Level*
	Before	After	
Normal	7 (11.5)	8 (13.1)	+ 1.6 %
Mild-Moderate	30 (49.2)	29 (47.5)	+ 1.7 %
Severe	23 (37.7)	23 (37.7)	0
Extreme	1 (1.6)	1 (1.6)	0

Table 4. Comparison of anxiety levels in the intervention group

Anxiety Level	Intevention, n (%)		*Δ Delta Anxiety Level*
	Before	After	
Normal	10 (16.4)	35 (57.4)	+ 41 %
Mild-Moderate	30 (49.2)	24 (39.3)	-9.9 %
Severe	18 (29.5)	2 (3.3)	-26.2 %
Extreme	3 (4.9)	0 (0)	- 4.9 %

Classical music therapy can be said to be effective if there is a minimum pain scale decrease of 1.67 and a minimum decrease in anxiety level of 0.1. Table 5 shows that menstrual pain before in the

control group was 6.11 ± 2.237 with the lowest pain being 2 and 10 being the highest pain. After being given 40Hz sound intervention in the control group, there was a decrease in menstrual pain by 0.05 the average menstrual pain became 6.07 ± 2,228 with the lowest and highest pain remaining the same. While the average menstrual pain in the intervention group before was 6.46 ± 1.659 with the lowest pain being 3 and 9 being the highest pain. After being given classical music therapy for 20 minutes, the average menstrual pain scale decreased by 3.07 to 3.39 ± 1.626 with the lowest pain being 0 and the highest pain being 7.

Table 5. Comparison of menstrual pain before and after menstrual pain in both groups.

Menstrual Pain	Before	After	Δ Effectiveness of Menstrual Pain	P Value
Control Group, Mean ± SD Median (min/max)	6.11 ± 2.237 6.0 (2 / 10)	6.07 ± 2.228 6.0 (2 / 10)	0.05	0.366
Intervention Group, Mean ± SD Median (min/max)	6.46 ± 1.659 7.0 (3 / 9)	3.39 ± 1.626 3.0 (0 / 7)	3.07	**<0.001**

The level of anxiety in both groups decreased but in intervention group the delta effectiveness was greater than the control group. Delta effectiveness in the control group was 0.02 and in the intervention group was 0.77**.** It was said to be effective at least there is a decrease in anxiety level of 0.1 and the intervention group has a decrease in anxiety level of 0.77 which means it exceeds 0.1 so it can be said to be effective.

The tabulation results shown in table 6 show that there is a significant difference between prior menstrual pain in the control group compared to prior menstrual pain in the intervention group. In addition, it can also compare menstrual pain after the intervention in the control group compared to menstrual pain after the intervention in the intervention group. The results were analyzed using Mann-U-Whitney and the P Value for the median difference between the control and intervention groups before the intervention was given was 0.337. After 20 minutes of intervention the p value for the median difference between the two groups was <0.001. This indicates that before the intervention, the two groups were not significantly different, indicating that the two groups had pain that was not much different at first.

Table 6. Comparison of the menstrual pain scale of the control group with the intervention group before and after the intervention

Menstrual Pain	Control Group	Intervention Group	P Value
Before Intervention, Mean ± SD Median (min/max)	6.11 ± 2.237 6.0 (2 / 10)	6.46 ± 1.659 7.0 (3 / 9)	0.337
After Intervention, Mean ± SD Median (min/max)	6.07 ± 2.228 6.0 (2 / 10)	3.39 ± 1.626 3.0 (0 / 7)	**<0.001**

Furthermore, to find out whether there is a significant difference in menstrual pain before compared to menstrual pain after intervention in the control group, the Wilcoxon statistical test was being done. It can also compare menstrual pain before compared to menstrual pain after being given classical music for 20 minutes which is shown in table 5. It was found that the p value in the control group was 0.366 which means that there was no significant difference between menstrual pain before and menstrual pain after in the control group. Meanwhile, the intervention group had a p value of <0.001 which means a significant difference between menstrual

pain before compared to menstrual pain after being given classical music therapy.

To compare anxiety before in the control group compared to anxiety before in the intervention group, Chi-Square analysis was carried out and the results are in table 7. It can be seen that in both groups there were more respondents who had abnormal anxiety, as many as 54 respondents in the control group and 51 respondents in the intervention group before the intervention. It was found that there was no significant relationship between prior anxiety in the control group and the intervention group because the p value was 0.601. This is a good thing because it indicates that the control group and the intervention group have a level of anxiety that is not much different at first place.

Table 7. Anxiety before intervention in control group and intervention group

Intervention Type	Anxiety Before		Total	OR (95% CI)	P value
	Normal n (%)	Abnormal n (%)			
Control	7 (11.5)	54 (88.5)	61	0.661 (0.234-1.868)	0.601
Intervention	10 (16.4)	51 (83.6)	61		

Table 8. Anxiety after intervention in control group and intervention group

Group	Anxiety After		OR (95% CI)	P value
	Normal n (%)	Abnormal n (%)		
Control	8 (13,1)	53 (86,9)	0,112 (0,046-0,276)	<0,001
Intervention	35 (57,4)	26 (42,6)		

Chi-Square analysis test was also conducted to compare anxiety after intervention in the control group compared to anxiety after in the intervention group. The results are shown in table 8 where there are still more control group respondents who have abnormal anxiety after the intervention, as many as 53 (86.9%). While in the intervention group, more respondents became normal anxiety after being given classical music therapy. In addition, found p value <0.001 which means there is a significant relationship between anxiety and the type of intervention after classical music therapy intervention.

Furthermore, to find out whether there is a significant difference between menstrual anxiety before compared to menstrual anxiety after intervention in the two groups, the Wilcoxon statistical test was carried out. The results are the p value in the control group is 0.317, which means there is no significant difference between anxiety before compared to anxiety after the intervention. Meanwhile, in the intervention group, a p value <0.001 was obtained, which means a significant difference between menstrual anxiety before compared to menstrual anxiety after being given classical music therapy.

Discussion

From the Mann-U-Whitney test in table 6, it was found that the median pain scale before classical music therapy was performed in the control group was 6 and in the group that would be given classical music therapy was 7. This difference was not statistically significant because p value = 0.337. Then the intervention group was given classical music therapy for 20 minutes and the pain scale after the intervention became 3. While in the control group who was not given classical music therapy intervention, the pain scale was the same as before it was given, namely 6. The median difference in pain between the control group and the control group intervention after being given classical music therapy was statistically significant with p value <0.001.

To see the difference in menstrual pain after getting the intervention in the

control group or the intervention group, a paired T-test can be done. However, the distribution of the data tested using the Kolmogorov-Smirnov got a P value <0.05, so the Wilcoxon test was carried out. The results in table 5 have p value = 0.366 in the control group so that the average difference is not significant between the pain scales before and after the intervention. Meanwhile, in the intervention group, p value <0.001 was found which was significant between the pain scale before and after classical music therapy was given.

Table 5 also shows the delta of the effectiveness of classical music therapy to reduce the menstrual pain scale. If there is a decrease in the pain scale of 1.76, it can be said to be effective based on previous research conducted by Juan Sebastian Martin-Saaverda and Angela Maria Ruiz-Sternberg. In this study it was found that the average decrease in menstrual pain after classical music therapy was given was 3.07 while the control group who was not given classical music therapy was 0.05. This shows that classical music therapy is effective in reducing menstrual pain.

The results obtained are in accordance with the research journal that has been conducted by Amirul Amalia where the average value of pain before the intervention was 4.84 and the average pain after the intervention was 3.03 with a scale of 1.8 reduction. From the results of the paired t-test, the p value = 0.00 where p <0.05 is statistically significant.

In addition, the research conducted by Dwi Augstiana Sari, Zulkhah Noor and Azizah Khoiriati also got similar results. Dwi's study found that the difference in pain scale before and after the intervention in the control group was not significant. While the difference in pain scale before listening to classical music therapy and after listening to classical music therapy for 15 minutes in the intervention group was significant. The data obtained in the previous study were the same as this study, namely after being given classical music therapy in the intervention group the results were significant. This is in accordance with the theory that the control group was not given classical music therapy which acts as a non-pharmacological therapy for dysmenorrhea. So that prostaglandins will be produced continuously by the uterus and increase in the blood so that the uterus will still experience contractions and pain occurs during menstruation. While the group given classical music therapy can stimulate relaxation and distract from the pain that is felt. Music therapy can also stimulate endorphins and reduce the production of prostaglandins. This is in accordance with Gate Control theory where classical music therapy works as pain modulation into sensory impulses where these sensory impulses will inhibit pain impulses by closing the gate in gate control theory. So the perception of pain will be reduced because it does not reach the cerebral cortex.[11,12]

This study can also determine the level of anxiety of the intervention group and control group. To compare anxiety before in the control group and anxiety before in the intervention group, a Chi-Square test was performed with the results listed in table 7. It was found that the intervention group was protective 0.661 times to reduce anxiety compared to the control group with p value = 0.601, which means it is not significant. The insignificant relationship before the intervention is a good thing because it indicates that the control group and the intervention group have a level of anxiety that is not much different at the beginning, namely before the intervention. After that, the intervention group was given classical music for 20 minutes, while the control group was given 40 Hz sound for 20 minutes. To compare anxiety after in the control group compared to anxiety after in the intervention group, it can be seen in table 8. It was found that the intervention group was protective 0.112

times to reduce anxiety compared to the control group with p value <0.001.

To see the difference in anxiety after getting the intervention, the Wilcoxon test can be done because the distribution of data is uneven. From the results, it was found that p value = 0.317 in the control group, so the average difference was not significant between the level of anxiety before and after the intervention. As for the intervention group, p value <0.001 was obtained, so the average difference was significant between the level of anxiety before and after being given classical music therapy. Based on previous research conducted by Juan Sebastian Martin-Saavedra and Angela Maria Ruiz-Sternberg, it is said to be effective if there is a decrease in anxiety levels of 0.1. In this study, it was found that the average decrease in anxiety levels after being given classical music therapy was 0.77, while the control group who was not given classical music therapy was 0.02. This shows that classical music therapy is effective for reducing anxiety during menstruation.

What was obtained was corresponding with the research journal that had been previously conducted by Juan Sebastian Martin-Saavedra and Angela Maria Ruiz-Sternberg that found a decrease in anxiety levels in the group given classical music therapy compared to the control group with p value = 0.049.[7] The theory also said that classical music therapy can produce the release of endorphin hormones in the descending control system which will stimulate alpha waves to provide calm and comfort. So that endorphins not only help to reduce pain but also help to reduce anxiety. Another effect of classical music therapy is relaxing because of the activation of the parasympathetic nervous system and decreasing sympathetic stimulation, thereby reducing adrenaline activity and epinephrine levels. This will result in a decrease in respiratory rate, heart rate, neuromuscular tension, oxygen consumption, muscle tension, blood pressure and metabolic rate.[11,13]

Conclusion

The results showed that classical music therapy was significantly effective in reducing dysmenorrhea pain and anxiety in Medical Students of Pelita Harapan University.

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WNT-Activated Medulloblastoma in A 6-Year-Old Boy

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Abstract

Background: Medulloblastoma is the most common malignant brain tumor of childhood. Prognosis is mostly favorable, but may be affected by histological and molecular subtypes. Long-term therapy-related morbidity also remains a significant concern.

Case Presentation: A 6-year-old boy with brainstem/midline cerebellum tumor. Histopathology found area of necrosis, sheets of malignant undifferentiated round cells with hyperchromatic nuclei and scanty cytoplasm, no nodule and no anaplasia. Immunohistochemistry found p53 wild-type staining pattern along with β-catenin diffuse cytoplasmic and focal nuclear staining. This indicated a diagnosis of WNT-activated medulloblastoma, World Health Organization (WHO) grade IV, with classic histological features.

Discussion: WNT-activated medulloblastomas with classic histological features and no anaplasia were reported to have the most favorable prognosis. The current patient showed negative staining for GFAP, Olig2, EMA, H3K27M, EZHIP, and LIN28A, with retained staining for INI1 and BRG1, thus excluding several differential diagnosis such as atypical teratoid/rhabdoid tumor, embryonal tumor with multilayered rosettes, small cell glioblastoma, Ewing sarcoma, high-grade neuroepithelial tumor with BCOR alteration or diffuse midline glioma. Histopathology in combination with immunohistochemical and molecular subtyping of medulloblastoma can help to refine diagnosis, exclude differential diagnosis, and improve counseling in regards to overall prognosis.

Introduction

Medulloblastoma is defined by the WHO as an embryonal neuroepi¬thelial tumor arising in the cerebellum or dorsal brainstem, presenting mainly in childhood and consisting of densly packed small round undifferentiated cells with mild to moderate nuclear pleopmorphism and a high mitotic count.[1] This condition is the most common malignant brain tumor of childhood.[2] In the United States, approximately 350 new pediatric cases of medulloblastoma are diagnosed every year, which represents about 30% of all pediatric brain tumors and 7–10% of all brain tumors.[3] The incidence of medulloblastoma is estimated to be 0.7 per 100 000 children per year with a male predominance, wherein the relative risk is 1.5 times higher in males. They can also occur in adults, although more than 70% of all medulloblastoma cases are found in children younger than 18 years old.[1,4] The majority of cases arise in children with a median age of 9 years, and a peak in

incidence between the ages of 3 and 7 years.[5]

This condition was initially described as cerebellar glioma until Bailey and Cushing named it medulloblastoma in 1925.[6] However, medulloblastoma has now been included in the group of embryonal neuroepithelial tumor (grade IV) of the World Health Organization (WHO) classification.[7] In modern classification, medulloblastoma represents a heterogeneous tumor with multiple subtypes. Medulloblastoma share a primitive embryonal phenotype, composed of malignant tumor cells which are dominated by neuronal antigen expression.[5] This highly invasive embryonal neuroepithelial tumor has a tendency to disseminate throughout the central nervous system early in its evolution. Prognosis is mostly favorable with a 5-year overall survival of approximately 75%, however, this might be affected by the histological and molecular subtypes, and long-term therapy-related morbidity also remains a significant concern.[5,8]

Diagnosis is mostly based on imaging and histopathological findings, while immunohistochemistry and molecular analysis can help to characterize the molecular subtype of medulloblastoma. This molecular characterization of medulloblastoma can help to better assess the risk or prognosis, and to refine treatment options.[5,8,9] Combination of histologic findings and immunohisto-chemistry may also help to exclude possible differential diagnosis.5 In view of that, this article will report a case of WNT-activated medulloblastoma in a 6-year-old boy with the main focus on the histopathological and immunohisto-chemical findings.

Case Report

A brainstem/midline cerebellum tumor tissue biopsy from a 6-year-old boy was evaluated in the histopathology laboratory. Routine H&E staining, special staining and immunohistochemical studies were performed after formalin fixation and paraffin-embedding. Light microscopy examination of the sections showed some brain tissue and tumor with extensive area of necrosis. Viable areas of tumor showed sheets of malignant undifferentiated round cells with hyperchromatic nuclei and scanty cytoplasm. No definite nodule formation can be seen. No anaplasia was seen. Mitoses were easily identified.

Immunohistochemical stains showed patchy reactivity for synaptophysin. There was negative staining for glial fibrillary acid protein (GFAP), OLIG2, epithelial membrane antigen (EMA), H3K27M, EZHIP, and LIN28A. There was retained staining for INI1 and BRG1. P53 showed a wild-type staining pattern. Beta-catenin showed diffuse cytoplasmic and focal nuclear staining. The NanoString expression profiling classifies this tumor as WNT activated

Discussion

A 6-year-old boy with a brainstem/ midline cerebellum tumor was diagnosis with WNT-activated medulloblastoma WHO Grade IV based on histologic findings and results of immunohisto-chemical studies. This tumor showed classic histological features with extensive area of necrosis and sheets of malignant undifferentiated round cells with hyper-chromatic nuclei and scanty cytoplasm. Neither definite nodule formation nor anaplasia was seen, and mitoses were easily identified. WNT-activated medullo-blastoma accounts approximately for 10% of all cases, is typically found in children between the age of 7 and 14 years old, and has an excellent prognosis with standard therapeutic approaches.[7,10]

Medulloblastoma is a high-grade embryonal neoplasm that composed of small round undifferentiated cells disposed in densely packed groupings and exhibits mild to moderate nuclear pleomorphism and a high mitotic index.[7,10] This primitive, small round blue cell tumor of the neuronal lineage may also demonstrates scattered apoptotic cells and foci of necrosis.

Neuronal differentiation is evidenced by diffuse synaptophysin positivity in most tumors, although focal glial, melanotic, or myogenic differentiation can be observed. Histologic subtypes of medulloblastoma include classic, large cell, anaplastic, nodular/desmoplastic, and extensive nodularity. The great majority of WNT-activated medulloblastoma has classic morphology at light microscopy, as was the case in the current patient, which denotes a low-risk tumor. The classic variant are by far the most frequent encountered in clinical practice, accounting for 72% of all reported medulloblastoma cases.[5,7]

Tumors with classic histology are characterized by cells with minimal cytoplasm and dense basophilic nuclei present in diffuse sheets. Homer Wright (neuroblastic) rosettes may also be seen.[4] Intrinsic desmoplasia is rare in classic variant tumors, and when desmoplasia presents it is typically associated with involvement of the leptomeninges by tumor. Similarly, nodules of differentiation are rare, and when present are not outlined by pericellular collagen as detected by reticulin staining.[5]

This tumor did not show any anaplastic features, and only very few cases of WNT-activated medulloblastoma were reported to show large cell/anaplastic pattern.[10] Cytological pleomorphism, increased nuclear size, brisk mitotic activity, and cell wrapping are considered as the key features of anaplasia in medulloblastomas. Anaplasia has been reported to be associated with poor prognosis in patients with medullo-blastoma. An increasing degree of anaplasia is significantly associated with shorter relapse-free survival time. Slight anaplasia might not influence prognosis, but patients with moderate and severe anaplasia were reported to have significantly worse outcome.[11]

Beyond histology, medulloblastoma classification may also be based on molecular differences and signaling pathways driving tumor development. Gene expression and methylation profiling is the gold standard for defining molecular groups of medulloblastoma.[10] The 2016 World Health Organization Classification of Tumors of the Central Nervous System has divided medulloblastoma into four molecular subtypes: WNT-activated, sonic hedgehog (SHH)-activated, group 3, and group 4.[7] Immunohistochemical markers help stratify medulloblastomas into each of the molecular subgroups: WNT-activated tumors typically show classic histology and immunostaining positive for β-catenin aberrantly located in cell nuclei; SHH-activated frequently show nodular/ desmoplastic histology and immuno-staining positive for GAB1; Group 3 and Group 4 tumors commonly have either classic or large cell/anaplastic histologic features and negative GAB1 and nuclear β-catenin immunostaining.[12]

WNT-activated tumors are characterized by expression of WNT pathway genes, contain mutations in exon 3 of the CTTNB1 gene in approximately 85%–90% cases, and exhibit loss or partial loss of chromosome 6 in 85%–90% cases. APC mutations can be identified in a high proportion of WNT-activated medulloblastoma lacking CTTNB1 mutations.[5] Other genes frequently mutated in this molecular subtype include TP53 (12.5% cases), SMARCA4 (27% cases), KMT2D (12.5% cases) and DDX3X (50% cases).[5,10,13,14] Around 85% MDB that are characterized by WNT pathway activation show monosomy 6 and/or harbor a CTNNB1 mutation in exon 3, and these genetic alterations determine the positive immunoexpression for beta-catenin antibodies in tumor cell nuclei.[10] The current patient showed a wild-type staining pattern of p53 expression. This TP53 mutations do not appear to carry the same poor prognosis in WNT tumors as they do in the SHH molecular group.[10,15] WNT-activated medulloblastoma are associated with a favorable prognosis in the pediatric population, whereas the prognosis in adults with this tumor subtype is still uncertain.[5]

The diagnosis of medulloblastoma should be considered in the context of any embryonal brain tumor in the cerebellum, cerebellar peduncle, or fourth ventricle. Rarely other malignant tumors with small cell morphology can be encountered in this region, such as atypical teratoid/rhabdoid tumor (ATRT), embryonal tumor with multilayered rosettes (ETMR), small cell glioblastoma, Ewing sarcoma, or high-grade neuroepithelial tumor with BCOR alteration (HGNET-BCOR). These can typically be excluded by a combination of subtle histologic findings or immunohisto-chemistry, using lineage markers or entity specific stains.[5]

The possibility of ATRT or ETMR can be suspected in the presence of specific histologic features such as rhabdoid cells or ependymoblastic rosettes, respectively. Immunohistochemistry can be of use in the absence of these specific histologic features. Malignant tumor other than medulloblastoma usually will not express neuronal markers such as synaptophysin or NeuN apart from ETMR and rarely ATRT. Furthermore, ETMR typically express high levels of LIN28A, whereas ATRT typically show loss of INI1 and Brg1 exprission, and is also found to have a polyimmunophenotype, where several different antigens such as EMA, smooth muscle actin, and GFAP are being co-expressed at the same time.[5]

Small cell glioblastoma and medullo-blastoma are usually hard to distinguish. However, widespread expression of GFAP, Olig2, or SOX10 and the absence of neuronal antigen expression favors the diagnosis of astrocytoma, while only a minority subset of medulloblastoma tumor cells may express Olig2 or SOX10. High-grade neuroepithelial tumor with BCOR alteration and Ewing sarcoma can usually be differentiated from medulloblastoma by BCOR or EWSR1 FISH immunohisto-chemistry, respectively.[5] Additionally, for tumor that arises in midline structures, diffuse midline gliomas may be considered as a differential diagnosis.

H3K27M mutations are the hallmark of diffuse midline gliomas, and thus the absence of this mutation may help exclude this diagnosis.[16] The immunohistochemical evaluation of EZHIP may also be considered to exclude the diagnosis of diffuse midline gliomas H3K27-mutant with EZHIP overexpression and posterior fossa ependymoma, group PFA (PFA-EPN).[17]

The current patient showed negative staining for GFAP, Olig2, EMA, H3K27M, EZHIP, and LIN28A, with retained staining for INI1 and BRG1, thus excluding all the aforementioned differential diagnosis.

Conclusions

Stratification of patients with medulloblastoma into low-risk and high-risk groups would enable more precise therapeutic intervention, so that the extent of treatment could be tailored to the degree of biologic aggressiveness. Histopathologic subclassification of medulloblastoma can help modify therapeutic planning, while molecular characterization of medulloblastoma is becoming increasingly important to help establish diagnosis, to exclude differential diagnosis, and to predict prognosis. Molecular subtyping based on genetic alterations, methylation profiles, and transcriptional patterns can better predict prognostic outcomes than histology alone and is increasingly used for medulloblastoma classification in clinical practice. WNT-activated medullo-blastomas are defined by activating mutations in the WNT/β-catenin signaling pathway, often associated with the loss of chromosome 6, and have the most favorable prognosis.

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Ultrasound-guided Genicular Nerve Ablation with Alcohol Solution for Knee Osteoarthritis: A Case Series

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Abstract

Genicular nerve ablation using radiofrequency (RF) is a common minimally invasive procedure for painful osteoarthritic knees. However, the high cost and unavailability of equipment in many healthcare centers made this inconvenient for some patients. Some case reports tried the cheaper and newer method, using an alcohol solution to ablate the genicular nerves, showing considerable improvement in the patient's pain, functional knee score, and quality of life. We have attempted the ultrasound-guided genicular nerve ablation using alcohol solution in 6 patients with knee osteoarthritis to complement the body of evidence. We found that the genicular nerve ablation using alcohol solution is an excellent method for relieving symptoms of knee osteoarthritis if knee pain is the main symptom.

Introduction

Genicular nerve ablation is a common non-surgical, minimally invasive choice for painful osteoarthritic knees. The common method is using radiofrequency (RF) to ablate the genicular nerve. However, the high cost and unavailability of equipment in many healthcare centres made this treatment inaccessible for some patients.

Instead of using RF, some case reports tried the cheaper and newer method, using an alcohol solution to ablate the nerves, and surprisingly showed a promising improvement or progresses in patient's pain symptoms, knee functional score, and their quality of life.[1,2] A recent trial also shows the effectiveness of the genicular nerve alcohol ablation. There is a significant improvement in VAS score, NRS score for walking, and WOMAC scores for the 1st and 6th months after the treatment.[3] To complement the body of evidence, we have attempted the ultrasound-guided genicular nerve ablation using alcohol solution in 6 patients with knee osteoarthritis. We found that the genicular nerve ablation using alcohol solution is an outstanding and cheap method for relieving symptoms of knee osteoarthritis if knee pain is the main symptom.

Case Illustration 1

A 71-year-old female presented with a history of left knee pain 19 years ago. She came to our clinic and complained about her persistent knee pain and stiffness that didn't go away. She rates her pain 5 out of 10 on a numerical rating scale (NRS). She still can walk far and go to the groceries alone while withstanding her pain. She still can do daily activities in the house but with moderate difficulty. She can't fully flex her knee because she says it's really painful. She had a history of multiple sodium hyaluronate injections and physiotherapy sessions, but it

wasn't helpful. Overall, the WOMAC score was 48. The knee x-ray shows that she has advanced knee osteoarthritis. She decided not to have knee replacement surgery because she was so scared that no one will take care of her. 1 week before the nerve ablation procedure, the diagnostic block was done and showed a great response. The NRS score became 5 from 10. The USG-guided superomedial genicular nerve, inferior-medial genicular nerve, and superolateral genicular nerve ablation were performed with 1 mL of 2% lidocaine followed by 1 mL of 96% alcohol at each nerve. She reported the NRS score dropped to 3 out of 10, 24 hours after the procedure. 1 month after the procedure, the patient said that her knee was better than before, but there were still some difficulties in daily activity. The WOMAC score became 35, but the NRS was still 3 out of 10.

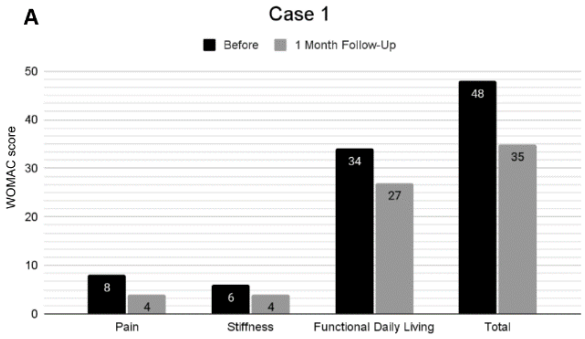

Figure 1. Western Ontario and McMaster Universities Arthritis Index (WOMAC) score results from case 1. There was significant improvement of WOMAC score in case 1, 4, and 5 (A, D, E).

Case Illustration 2

A 60-year-old male presented with a history of left knee clicking and stiffness with moderate pain since 10 years ago. He told that he cannot do full knee flexion because it is painful. He still can walk far about 100 meters without pain. The overall NRS score was 6 out of 10 and the WOMAC score is 38. The knee x-ray showed he had grade IV knee osteoarthritis. He had a history of left knee astroscopic lavage and debridement in 2016 but he feels no improvement. He also had a history of dyslipidaemia and benign prostate hyperplasia, controlled with medicines. 1 week before the genicular ablation, the diagnostic block with lidocaine was done. He said he felt better for about 3 days after the injection, with the NRS score dropping to 4. The same ultrasound-guided genicular nerve ablation procedure was done with 1 mL of 2% lidocaine followed by 1 mL of 96% alcohol at each nerve. After the procedure, he felt better with the NRS score dropping to 3, but he noted that the mechanical symptoms stills annoyed him. 1 month after the procedure, the patient said that overall there is no improvement in his knee symptoms after treatment, with the NRS score still 3 and the WOMAC score became 40. Note that he complained more about his knee mechanical symptoms, rather than his knee pain.

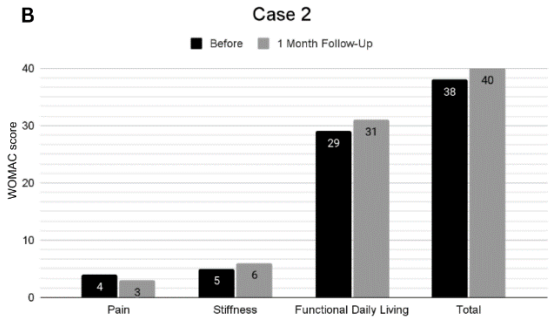

Figure 2. Western Ontario and McMaster Universities Arthritis Index (WOMAC) score results from case 2. In cases 2, 3 & 6 (B, C, F), the WOMAC score before and after treatment are relatively the same.

Case Illustration 3

A 61-year-old female came to the clinic complaining about her left knee stiffness since 2019 that got worse 2 weeks ago. She felt stiffness every day, especially when sitting or resting for too long. She felt better when she moved her legs. She also told that she felt a clicking sensation from her left knee and the clicking got louder when she walks on the uneven surface. The NRS score was 6 out of 10 and the WOMAC score was 51. She went to a physical therapy session once, but she didn't like it because she said that it made her knee

pain. She had a history of uncontrolled primary hypertension. The nerve block was done and she felt better for a while because of her knee pain reduction, but she was still annoyed by her knee mechanical symptoms. The same ultrasound-guided genicular nerve ablation procedure was done with 1 mL of 2% lidocaine followed by 1 mL of 96% alcohol at each nerve. After the procedure the NRS score dropped to 2. 1 month after the procedure, the patient said that her mechanical knee symptoms got worsened. After a more in-depth history taking, the overall NRS score was still 2 but the mechanical symptoms made her uncomfortable. She said that her left knee became really stiff and very difficult to walk now, even on flat surfaces. The clicking sensation also got worse. The WOMAC score became 63.

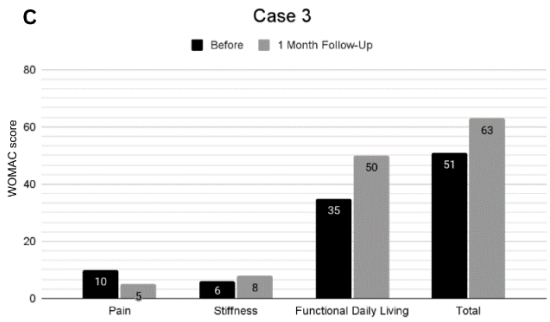

Figure 3. Western Ontario and McMaster Universities Arthritis Index (WOMAC) score results from case 3. In cases 2, 3 & 6 (B, C, F), the WOMAC score before and after treatment are relatively the same.

Case Illustration 4

A 64-year-old male came to the clinic with a chief complaint of pain in his left knee since 2011 which got worse in the past few weeks. The pain in his left knee worsen when she walked for about 20 meters, pain especially when he was having stairs, sitting for a long amount of time, and when he tried to flex her knee fully. She also felt a clicking sensation, especially when getting on vehicles on her left knee with minimal stiffness present. The patient also had a varus deformity present with a history of grade III knee osteoarthritis previously. The NRS score was 5 out of 10 with a WOMAC score of 43. The patient several times were having an intraarticular injection which could last for more than 1 year, but as of now gradually does not last that long. An ultrasound-guided genicular nerve ablation procedure was done with 1 mL of 2% lidocaine followed by 1 mL of 96% alcohol at each nerve. After the procedure was done, the overall NRS score was 0. 1 month after procedure, a detailed history taking was done and He told after the procedure about 80% of the symptoms subsided. The residual symptoms as of now were minimal but increased in certain activities such as getting on vehicles, standing and walking for a long time. The WOMAC score became 35.

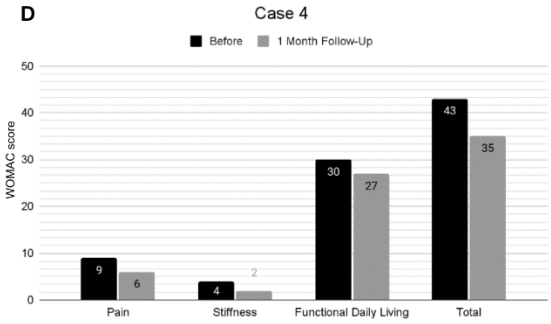

Figure 4. Western Ontario and McMaster Universities Arthritis Index (WOMAC) score results from case 4. There was significant improvement of WOMAC score in case 1, 4, and 5 (A, D, E).

Case Illustration 5

A 79-year-old female came to the clinic with a complaint of pain in her right knee for 9 months. She felt the pain in her right knee accompanied by a clicking sensation. The pain was felt especially when she walked around her house, climbing stairs which also need the assistance of others, and every morning she also felt stiffness. She felt her activity was slightly limited but overall didn't need assistance except for climbing stairs. She had a history of filariasis on her left leg. The NRS score was 6 out of 10 with a WOMAC score of 53. An ultrasound-guided genicular nerve ablation procedure was done with 1 mL of 2% lidocaine followed by

1 mL of 96% alcohol at each nerve. After the procedure was done, the overall NRS score was 4. Following the procedure, she could walk on her own without assistance to the parking lot from the orthopaedic outpatient department. After 1 month, she was able to bend her knee more confidently than before but climbing stairs still has been a challenge for her. The WOMAC score was 35 with an NRS score of 1 out of 10.

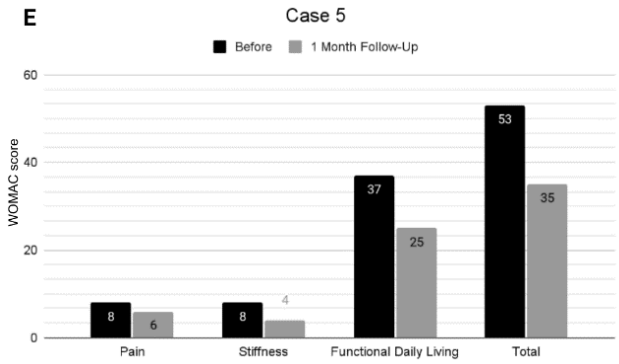

Figure 5. Western Ontario and McMaster Universities Arthritis Index (WOMAC) score results from case 5. There was significant improvement of WOMAC score in case 1, 4, and 5 (A, D, E).

Case Illustration 6

A 65-year-old female came to the clinic with stiffness in her left knee for 1 year. She felt a clicking sound when she moved her knee but otherwise not too disturbing or experiencing any pain. She complained of knee stiffness especially in the morning when she woke up and felt extreme pain. The Pain also comes and goes when getting up from sitting, walking about 100 meters, climbing, or getting downstairs but otherwise did not need any crutches, walker, or assistance. The NRS score was 8 out of 10 with a WOMAC score of 50. An ultrasound-guided genicular nerve ablation procedure was done with 1 mL of 2% lidocaine followed by 1 mL of 96% alcohol. Due to very low pain tolerance, only superomedial genicular nerve (SMGN) and inferior medial genicular nerve (IMGN) were ablated, leaving the inferior lateral genicular nerve (ILGN). After the procedure, the NRS score became 0. After 1 month, the pain decreased. However, the stiffness got worse according to her. The overall WOMAC score was 52 with an NRS score became 4 out of 10.

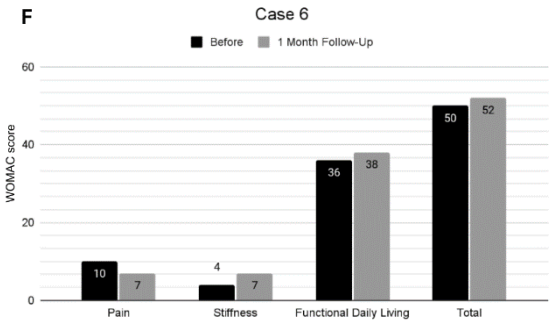

Figure 6. Western Ontario and McMaster Universities Arthritis Index (WOMAC) score results from case 6. In cases 2, 3 & 6 (B, C, F), the WOMAC score before and after treatment are relatively the same.

Discussion

Our case report showed that genicular ablation using alcohol solution may become a viable option for chronic painful knee osteoarthritis. After the procedure, the pain section from the WOMAC score was increased and the NRS was reduced in all patients after a month. RF (radiofrequency) is popularly used for neurolysis procedures and is supported by many studies.[4-7] However, it has its disadvantages due to higher costs. In the current evidence, alcohol neurolysis is a safe, effective, and low-cost procedure with preferably good results. Since alcohol causes iatrogenic neural degeneration, it spares the motoric function of the nerve. Thus, alcohol neurolysis can be reliable as a palliative treatment for chronic painful osteoarthritis without altering the patient's ambulatory.

To our knowledge, the alcohol neurolysis to the genicular nerve procedure was first introduced in a case report by Dass et al.[1] Our case report has a similar procedure, using about 50% alcohol concentration to avoid permanent neurolysis of the genicular nerve.[9]

However, we didn't use contrast dye in the mixture and fluoroscopy machine. Since fluoroscopy increases the accuracy of the injection site, unnecessary damage to another soft tissue/structure can be avoided. However, in our preference, using ultrasonography alone is still reliable enough as a guidance tool and also has lower radiation exposure. Following Dass et al., the study done by Ahmed et al. tried to ablate the middle genicular nerve (MGN), recurrent peroneal nerve (RPN), and inferior lateral genicular nerve (ILGN) and showed good results in 1-month and 6 months follow-ups.[2] Future studies were needed to look at the long-term effect of alcohol neurolysis on the genicular nerve for longer than 6 months. A recent trial by Elashmawy et al. also looks at the efficacy of alcohol neurolysis, compared to nerve block alone. All 23 patients treated with alcohol neurolysis maintained the VAS score, NRS, and WOMAC score after 6 months.[3] Ahmed et al. and Elashmawy et al. used alcohol and an anaesthetic solution, instead of injecting the anaesthetic and alcohol separately.

Besides the advantages, alcohol neurolysis is an excruciating procedure in most of our patients. In our experience, it will be more pleasant for the patient if we inject the alcohol really slowly to the genicular nerve. The procedure also most likely doesn't work out for the patient if they are more concerned with the mechanical symptoms of the knee rather than the knee pain.

We use the WOMAC (Western Ontario and McMaster Universities Arthritis Index) to assess patient feedback and treatment satisfaction. WOMAC was first developed in 1982 and widely used to evaluate knee or hip osteoarthritis patients. All of the cases had improved pain scores. Some of the patients who satisfied with the procedure were also improved their quality of life/physical function and stiffness score. However, in case 2, 3, and 6; the patients mostly complained about the mechanical symptoms of the knee, e.g. clicking and catching sensation.

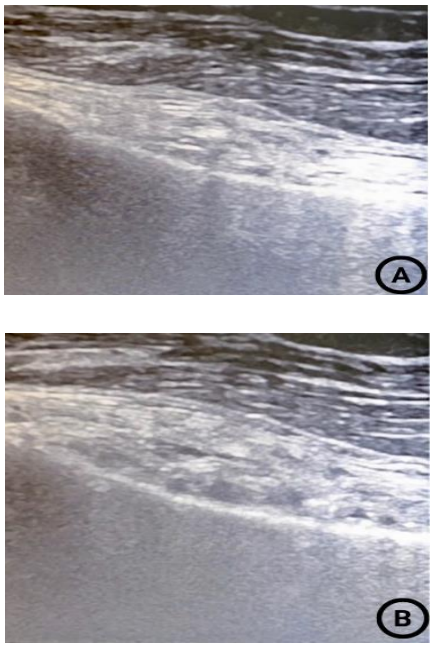

Figure 7. Inferior medial genicular nerve (IMGN) before ablation using alcohol solution (A). IMGN after ablation using alcohol solution (B).

Conclusion

In conclusion, alcohol may become a great tool as a neurolysis agent besides radiofrequency (RF). However, future high-quality randomized controlled trials were needed to confirm the efficacy of alcohol neurolysis compared to RF.

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Strangulated Left Lateral Inguinal Hernia in a 54-Year-Old Woman: A Case Report

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Abstract

Introduction: Around 20 millions of hernia repairs were done annually with women presenting least cases. The occurrence of inguinal hernia in female patients is 3-6%, which is lower than men (27-43%). Inguinal hernia itself may present as a bulge in the groin in which the definitive treatment is through surgery. Although many research were done for hernia repair in men, guidelines for women are still currently observed with less favourable outcomes.

Case illustration: A 54-year-old woman came to the ED complaining of pain of protruding bulge in the groin area for two hours. The patient has had a history of bulging for three years, which was previously reducible. Examination of the inguinal region revealed a lump with a diameter of +/- 4 cm and painful when palpated. Abdominal USG showed a left inguinal hernia consisting intestinal tissues. Open herniotomy with mesh grafting was performed and the patient got discharged after 4 days of hospitalisation.

Conclusion: Lifetime risk for development of inguinal hernia is higher in men compared to women, but the rate of emergency procedures in women is 3 to 4-fold higher than in men. Guidelines for hernia repair in women show less favourable results than in men. Therefore, special steps must be taken in the repair of inguinal hernia in women.

Introduction

Around 20 millions of hernia repairs were done annually, with inguinal hernia being the most common type of groin hernia. Other types of groin hernia include scrotal and femoral hernia. The term hernia itself has the meaning of protrusion. Therefore, inguinal hernia means protrusion of a peritoneal pouch that consists of intestinal organs caused by a weakness or defect in the abdominal wall.[1] Prevalence of inguinal hernia is higher in men than women with 27-43% occurrence in men and 3-6% occurrence in women. Incidence of inguinal hernia is also higher around the age group of 40-59 years old.[2] Inguinal hernia can be acquired or a form of congenital disease in some cases.[3]

Inguinal hernia is also classified into two groups, direct inguinal hernia and indirect inguinal hernia.[4] Indirect inguinal hernia are about twice as common as direct inguinal hernias. There is a hypothesis that all indirect inguinal hernias result from a processus vaginalis that had never closed, this hypothesis is supported by research by Jiang and Mouravas that adult indirect

inguinal hernias may develop after the long-term build-up of pressure on a processus vaginalis that had closed along its entire length except at the neck of the hernia sac.[5,6]

Inguinal hernia usually presents with a bulge in the groin. It may become more noticeable when the patient is standing up, coughing, or straining. It can be accompanied with a mild burning or sharp pain that radiates to the scrotum, testes, or inner thigh. Although, if presented with a severe pain and constipation, it might be signs for incarcerated or strangulated hernia. Management of inguinal hernia is through surgery by returning the abdominal contents back and closing the hernial defect with a mesh graft to ensure a lesser chance of recurrency.[3]

There was an anatomical study of the inguinal region focusing on the anatomic differences in men and women and the relationship to hernial formation.[7] The result of the study is there was a significant difference between the diameters which were almost twice as large in men, while the width of the rectus abdominis muscle was significantly greater in women. These anatomical differences are the possible explanation of why the risk involving groin hernia development might be lower in women than men.[7] Higher incidence of inguinal hernia in men leads to the question of management differences of inguinal hernia in men and women. There is a growing problem in the lack of data involving inguinal hernia repair in women.[7] Although guidelines for inguinal repair in women are currently observed, less favourable outcomes are still visible. In this case report, we illustrated the treatment given for a woman patient with inguinal hernia. The authors are hopeful that this information will be helpful for further research around this topic.

Case Illustration

A 54-year-old lady came to the emergency ward complaining of pain and protruding bulge in the groin area for two hours. The characteristic of the pain was described as sharp with a pain scale of 8/10. The pain radiated to the left knee and felt constantly. The patient has had a bulge in the groin area for 3 years now. The bulge was reducible until 17 hours ago when it became irreducible. The patient felt that the bulge became bigger over time. The patient denied any redness and swelling on the bulge. The patient vomited water and food once in the emergency ward with no sign of bleeding. There were no signs of fever and extreme weight loss. The patient has hypertension and consumes amlodipine 10 mg once a day regularly. The patient does not have any history of diabetes mellitus and cholesterol.

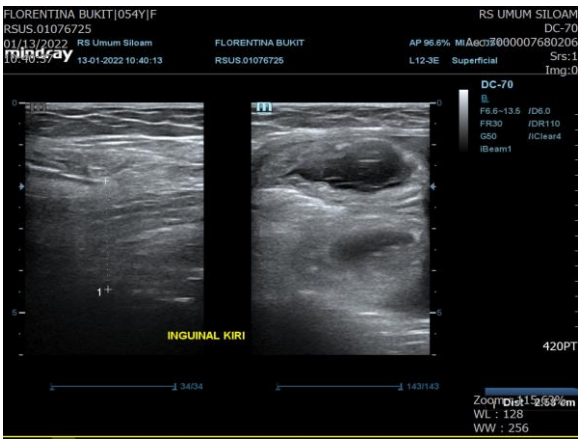
When she first arrived in the emergency ward, she was screened for COVID-19. The result came back negative. The vital signs were stable. The examiner found a lump on the inguinal region with a diameter of +/- 4 cm, immobile, soft and painful when palpated. Examination of other regions was unremarkable. The result of blood work was elevated ESR of 22 mm/hour and reduced potassium level of 3.4 mmol/L. Abdominal ultrasound was performed and showed a left inguinal hernia with a defect of +/- 2,58 cm consisting intestinal tissues.

She was diagnosed with strangulated left lateral inguinal hernia. The plan was to do an urgent open herniotomy with mesh grafting. She was given antibiotic ceftriaxone 1 gram intravenously twice daily and omeprazole 40 mg intravenously twice daily. Fluid administration of Lactated Ringers 500 mL every 8 hours intravenously was given. Intraoperative findings revealed

hernial sac consist of one viable loop of intestinal tissues which is then pushed back into the peritoneal wall. After the removal of hernial sac, the operator proceeded to place a mesh graft on the inguinal floor. One day post-herniotomy, the patient complained of abdominal pain around the incision site when in a sitting position. Vital signs were normal. Examination of the incision site was unremarkable. Day two post herniotomy, the patient still complained of abdominal pain around the incision site, but she felt much better. Vital signs were normal, and examination of the incision site was unremarkable. The patient was discharged on day three post-herniotomy and given oral drugs such as cefixime 200 mg twice daily, metronidazole 500 mg thrice daily, ketorolac 10 mg thrice daily and omeprazole 20 mg twice daily.

Imaging and Intraoperative Pictures

Figure 1. Protruding bulge in the groin area



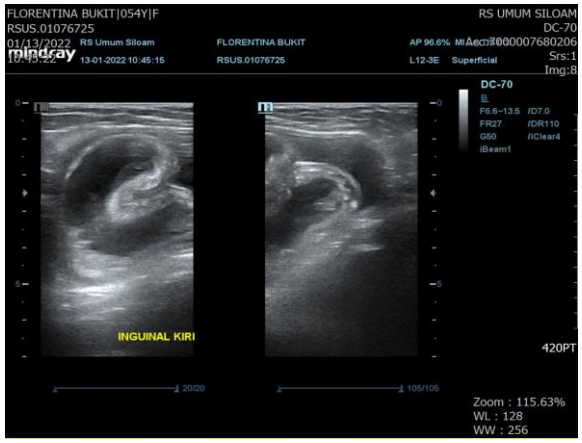


Figure 2 and 3. Abdominal ultrasound showed a left inguinal hernia with a defect of +/- 2,58 cm consisting intestinal tissues

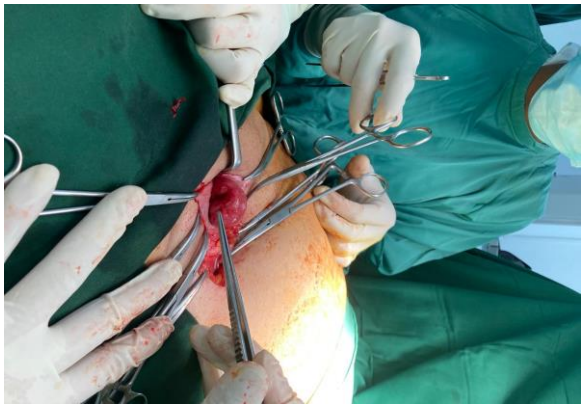


Figure 4. Opened hernial sac revealed one viable intestinal loop

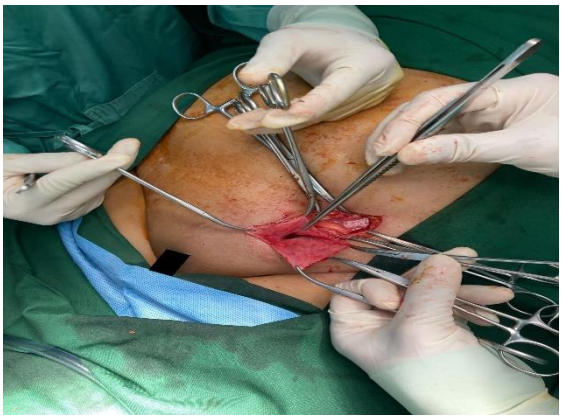


Figure 5. Opened hernial sac

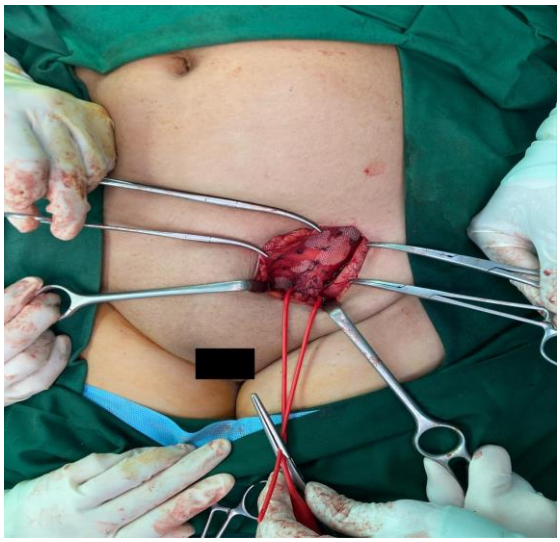


Figure 6. Placed mesh grafting on the inguinal floor

Discussion

Inguinal hernia in women occurs when the inguinal canal is being weak. This canal run diagonally from the hip bone down to pubic bone, making the groin area connected to the abdomen. The canal contains blood vessels, nerves, lymphatic vessels, and it also contains the round ligament that supports the uterus. When the part of the abdominal content bulges through a gap in the abdominal wall this leads to inguinal hernia. The inguinal canal in women is narrower therefore inguinal hernias are much less common in women than men, but weakness of the connective tissue can increase the risk of having an inguinal hernia in women.[8]

Surgery for tension-free inguinal hernia is highly considered in women than men because women have higher risk of complication. During surgery, the abdominal content is moved back into the abdominal cavity and the sac is excised. The gap in the abdominal wall is then closed off with synthetic mesh or reinforced with tissue from another part of the body. Adding synthetic mesh strengthens the abdominal wall better than only sewing the gap with the neighbouring connective tissue and this also makes faster recovery post- surgery.[9]

During surgery of the inguinal hernia in women, a femoral hernia should always be ruled out because women who have an inguinal hernia are more likely to have a hidden femoral hernia and this can only be assessed during surgery. The incidence of femoral hernia in women is 16.7-37%.[7] If a femoral hernia is not reliably ruled out or not appropriately treated, recurrence rate might be higher. Based on systematic review and meta-analysis there is a higher recurrence rate in females caused by femoral hernias being overlooked during primary surgery. This is true for the lichtenstein open techniques, where the transversalis fascia is not routinely opened.[10,11]

A systematic search performed by Ferdinand K et al in 2019, showed that there is a lifetime risk of 3-5.8% of developing hernia in women. The proportion of emergency procedures done in women is 14.5%, which is higher than men with the proportion of 3.0%. The number of participants in each gender may also greatly affect the number. But we can conclude that there is a higher chance of women getting into an emergency procedure than men by 3 to 4-fold. From the research, they discussed the surgical intervention suited for inguinal hernia repair in women. The guidelines recommended Total Extraperitoneal Patch (TEP) and Transabdominal Peritoneal Patch (TAPP) laparo-endoscopic techniques or open preperitoneal mesh placement technique if femoral hernia is present. The research also

concluded no recurrence when performing modified Nyhus-Condon femoral hernia repair with mesh and Lichtenstein repair with insertion of a cone of polypropylene mesh into the femoral canal. Although, a high early recurrence rate might occur when presence of femoral hernia is overlooked. Women also have a higher chance of chronic postoperative pain that occurred in 24.2% of patients.[7]

Studies done in 2011 by Jonathan C et al showed the importance of doing a laparoscopic repair in women in the detection of previously undiagnosed femoral hernia, which may occur in 40% of cases. Although, in a retrospective chart review done in 2012 by A. Ashfaq showed a far lower rate (2%) in femoral hernia detection. There were no statistically significant differences between laparoscopic versus open approach in recurrence of hernia (45% versus 55% respectively).[12,13]

Conclusion

There are so many special characteristics for inguinal hernia repair in women that must be taken into account, so it is very important to know all the guidelines including the specific recommendations for the diagnosis and treatment of female inguinal hernia. Beside the consideration of choosing the right guideline, the outcome of the treatment is less favourable in women than in men therefore repair of inguinal hernia in women should be performed by an experienced surgeon that can be aware of all the specific aspects and consideration of the guideline.

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Intramedullary Spinal Cord Cavernoma; A Case Report and Literature Review

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Keywords: Spinal cord; Intramedullary lesion; Cavernous malformation; Cavernoma
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Abstract

Background: Spinal cord intramedullary cavernous malformation (SICM) is kind of rare vascular disease, and the therapeutic strategy is still under debate. Cavernous malformation (CM) can be found throughout the central nervous system (CNS) but only rarely occur within the spinal cord. The purpose of this article is to describe natural history, clinical presentation and outcome of SICM case which treated surgically

Case Presentation: A 70-year-old healthy woman presented with lower extremity weakness. A posterior laminectomy was performed, and a diagnosis of intramedullary spinal cord cavernous malformation was established. Neurological improvement was seen in one month after surgery

Conclusion: Intramedullary CM is a rare disease but one with significant consequences if not managed appropriately. whenever safely feasible, gross total resection is suggested, to prevent rebleeding and further worsened of neurological deficit.

Introduction

Cavernous malformations are well circumscribed vascular lesions made up of thin-walled sinusoidal channels.[1] Cavernous malformations (CMs) are not uncommon, but most of them are found to be located intracranially. Intramedullary CMs are rare, which comprise 3–5% of identified total central nervous system lesions and account for 5–12% of all spinal cord vascular lesion, with annual risk haemorrhage 2.1-2.5%.[2,3,4,5] Appropriate management of these lesions requires understanding their clinical, radiographic characteristics and a thorough knowledge of the anatomy of the spine and spinal cord.

Case Presentation

A 70-year-old healthy woman presented after an episode of back pain since the last 1 month, followed by progressive lower extremity weakness (motor strength 4/5) and dysesthesias. Magnetic resonance imaging demonstrated a T1W mix density, predominantly hyperintense lesion from T-2 through T-4 Differential diagnosed with an intramedullary spinal cord tumour haemorrhage or spinal intramedullary CM.

A posterior laminectomy was performed. After opening the dura we found bluish discoloration, then a posterior median sulcus myelotomy was performed over this area. We then exposed the hematoma, blood products were suctioned then we resected the lesion piece by piece along the gliotic plane, leaving the hemosiderin margin as a guide for the

cleavage plane of the lesion. Intraoperative somatosensory evoked potentials (SSEPs) and motor evoked potentials (MEPs) were monitored. After complete resection of the lesion, we sutured the pia mater, arachnoid membrane, and duramater.

No transient deficit postoperatively. One month after surgery, her motor examination was entirely normal but her dysesthesias persist.

Figure 1. Contrast Sagittal T1-weighted MR image demonstrating heterogeneous mixed signal intensity at T2-T4 with no enhancement

Figure 2. Sagittal T2-weighted MR image demonstrated mixed signal with near complete T2 hypointense rim at T2-T4

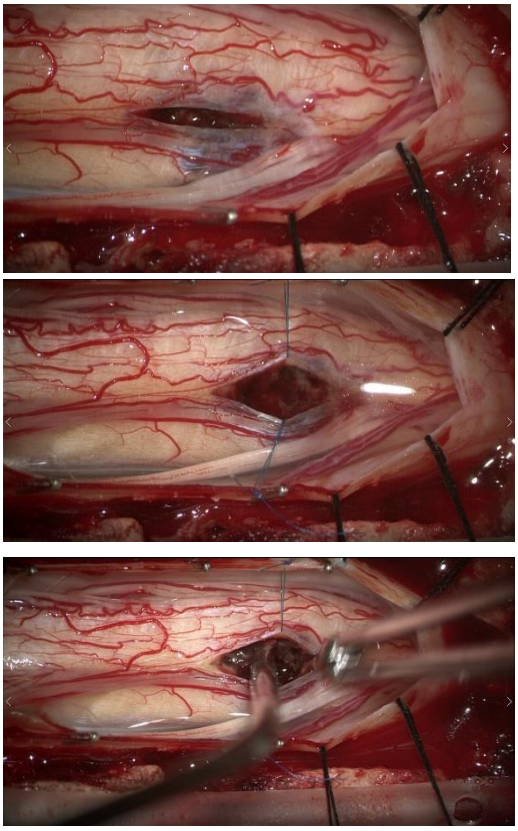

Figure 3. Posterior intramedullary cavernoma can be seen under the duramater. A small myletomy was made over the hemosiderin staining and the hematoma cavity was entered.

Discussion

Cavernoma is a vascular malformation, raspberry-like lesion filled with blood that flows very slowly through vessels that like “caverns”. The caverns is composed of dilated thin wall capillaries that consist of single layer of endothelial cells, very few intact tight junction between the endothelial cells and no elastic fiber. Cavernoma are dynamic lesions, some will remain stable without bleed for a very long period, some might bleed once than remain stable, some might grow, but some could bleed repeatedly. Patient with repeated bleeding will have progressive declining of neurological state. Although it is recovering, but the functional state never get back to the function prior to the last bleed. Complete removal of cavernoma is essential to prevent rebleeding.[1]

In line with our literature study, thoracic region is the most common site. On fourty one publications with 1032 patients of spinal cord cavernoma in the past 10 years.[2,3,6-47] (Table 1). The mean age at symptom onset was 41 years. The male/female ratio was nearly the same 1.24:1. Fifty nine percent (611 cases) of lesions were located at thoracic spine, 35% (368 cases) at cervical, 1% (11 cases) at lumbar region, 1.7 % thoracolumbar, 1.6 % cervicothoracal, 0.2 % conus medullaris 0.09% cervicomedullary, and 0.4 % unspecified location.

Although it was not found in our case, on our literature studies, we found 29 (9%) of 298 patients evaluated for a family history of these lesions had at least one family member with at least one CM.[3,6,7,8] Fifty four (38%) of 141 patients described in 4 series had synchronous intracranial CMs.[3,7,8,9].

Extremity weakness is the most common presentation, as seen in our case. It is consistent with 38 publications with 898 patients provided information on patient clinical presentations, 577 patients (64%) presented with motor weakness, 510 patients (56.8%) had sensory deficit, at least 358 patients (39.8%) had pain, and 320 patients (35.6%) had bowel or bladder dysfunction.

Table 1. Clinical data from series of SICM [6-47]

Authors & year	Patients	Mean Age (yr)	M: F Ratio	Lesion location No of lesion	Clinical presentation No of patients	Onset, No of patients	Family history
Bozinov, et al. 2011	6	27.5	3:3	Cervical 2, Thoracal 4	Weakness 4, sensory deficit 4, B/B 1	Acute 2, progressive 4	-
Choi,et al. 2011	21	39.3	8: 13	Cervical 9, Thoracal 9, Lumbal 1 Cervicomedullary 1 Thoracolumbar 1	Weakness 12, sensory deficit 11. B/B 4, pain 9	Acute 8, progressive 8, recurrent 5	-
Liang et al. 2011	96	34.5	1,67:1	Cervical 25 Thoracal 68 Lumbal 3	Weakness 84, sensory deficit 46 B/B 68, pain 39	Acute 6 Progressive 90	0
Pearl et al. 2012	2	52	2:0	Thoracal 2	Sensory deficit 2	Progressive 2	-
Savasta et al.2012	1	9	0:1	Thoracal 1	Pain 1	Acute 1	-
Soriasno et al. 2012	1	42	0:1	Thoracal 1	Sensory deficit 1 Pain 1	Acute 1	-
Tong et al. 2012	20	34	1:3	Cervical 9 Thoracal 7, Cervicothoracal 4	Weakness 14, Sensory deficit 9, pain 5, B/B 2	Progressive 20	-
Babu et al. 2013	8	43	-	Thoracal 4 Others 4	Weakness 6 , sensory deficit 6, pain 5, B/B 1	Progressive 8	-
Eicker et al. 2013	1	20	0:1	Cervical 1	Sensory deficit 1 Pain 1	Progressive 1	-
Endo T et al. 2013	8	57	5:3	Thoracal 8	Weakness 2, sensory deficit 2, pain 4	Acute 5 Progressive 3	-
Lanotte, et al 2013	1	24	0:1	Cervical 1	Sensory deficit 1	Progressive 1	-
Grasso et al. 2014	1	34	0:1	Thoracal 2	Weakness 1 sensory deficit 1 , B/B 1	Acute 1	-

Matsui et al.2014	1	42	1:0	Conus medullaris 1 Skin associated lesion 1	Weakness 1 sensory deficit 1 , B/B 1	Acute 1	-
Qing et al. 2014	20	48.5	8: 12	Cervical 9 Thoracal 11	Pain 20	Progressive 20	-
Ardeshiri et al, 2015	25	46	14: 11	Cervicothoracal 11 Thoracolumbar 14	weakness 16, sensory deficit 21 B/B 4	Acute 1 Progressive 16 Recurrent 3	-
Reitz M et al, 2015	48	41.3	25:23	cervical 19 thoracic 27 thoracolumbar 2	Asypmtomatic 3	Acute 20 Progressive 9 Recurrent 16	-
Zhang et al. 2016	85	40.5	51:34	cervical 40 thoracal 40 lumbar 5	weakness 62 sensory deficit 67 pain 33 B/B 20	Acute 41 Progressive 40 Recurrent 4	-
Kodeeswaran et al, 2016	1	15	1:0	Cervical 1 Synchronous intracranial lesion 1	Weakness 1	Progressive 1	-
Scherman et al, 2016	1	56	0:1	Cervical 1	Weakness 1 Sensory deficit 1 B/B 1	Progressive 1	-
Salinas et al, 2017	1	62	1:0	Thoracal 1	Weakness 1 Sensory deficit 1	Progressive 1	-
Ahmed NF, et al, 2017	1	45	1:0	Cervical 1	Weakness 1, sensory deficit 1, Pain 1	Progressive 1	-
Huntley et al. 2017	1	58	1:0	Thoracal 1	Weakness 1, Sensory deficit 1, B/B 1	Progressive 1	-
Imagama S, et al, 2017	41	39	18:23	Cervical 17 Thoracal 24	Weakness 26	-	-
Azad TD et al. 2017	32	44.2	13:19	Cervical 16 Thoracal 16 Synchronous intracranial lesion 9	Weakness 5 sensory deficits 9 Pain 16 B/B 2	Acute 19 Progressive 13	6
Sun I et al.2017	10	45	1:1	Cervical 6 Thoracal 4	-	Acute 4 Progressive 6	-
Li et al. 2018	83	39	40:43	Cervical 34 Thoracic 47 Lumbar 2	Weakness 47 Sensory deficits 9 Pain 25 B/B 13	Progressive 83	6
Nagoshi et al. 2018	2	37.5	2:0	Cervical 2	Weakness 1 Sensory deficit 1 Pain 1	Acute 2	-
Oh HM et al.2018	1	79	0:1	Cervicothoracal 1	Weakness 1 Pain 1 Sensory deficit 1	Acute 1	-
Ren et al.2018	10	39.9	5:5	Cervical 2 Thoracal 8	Weakness 5 Sensory deficit 7 Pain 7 B/B 3	Progressive 10	-
Winkler AE et at. 2018	1	28	1: 0	Thoracal 1	Weakness 1 Conus medullaris syndrome 1	Acute 1	-
Apostolakis et al. 2019	1	77	1:0	Conus medullaris 1	Pain 1	Progressive 1	-
Goyal et al. 2019	107	17.3	59:48	Cervical 43 Thoracal 63 Conus medullaris 1 Synchronous intracranial lesion 24	Motor 14 Sensory 16 Pain 17 B/B 15 Asymptomatic 22	Acute 28 Progressive 56	11

Kang MG, et al. 2019	1	61	1:0	Thoracal 1	Weakness 1 Pain 1	Progressive 1	-
Moldovan K, et al. 2019	1	54	1:0	Thoracal 1	Motor weakness 1	Acute 1	-
Ren J et al. 2019	20	14	16: 4	Cervical 5 Thoracal 15	Weakness 19 Sensory deficit 20 Pain 10 B/B 12	-	-
	234	38.3	132: 102	Cervical 62 Thoracal 172	Weakness 197 Sensory deficit 224 Pain 133 B/B 145	-	-
Ren J et al. 2019	40	40.6	2.1:1	Cervical 17 Thoracal 23	weakness 34 sensory deficits 37 pain 16 B/B 17	Acute 36 Progressive 4	-
Couldwell WT et al. 2020	1	36	1:0	Cervical 1	Weakness 1	Progressive 1	-
Gendle C et al 2020	1	5 mo	1:0	Thoracolumbar 1	B/B 1	Progressive 1	-
Nwachuku et al. 2020	1	63	1:0	Cervical 1	Weakness 1 Sensory deficit 1 B/B 1	Progressive 1	-
Oishi M et al 2020	1	37	1:0	Cervicothoracal 1	Weakness 1 Pain 1 B/B 1	Acute 1	-
Panda A et al. 2020	76	49	39:37	Cervical 35 Thoracal 41 Synchronous intracranial lesion 20	Asymptomatic 17	Acute 9 Progressive 29 Recurrent 21	6
Zhang et al. 2020	18	12.9	2: 1	Cervical 9 Thoracal 9	Weakness 15 Pain 10 Sensory deficit 8 B/B 6 Spinal deformity 1	Acute 11 Progressive 7	

Although the clinical presentation may be variable, the majority of patients seek medical attention due to acute onset of hemorrhage into the spinal cord parenchyma as seen in aour patient. Ogilivy et al describe four types of clinical presentation. First, acute neurological deterioration over a period of months or years with gradual, partial improvement in between episodes. This probably the result of episodes of small hemorrhages from the lesion. Second, slowly progressive neurological deterioration which lasted several months to years. This suggests an enlargement of the lesion resulting from repeat microhemorrhages, the gliosis neurotoxic effect of hemosiderin, impaired microcirculation due to local pressure, or progressive hyalinization and thickening of the vascular walls or gradual thrombosis. Third, acute onset of neurological deterioration with a rapid neurological decline. Fourth, acute onset of pain and mild symptoms of neurological deterioration with gradual decline over weeks to months to the final syndromes.[48]

Magnetic resonance imaging is the gold standard for diagnostic. A typical lesion on an MR image is a lobulated, commonly said as popcorn appearance. Internal blood-fluid levels on either axial or sagittal sequences can also be found. Hemosiderin deposition resulting in a hypointense rim around a mixed signal intensity is the pathognomonic appearance of CMs on T2w. Adjacent intramedullary hemorrhage can also be founded separately from T2w hypointense rims.[8,12]

Based on the signal characteristics, SCMs were also classified into 4 types according to Zabramski's criteria Type I (subacute hemorrhage) if it was hyperintense on T1w and hypo/hyperintense on T2w with an incomplete or absent T2w hypointense rim. Type II ("classic") if it was heterogeneous on both T1w and T2w with complete/near complete Tw2 hypointense rim. Type III (chronic hemorrhage) if it was isointense/hypointense on T1w and T2w with varying extent of T2w hypointense rim. It was considered type IV (punctate hemorrhage) if it was not well seen on T1w and T2w.[8,49]

Cavernous malformations must remain in the differential diagnosis of intradural intramedullary lesions. The broader differential includes multiple sclerosis, spinal ependymomas, astrocytomas, metastatic disease, hemangioblastomas, spinal AVMs, and transverse myelitis. Spinal angiography will facilitate the diagnosis of a spinal vascular malformation.[12] Moreover, in particular case, spinal angiography enhanced with flat-panel catheter angiotomography (FPCA) is suggested to identify spinal developmental venous anomaly in cavernous malformations to prevent higher risk of surgical complication.[13]

Resection is the only definitive treatment since this leads to a permanent elimination of the risk for further growth or hemorrhage. The resection of the active cavernoma tissue is thought to be sufficient. Excision of hemosiderin infiltration in the surrounded healthy tissue is not recommended, since it poses a significant risk of morbidity. Incomplete resection may lead to recurrence and even progressive deterioration due to bleeding from the residual malformation.[10,12]

Across 23 literature studies with 825 patients, 671 CMs (81%) were totally resected.[3,7,9,10-12,16,17-19,24-26,28,29,32,34,36-38,41-43] Transient early postoperative morbidity was reported in 15 out of 116 patients (12%) in 3 series, At the long-term follow-up 224 patients were improved (27.15%), 393(47.5%) were unchanged, and 72 (8.7%) were worsened, as compared with their preoperative status. These overall results are summarized in Table 2.

Table 2. Outcome on surgically treated SICM [3,7,9,10-12,16,17-19,24-26,28,29,32,34,36-38,41-43]

Authors & year	No of patients	Total resection rate	Early transient morbidity	Mean FU in months	Long term outcome No of patients
Bozinov, et al. 2011	6	6/6			Improved 6
Choi,et al. 2011	21	21/21		33.21 (1-73)	Improved 10 same 9 worsened 2
Liang et al. 2011	96	64/96	5	45.8 (10–183)	Improved 23 Same 35 worsened 6
Tong et al. 2012	20	20/20	8		Improved 7, same 5
Babu et al. 2013	8	8/8		15.9 (36.7 ± 10.4)	Improved 4, same 2, worsened 2
Eicker et al. 2013	1	1/1		3	Improved 1
Endo T et al. 2013	8	8/8		28.9 (15 to 52)	Improved 5 same 2 worsened 1
Ardeshiri et al, 2015	25	20/25		6.3 (2-17)	Improved 2, same 18
Reitz M, 2015	48	48/48		79.3 ± 35.2	Improved 6 Same 26 Worsened 16
Zhang et al, 2016	85	58/85		42.8	Improved + same 79 : Worsened 6
Kodeeswaran et al, 2016	1	1/1		6-8	Improved 1
Scherman et al, 2016	1	1/1		11	Improved 1
Salinas et al, 2017	1	1/1		10	Improved 1
Imagama S, et al, 2017	41	41/41		10 years (2-24 years)	Improved 11 Same / worsened 15
Azad TD et al. 2017	32	32/32	2	6	Improved 6 Same + worse 20
Li et al. 2018	83	82/83		0.5-6 years	Improved 19 same 38 worsened 5
Oh HM et al. 2018	1	0/1		3	Improved 1

Ren et al.2018	10	10/10	1.4 years (3 mo – 6.8 mo)	Improved 2 same 8
Winkler AE. Et at. 2018	1	1/1	7 week	Improved 1
Goyal et al. 2019	107	32/107		Improved 10 Same 15 Worsened 7
Moldovan K, et al. 2019	1	1/1	6 week	Improved 1
Ren J et al. 2019	15	15/15	42.7 ± 36.8 (6 - 164 mo)	Improve 5 Same 9 worsened 1
	176	176/176	46.4 ± 34.6 (6 - 164 mo)	Improve 57 Same 113 Worsened 6
Ren J et al. 2019	37	24/ 37	40.5 ± 38.9 months	Same 17 Improved 5 Worsened 2

Gross-total resection is the most important factor in eliminating the risk of a new haemorrhage in the future, It is achieved in 94% The transient worsening of patients immediately following the surgery is seen in 24–50% cases and the majority resolves during the first 3 months.[4,5] Another study reported on 7 % of patients which suffered from neurological worsening that unimproved during the long-term follow-up. Only a minority of published studies have reported results of conservatively treated patients.[12] Based on these studies surgical resection is the chosen way of treatment for our patient.

Intramedullary cavernomas may be located superficially or deep-seated; anteriorly, laterally, or posteriorly. Posterior approach is the most frequently elected, because it's provide extensive exposure of the spinal cord, relatively safe, and furthermore, it is an approach which all neurosurgeons are familiar with. A lateral lesion can be approached posteriorly by releasing dentate ligament to allow cord rotation to perform direct entry to the lesion. For a centromedullary lesion without any surface discoloration, a myelotomy should be performed during the operation, which might involve a higher surgical risk. Furthermore, SSEP and MEP monitoring is useful in protecting neurological function.

Length of symptoms and pre operative neurological state is an important factor predicting postsurgical recovery. In long-term follow-up, Svoboda et al reported 42% improved (11 patients), 46% remained stable (12 patients), and 12% (3 patients) deteriorated compared to their presurgical neurological status.[50] It is general agreement that patients with motor deficits have the highest possibility of postsurgical improvement reaching up to 86%.[50] Interestingly, several studies pointed out that sensory deficit, pain (radicular or central), and bladder dysfunction often do not favor a full recovery following the surgery.[4,5,31] Patients having symptoms of less than 3 months were found to have better postsurgical outcomes Similarly, patients with acute or stepwise clinical course are prone to benefit more significantly from surgery when compared to those with progressive neurological decline.

Conclusion

Spinal cord intramedullary cavernoma are rare vascular malformation of the spinal cord. Removal of intramedullary spinal cavernomas may lead to clinical improvement, so it may be considered as a curative option to reduce the risk of new hemorrhage. We would consider surgical removal of symptomatic intramedullary spinal cavernomas with proven growth or bleed with significant initial symptom.

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