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Moyamoya disease among Polish population: single clinic experience and literature review

Choroba Moyamoya wśród ludności polskiej: doświadczenia jednego ośrodka i przegląd piśmiennictwa

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Keywords

Moyamoya disease, epidemiology, MMD, polish population

Słowa kluczowe

choroba Moyamoya, epidemiologia, MMD, populacja polska

Summary

Introduction. Moyamoya disease (MMD) is an extremely rare condition with unknown ethology. The pathological process occurring in intracerebral vessels results with stenosis or occlusion of the arteries situated on the base of the scull. The progressive stenosis usually occurs at the distal part (supraclinoid) of the internal carotid artery (ICA) and proximal portion of anterior cerebral artery (ACA) and medial cerebral artery (MCA) and development of an abnormal vascular network is observed. Patients usually suffer from ischemic attacks, mostly among paediatric population or an intracranial haemorrhage most often among adults.

Aim. The aim of this study is to determine the epidemiological data of Moyamoya disease among patients, who underwent treatment in Neurosurgery Department in Lublin.

Material and methods. Retrospective analysis of twelve cases of Moyamoya disease treated in the Department of Neurosurgery and Paediatric Neurosurgery in Lublin between 2006 and 2016 was performed. The analysis is focused on epidemiological features: age, gender, affected hemisphere, treated artery, symptoms and number of burr holes.

Results. All patients were classified with Moyamoya disease. Among 12 patients 83% of them were female and 18% were male. The female-to-male ratio was 5. The mean age of the population was 11.2 years and 8.6 years when only paediatric population is analyzed. Among all cases the most common symptom was hemiparesis (92%), which occurred with equal frequency on both sides (50% on the left side and 50% on the right side). There was also one case of tetraparesis. Among our patients we also observed dysphasia (50%), cognitive impairment (33%), headaches (25%), epilepsy (17%) and numbness of the limbs (9%). All patients underwent multiple burr hole surgery with the number of holes between 6 and 20 (mean hole number – 11.5).

Conclusions. Moyamoya disease is very rare in Polish population and mostly affect paediatric patients. MMD mostly affect women and children. It is very important for the pediatrist, neurologist and neurosurgeon to remember about MMD when dealing with child suffering from ischemic stroke, which are very rare in paediatric population.

Streszczenie

Wstęp. Choroba Moyamoya (MMD) jest bardzo rzadką chorobą o nieznanej etologii. Proces patologiczny zachodzący w naczyniach wewnątrzczaszkowych prowadzi do zwężenia lub całkowitego zamknięcia tętnic usytuowanych na podstawie mózgowia. Postępujące zwężenie występuje zwykle w dystalnej części (nadklinowej) tętnicy szyjnej wewnętrznej, bliższej części tętnicy przedniej mózgu lub tętnicy środkowej mózgu, z towarzyszącym mu rozwojem drobnych patologicznych naczyń. Głównym objawem choroby są udary niedokrwienne, głównie u dzieci, lub krwawienia śródczaszkowe u dorosłych.

Cel pracy. Celem pracy jest analiza danych epidemiologicznych choroby Moyamoya wśród pacjentów, którzy byli leczeni w Klinice Neurochirurgii w Lublinie.

Materiał i metody. W latach 2006-2016 przeprowadzono retrospektywną analizę 12 przypadków choroby Moyamoya leczonych w Klinice Neurochirurgii i Neurochirurgii Dziecięcej w Lublinie. Analiza koncentruje się na danych epidemiologicznych: wieku, płci,

Conflict of interest
Konflikt interesów

None
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uszkodzeniach półkul mózgu i tętnic objętych zmianami, objawach klinicznych i liczbie wykonanych otworów trepanacyjnych.

Wyniki. U wszystkich pacjentów rozpoznano chorobę Moyamoya. Wśród 12 pacjentów 83% stanowiły kobiety, a 17% mężczyźni. Stosunek kobiet do mężczyzn wynosił 5. Średni wiek populacji wynosił 11,2 i 8,6 roku, gdy analizowano populację dziecięcą. Wśród wszystkich przypadków najczęstszym objawem był niedowład połowiczy (92%), który wystąpił z równą częstotliwością po obu stronach (50% po stronie lewej i 50% po stronie prawej). Był też jeden przypadek niedowładu czterokończynowego. Wśród naszych pacjentów zaobserwowano także: zaburzenia mowy o typie dyzfazji (50%), upośledzenie funkcji poznawczych (33%), bóle głowy (25%), napady padaczkowe (17%) i drętwienie kończyn (9%). Wszyscy pacjenci byli poddani leczeniu operacyjnemu polegającemu na wielokrotnym nawierceniu otworów trepanacyjnych od 6 do 20 (średnia liczba otworów – 11,5).

Wnioski. Choroba Moyamoya jest bardzo rzadka w populacji polskiej i dotyczy głównie dzieci, zwłaszcza płci żeńskiej. Ważne jest, aby pediatrzy, neurolodzy i neurochirurdzy pamiętali o chorobie Moyamoya podczas leczenia dzieci z udarami niedokrwiennymi.

INTRODUCTION

Moyamoya disease (MMD) is an extremely rare condition with unknown ethology. The pathological process occurring in intracerebral vessels results with stenosis or occlusion of the arteries situated on the base of the scull. The progressive stenosis usually occurs at the distal part (supraclinoid) of the internal carotid artery (ICA) and proximal portion of anterior cerebral artery (ACA) and medial cerebral artery (MCA) and development of an abnormal vascular network is observed (1). MMD mostly occurs in Asian population an among women. In Japanese "Moyamoya" means puff of smoke. Affected vessels as pathologic analysis revealed did not found any arteriosclerotic or inflammatory changes. Assays of dura and scalp has been harvested and analyzed in patients with Moyamoya syndrome. The test revealed elevated basic fibroblast growth factor in those assays as well as in cerebrospinal fluid sampled during a surgery. This founding may suggest systemic process underlying as a cause of the disease (2-6). Although the cause of the disease remains unknown some cases are linked with specific genetic mutations. Studies identified RNF213 in the 17q25-ter region as an important susceptibility gene of MMD among East Asian populations (7) and RNF213/ Mysterin may also be considered as a major cause of MMD occurrence among white patients (8).

Patients usually suffer from ischemic attacks, mostly among paediatric population or an intracranial haemorrhage most often among adults. The process and prognosis of the disease is difficult to foreseen because the progression of MMD can be slow and stable with rare disease events or it can cause fast neurological deterioration (9, 10). Suzuki and Takaku radiological scale may help to predict the prognosis and asses permanent neurological deficits.

AIM

The aim of this study is to determine the epidemiology among Polish population treated in Neurosurgery Department in Lublin. This is the first study describing Moyamoya disease epidemiology among Polish patients.

MATERIAL AND METHODS

This study was approved by the University in Lublin Ethical Committee. Retrospective analysis of twelve cases of Moyamoya disease treated in the Department of Neurosurgery and Paediatric Neurosurgery in Lublin between 2006 and 2016 was performed. Diagnosis was based on neuroimaging test results: MR angiography and CT angiography and DSA, characteristic for the disease and criteria stated by the Research Committee on Spontaneous Occlusion of the Circle of Willis (Moyamoya disease) in Japan. Embase, Pubmed and Google Scholar bases were searched using key words: "Moyamoya disease", "MMD epidemiology". Each patient underwent a burr hole surgery. The analysis is focused on epidemiological features: age, gender, location, traded artery, symptoms and number of burr holes. We used Suzuki and Takaku grading scale with Fukuyama and Umezu modification to determine the progress of the disease.

RESULTS

All patients were classified with Moyamoya disease. Among 12 patients 83.4% of them were female and 16.6% were male (fig. 1). The female-to-male ratio was 5. Research was performed mostly on paediatric population (age 1-16), one patient was an adult (39 y.o.). The mean age of the population was 11.2 years and 8.6 years when only paediatric population is analyzed. We diagnosed 8 patients (67%) with ischemic stroke, all of them were female and 4 patients (33%) with transient ischemic attacks (TIA) (fig. 2). The disease was diagnosed unilateral in 17% of all cases and 83% of all cases were bilateral. MMD mostly affected the right hemisphere (57%) when diagnosed unilateral and 43% of all cases considered the left hemisphere. MMD causes vessel stenosis and occlusion. In our research in 100% of all cases we found pathological changes in ICA and MCA and in 92% of all cases in ACA. The pathological changes in internal carotid artery were mostly bilateral (83%) rather than unilateral where we found changes only in 17% of all cases and always in the right ICA. The pathological process in medial cerebral artery was also mostly bilateral (50%), when unilateral mostly

in the right MCA (33%) than left (17%). Unlike the previous vessels, the anterior carotid artery was occupied mostly unilaterally. The pathological process included the right ACA in 42% of all cases, the left ACA in 25% of all cases and 33% of all cases were bilateral. Among all cases the most common symptom was hemiparesis (92%), which occurred with equal frequency on both sides (45% on the left side and 45% on the right side). There was also one case of tetraparesis. Among our patients we also observed dysphasia (50%), cognitive processes abnormality (33%), headaches (25%), epilepsy (17%) and numbness of the limbs (9%) (tab. 1). All patients underwent multiple burr hole surgery with the number of holes between 6 and 20 (mean hole number – 11.5). We used Suzuki and Takaku grading scale with Fukuyama and Umezu modification to determine the progress of the disease. Among all patients 50% of them were diagnosed with stage 3c of MMD, 42% with stage 3a and 8% with stage 3b.

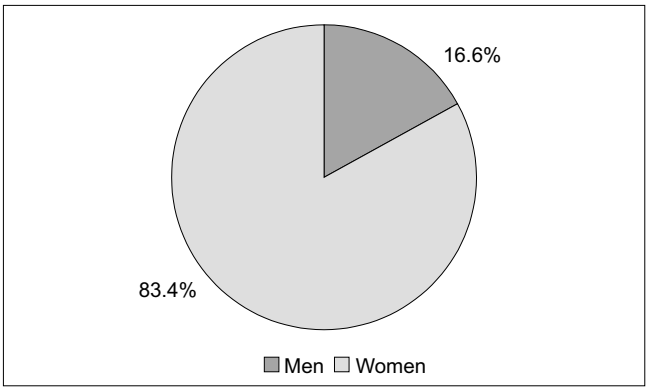

Fig. 1. Sex distribution of Moyamoya disease in 12 patients

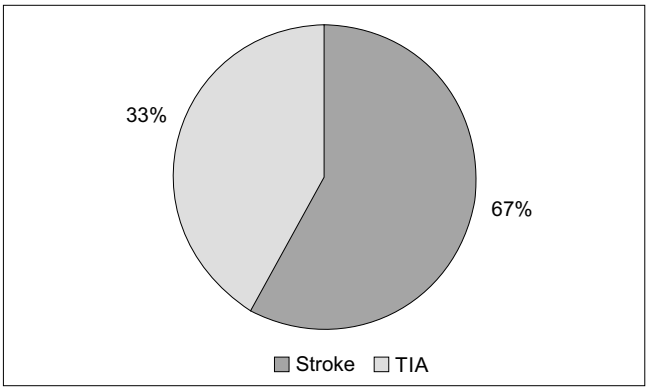

Fig. 2. Presenting symptoms in 12 Moyamoya patients

Tab. 1. Moyamoya disease: epidemiology: a single Polish centre experience

Symptom	Patient No.	Percent
Hemiparesis	11	92%
Speech abnormality	6	50%
Cognitive impairment	4	33%
Headache	3	25%
Epilepsy	2	17%
Limb numbness	1	9%

DISCUSSION

MMD mostly occurs among Asian population mainly in Korea, Japan, Taiwan and China. This is the first study to report the Polish national epidemiology of MMD. Prevalence was estimated by several authors (tab. 2) for instance the prevalence of MMD according to a research performed in Japan in 1995 was 3.16/100,000 population (11) and according to a survey performed in 2004 the prevalence was 6.03/100,000 population (12). Study in Korea revealed the prevalence was 9.1/100,000 population in 2004 (13) and in Taiwan the research reports that the prevalence was 1.63/100,000 population (14). In Poland in 2013 there were 34 registered cases of Moyamoya disease which results with prevalence of 0.089/100,000 population.

Tab. 2. Moyamoya disease prevalence – literature review

Authors/Year	Country	Patient No.	Sex ratio (female/male)	Prevalence per 100,000
Wakai et al. 1997 (11)	Japan	1176	1.8	3.13
Uchino et al. 2005 (20)	Washington state and California	298	2.2	ND
Kuriyama et al. 2008 (19)	Japan	1240	1.8	6.03
Baba et al. 2008 (12)	Japan	267	1:2.2	10.5
Kraemer et al. 2008 (21)	Germany	21	4.25	ND
Shoukat et al. 2009 (23)	Pakistan	13	1:1.16	ND
Yim et al. 2012 (13)	Korea	4517	1.94	3.92
Chen et al. 2014 (14)	Taiwan	422	1.4	1.61
Saarela et al. 2016 (22)	Finland	61	4.54	ND
Our research 2017	Poland	12	5	0.089

ND – no data

Children are more probable to present with ischemic stroke or transient ischemic attacks (TIA) and among the adult group haemorrhage is a more common symptom (15, 16). According to Hoshino the most common symptom in their population was TIA in 46%, infarction in 20%, haemorrhage in 21%, headache in 4%, symptomatic in 3% and others in 2% (17). Data presented by Edward is pretty similar, where stroke is the most common symptom in 67.8%, TIA in 43.4%, seizures in 6.3% headache in 6.3% (18).

In our analysis stroke was present among 58% of population, TIA in 42%, headache in 25% and seizures in 17% of population. The most common symptom observed was hemiparesis, which was present among 92% of all cases, cognitive impairments in 33% and dysphasia in 50%. Those symptoms were caused by ischemic stroke or TIA. Among TIA patients 3 out of

4 patients suffered from hemiparesis that withdrew within 24 hours.

In our study 83% of population were female and 13% were male, which gave female-to-male ratio 5. As we can see in researches done among Asian population the female-to-male ratio is usually around 2, for example Wakai et al. (11) claim it equals 1.8 among Japan population, according to Kuriyama et al. it is 1.8 as well in Japan (19), according to Yim et al. it is 1.94 in Korea (13), according to Chen et al. it equals 1.4 in Taiwan (14) and according Uchino et al. it equals 2.2 in Washington state and California (20), according to Kraemer et al. the ration equals 4.25 in european population (21), and in Saarela et al. research the ratio equals 4.55 (22) so it is similar to our results. On the other hand in research made by Baba et al. (12) the female-to-male ratio equals 1:2.2 in favour to male population in Japan. As we can see in our research there is a big female domination among patients with MMD.

Usually in epidemiological studies concerning Moyamoya disease authors reports two peaks of age distribution. In study made by Wakai in Japan the age of the patients is set between 10-14 in both sexes, 40-45 in women and 45-50 in men (11). According to Kuriyama et al. the firs peak of age distribution is between 10-14 among men population and 20-24 among women and the second one is between 35-39 among men and 50-54 among women (19). Studies made in Korea by Yim et al. revealed that the first peak of age distribution is set between 10-19 in both sexes and the second one is set between 40-49 as well (13). Our population was mostly paediatric except one patient, whose age is 39. Most of the patients are assigned to 9-16 age group, which consists of 6 patients and to 1-9 age group, which consists of 5 patients. According to Kraemer et al. (21) the mean age at the time of diagnosis was 34.52 years and at onset of symptoms was 31 on the other hand based on research made in Pakistan by Shoukat et al. (23) we can find out that the mean age at presentation was 16.57 years. Saarela et al. claim that the mean age at the disease onset in their research was 31.5 ± 17.9 years (22). According to our research the mean age at the disease onset is 11.2 years and 8.64 years for the paediatric population only.

Our patients underwent surgical treatment using multiple burr hole surgery. The treatment was invented accidentally by Endo et al. in 1984 when they traded a child using bilateral frontal burr hole for ventricular drainage (24) and after three months they noticed neovascularization through the burr holes on follow-up angiogram. Through the years this technique was developed and thoroughly analyzed. In 1996 Kawaguchi et al. shared their experience with this technique. They used between 1 and 4 burr holes over each hemisphere and reported neovascularization process in 41 out of the 43 burr holes (25). In 2006 there comes another paper reporting the results using burr hole technique by Sainte-Rose et al. They made 10 to 24 burr holes over each hemisphere. To make sure they cover all the pathological areas of the brain they decided to increase the number of burr holes (26). Oliveira et al. also used burr hole technique, drilling 10 to 20 burr holes and reported neovascularization process via burr holes (27). We made 6 to 10 burr holes over each hemisphere sometimes bilateral, reaching up to 20 burr holes. Mean number of burr holes we made was 11.5 total and 8.06 burr hole per hemisphere. A skin flap was made in the fronto-temporalo-parietal area, periosteum was dissected from the skin flap. We usually drill burr holes in three rows, which we can see in the figure 1. The number of the burr holes depends on the extension of the disease. Afterwards we make a V shape incision of the dura mater and a puncture cut of the pia mater and cerebral cortex in every burr hole. We insert the periosteum into each burr hole starting from the base of the skin flap. There are several techniques involving direct and indirect surgeries too treat MMD. In paediatric population indirect surgery as encephalo-duro-arterio-synangiosis (EDAS) or encephalo-duro-arteriom-myo-synangiosis (EDAMS) are more beneficial and should be considered as a primary treatment comparing to direct surgery techniques, which are more beneficial among adult population (28).

Suzuki and Takaku classified the stages of MMD into 6 stages and Fukuyama with Umezu then divided stage 3 into 3 subdivisions. Stage 1 describes narrowing of carotid the carotid fork (ICA bifurcation), stage 2 is described as dilated ACA, MCA and narrowed ICA bifurcation with Moyamoya change. Stage 3 with its subdivisions: stage 3a described as partial non-filling of the anterior and middle cerebral arteries, stage 3b as partial preservation of the anterior and middle cerebral arteries and stage 3c as complete lack of the anterior and middle cerebral arteries, stage 4 as minimalisation of the "Moyamoya vessels" and disappearance of the posterior cerebral artery, stage 5 as reduction of the "Moyamoya vessels" and disappearance of the main arteries arising from the internal carotid artery, stage 6 is described as disappearance of the Moyamoya vessels at the base of the brain with preserved collateral circulation from the external carotid artery. We used modified Suzuki and Takaku scale because it eliminates the inconvenience of the basic scale, where many cases can be assigned to stages 3-5 and the classification was too subjective. Stages of Moyamoya disease are not strongly related to clinical symptoms but are very useful while estimating prognosis. Most of our patients (50%) were classified as stage 3c, 42% of our patients were classified as stage 3a and 8% as 3b. Prognosis is also related with age according to Kim et al., who presented increased probability of preoperative stroke and less beneficial outcome in patients with age less than 3 years old (29). Despite the fact that surgery results in decreased incidence of TIA and stroke probability in MMD population, stroke diagnosed preoperatively happens to be a poor prognostic factor for the effectiveness of the procedure (30).

CONCLUSIONS

Moyamoya disease is very rare in Polish population and mostly affect paediatric patients. MMD mostly affect women and children. It is very important for the pediatrist, neurologist and neurosurgeon to remember about MMD when dealing with child suffering from ischemic stroke, which are very rare in paediatric population. Preferable treatment for this population for now is indirect surgery technique. There were only 12 cases of MMD in our department, which has the biggest experience in treating MMD in Poland. It is important to increase the awareness of the disease which may cause, therefore, increase recognisability.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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