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Moyamoya disease during pregnancy and childbirth

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ABSTRACT

Moyamoya disease (MMD) is a chronic vasculopathy characterized by progressive bilateral stenosis and occlusion of the terminal portion of the internal carotid artery (ICA) and the presence of an abnormal vascular network at the base of the brain, termed Moyamoya vessels (MMV). The main presentations of MMD are ischemia and hemorrhage, and diagnosis is done via angiography. Cerebral events were reported in 5.1% of pregnancies of MMD diagnosed mothers, in Japan. In the case of MMD diagnosis due to cerebrovascular events during gestation, 34.7% of patients presented with an ischemic event, while 69.5% suffered from hemorrhage. During gestation, hemorrhagic events were found to occur mostly antepartum, after 24 weeks of gestation, while cerebral infarction peaked 3-7 days after delivery. No treatment has been found to halt or reverse the progress of the disease. Interventions focus on reducing the risk of stroke and cognitive disfunction as a result of ischemia. In the case of pregnant women suffering hemorrhage due to MMD, conservative treatment, as well as ventricle puncture and drainage were to be efficient, and did not severely impact the child. When diagnosed before pregnancy occurs, MMD under treatment does not pose a significantly increased risk of complications, compared to pregnancies in unaffected women. No evidence suggests that MMD is a contraindication for pregnancy.

Keywords: moyamoya disease, pregnancy, bypass surgery, ischemia, hemorrhagic stroke

INTRODUCTION

Moyamoya disease (MMD) is a rare, chronic vasculopathy of unknown etiology, characterized by progressive bilateral stenosis and occlusion of the terminal portion of the internal carotid artery (ICA) and the presence of an abnormal vascular network at the base of the brain, termed Moyamoya vessels (MMV). The disease poses a risk of ischemic attack and intracranial hemorrhages in both adults and children. Symptoms are most common around ages 10 and 30-45 year-old [1], [2]. MMD is more common in women, and the symptoms peak at the ages 30-45, which may coincide with pregnancy [3]. Pregnancy is a potential aggravating factor for women with MMD, due to a number of factors: increased estrogen and progesterone levels, causing vasodilation [4], activation of the renin-angiotensin-aldosterone system, causing hypervolemia, as well as augmented coagulation, associated with decreased fibrinolytic activity [5].

MATERIALS AND METHODS

MMD is most prevalent in the Asian continent, predominantly Japan, Korea and China [6]. Thus, most literature on this topic is sourced in these areas, but studies including European patients, as well as women from the USA have been sourced. This article is based on a number of relevant studies published since (INSERT AN), including meta-analyses, reviews and case reports. Pregnant patients were

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included, as well as studies on delivery methods and postpartum follow-ups.

RESULTS

Epidemiology

MMD is found predominantly in patients originating from countries in Eastern Asia, such as Japan, Korea, China and Taiwan. Studies have shown that prevalence in Japan varies from 3.16-10.5/100 000 people [7]–[9], and from 6.3-16.1/100 000 in Korea [10][11], while 3.92/100 000 people in China were found to suffer with MMD [12], as well as 1.61/100 000 in Taiwan [13]. The female to male ratio of affected patients was found to be larger than 1, but few studies have reported it as greater than 2 [7]–[13]. The incidence of familial MMD in Eastern Asian countries was found to be 15%, suggesting a genetic component to the disease. The RNF213 gene in the 17q25-ter region was found to be a susceptibility factor for MMD [14].

Histology and pathophysiology

MMD is characterized by occlusion of the distal ICA, and the formation of collateral vessels from the dilated portion of the ICA – termed Moyamoya vessels (MMV) [15].

Vessels affected by MMD are characterized by fibrocellular thickening of the intima (19.4μm, compared to 8μm in the control intima), associated with irregular disposition of the internal elastic laminae, thinning of the media and decreased outer diameter [16] [17]. Evidence has shown that MMD occurs mainly due to proliferation in the intima [15].

MMVs are perforating arteries, originating from the dilated part of the ICA, characterized by fibrin deposits in the arterial wall, attenuated media and the potential of generating microaneurysms [16]. These vessels may be a compensatory mechanism for the reduced cerebral perfusion caused by ICA stenosis [15].

Diagnosis

MMD diagnosis is done based on angiographic findings that respect the following criteria: stenosis or occlusion of the terminal portion of the intracranial ICA or proximal portions of the anterior cerebral artery (ACA) and/or the middle cerebral artery (MCA), as well as presence of abnormal vascular networks near the occlusive or stenotic lesions [18].

Delivery methods

Nationwide surveys in Japan have revealed a 69.7–76.3% prevalence of cesarean section deliveries in mothers diagnosed with MMD [19], while vaginal delivery was shown to be preferred in the USA. A Japan-based study reported that elective C-sections made up 58.3% and 40% of delivery methods in pregnant women diagnosed with MMD before and during pregnancy, respectively. Emergency cesarean sections accounted for 6.8% of births in the case of patients diagnosed with MMD before pregnancy, but 40% of those diagnosed during pregnancy [3]. Another study, based in an European hospital reported that c-sections totaled 19% of patients diagnosed while pregnant underwent c-section, while 100% of patients diagnosed before pregnancy opted for the same delivery method [20].

No significant differences have been found between the two delivery methods, regarding MMD complications [3]. Both delivery methods have been associated with a low (<5%) risk of transient ischemic attack [19].

Symptoms and complications

The main presentations of MMD are ischemia and hemorrhage, the latter being caused by compensatory mechanisms for ischemia. Ischemic stroke and transient ischemic attacks (TIAs) are the symptoms at presentation for 50-75% of MMD patients, while hemorrhage was found in 10-40% of cases [21]. Cerebral events were reported in 5.1% of pregnancies of MMD diagnosed mothers, in Japan [19]. Another study found the risk of hemorrhage in MMD diagnosed mothers to be 2.8% per pregnancy, similar to that of MMD patients that are not pregnant (3.3%) [22].

In the case of MMD diagnosis due to cerebrovascular events during gestation, 34.7% of patients presented with an ischemic event, while 69.5% suffered from hemorrhage [3].

During gestation, hemorrhagic events were found to occur mostly antepartum, after 24 weeks of gestation, while cerebral infarction peaked 3-7 days after delivery [5].

Pregnancy itself poses a risk of pre-eclampsia and eclampsia, toxemia and pregnancy induced hypertension [3].

TREATMENTS

No treatment has been found to halt or reverse the progress of the disease. Interventions focus on reducing the risk of stroke and cognitive disfunction as a result of ischemia. Nonsurgical therapy, such as administration of antiplatelet and avoidance of dehydration and smoking represent protective factors [23]. Surgical therapy involves revascularization of the areas served by the stenotic carotid artery, by direct or indirect bypass, involving procedures such as anastomosis between the superficial temporal artery (STA) and MCA [6], the STA and the ACA [24], the occipital artery and the posterior cerebral artery [6].

Surgical revascularization has been shown to eliminate TIAs and headaches in 91.7% and 91% of patients, respectively [25]. It was also proven to improve cerebral perfusion and lower the risk of rebleeding in the case of patients presenting hemorrhage due to MMD [6]. In the case of pregnant women, surgical bypass previous to pregnancy may result in lower maternal and fetal morbidity and mortality, as well as a lower risk of ischemic cerebrovascular incidents during childbearing, but studies were not able to reach a final conclusion, and results are often controversial [20], [26]. Antiplatelet therapy with aspirin, advised after bypass surgery, was not found to be impactful on the child when continued up to the 34th week of gestation [27].

Surgical treatment also includes hematoma evacuation and the placement of a drain [3].

In a group of women diagnosed with MMD due to cerebrovascular events during pregnancy, 57.2% underwent neurosurgical treatment, and 80% underwent cesarean section with 13.6% maternal and 23.5% fetal mortality rates [3].

In the case of pregnant women suffering hemorrhage due to MMD, Liu et. Al. found conservative treatment, as well as ventricle puncture and drainage to be efficient, and did not severely impact the child (APGAR score at birth varied from 6 to 9) [22].

CONCLUSION

MMD poses a lifelong risk of ischemic and hemorrhagic events, with a peak that overlaps the childbearing age of most women. When diagnosed before pregnancy occurs, MMD under treatment does not pose a significantly increased risk of complications, compared to pregnancies in unaffected women. No evidence suggests that MMD is a contraindication for pregnancy [22].

There is no conclusive evidence that treatment prior to pregnancy or a certain mode of delivery decrease the chance of MMD-related events.

When they occur, cerebrovascular events related to MMD should be treated according to symptomatology, either conservatively or surgically, taking into account the condition of the child. Close collaboration between the patient's neurosurgeon and obstetrician is advised [28].

The rarity of this disease, as well as the unknown etiology and unique geographical distribution impose a limitation on studies.

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