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Clinical Study

Five-year experience of 101 adult patients with moyamoya disease at a single institution in Eastern China

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ABSTRACT

This retrospective study included 101 adult moyamoya disease (MMD) patients of whom 58 were females and 43 were males in Wenzhou, China. Clinical and diagnostic features, surgical treatment, follow-up information and outcomes constitute this review. The modified Rankin Scale (mRS) was used to determine the neurological functional outcome. The Kaplan–Meier method was used to estimate recurrent stroke and mortality risk based on drug treatment alone or in combination with revascularization. The mean age at symptom onset was 43.3 (range, 18–64) years. The initial symptom was either hemorrhage, ischemia or transient ischemic attack (TIA) in 90, 6 and 5 patients, respectively. The median follow-up time in 84 patients was 26.5 (range, 6–62) months. Ten patients were treated with revascularization. In the remaining drug-treated group, the 5-year risk of recurrent stroke and death was 8% following onset of initial symptoms, while it was 25% in the revascularization group. However, the difference between these two groups was not significant ($p > 0.05$). There was also no difference in mRS between these two groups upon patient discharge, but in the revascularization group was lower than that in the drug-treated group at their last follow-up ($p < 0.05$). Adult MMD patients were most ikely to present with hemorrhage and had a better neurological functional outcome after revascularization than from medical therapy. However, revascularization did not decrease the recurrent stroke incidence or mortality risk. These results are different from those reported by other Chinese and foreign institutions.

1. Introduction

Moyamoya disease (MMD) is a chronic, occlusive cerebrovascular disease with an unknown etiology characterized by bilateral stenoocclusive changes at the terminal portion of the internal carotid artery and an abnormal vascular network at the base of the brain [1,3]. MMD is a rare disease in most parts of the world, but it develops mostly in eastern Asian countries including Japan, Korea, and China [2]. One of the well-known specific features of MMD is its pattern of age distribution. The incidence peaks in two age groups: children who are approximately 10 years of age and adults in their mid-40s, with a higher incidence in childhood [2,4,5]. However, recent studies revealed a higher incidence in adults, particularly in female patients, compared to children [5,8,17,18]. In fact, with recent advances in neuroradiological diagnostic modalities, including magnetic resonance angiography (MRA) and three-dimensional CT angiography (CTA), the diagnosis of adult onset MMD has become more frequent than in the past. Thus, there is a need to improve the identification and management of adult onset MMD.

However, there is little detailed demographic, clinical data and follow-up information about Chinese adult patients with MMD. This limitation is accentuated by the lack of agreement between different studies. For example, in Asia, hemorrhagic stroke predominated in adult MMD [4,5], which essentially agreed with a previous Chinese study [8]. However, another extensive study on adult MMD patients found that ischemic rather than hemorrhagic stroke is predominant in China, and only 20% of these adult patients had intracranial hemorrhages [9].

So, in this investigation, we present a retrospective analysis of adult patients with MMD admitted and treated during the last 5 years at the First Affiliated Wenzhou Medical University Hospital, located in Wenzhou, a medium sized city in eastern China. Our detailed demographic analysis is presented here along with description of clinical characteristics and outcomes. This report describe how we identified and cared for such patients afflicted with this life compromising disease.

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2. Patients and methods

2.1. Patient selection

This study retrospectively analyzed patients diagnosed with MMD, who were admitted and treated at our facility from January 2010 to December 2014. MMD was definitively identified based on the guidelines for the diagnosis of this disease [3]. Diagnostic criteria of MMD is that digital subtraction arteriography (DSA) or CTA/MRA include: (1) Stenosis or occlusion of the terminal portion of the intracranial internal carotid artery or proximal portions of the anterior and/or the middle cerebral artery. (2) Abnormal vascular networks in the vicinity of the stenotic or occlusive lesions in the arterial phase. (3) Bilateral character of findings (1) and (2). Patients excluded from this study included those presenting with either atherosclerosis, autoimmune disease (systemic lupus, antiphospholipid antibody syndrome, arteritis nodosa, and Sjögren syndrome), meningitis or prior skull-base radiation therapy.

2.2. Retrospective chart review

Clinical records including hospital charts, clinic notes and radiological studies were reviewed. All data were collected through May 2015. The Research Ethics Board at the First Affiliated Wenzhou Medical University Hospital approved the study design.

2.3. Surgical treatment

Surgical revascularization was performed to prevent recurrent stroke and to improve neurological outcome. Two general methods of revascularization were used: direct and indirect. The superficial temporal artery to middle cerebral artery (STA-MCA) bypass was the most commonly used direct revascularization procedure. Indirect revascularization procedures most commonly used were ence phalo-duro-arterio-myo-synangiosis (EDAMS—in which the intact and continuous STA is moved close to the cerebral surface and sutured to the dural edges), encephalo-myo-synangiosis (EMS—in which the inner surface of the temporalis muscle is moved close to the cerebral surface) and various combinations were used for both the direct and indirect procedures.

2.4. Clinical follow-up

After hospital discharge, outcome was monitored for periods lasting from 0.5 to 5 years. Our evaluation entailed either clinical visits, telephone or letter interview. The modified Rankin Scale (mRS) determined the neurological functional outcome.

2.5. Statistical analysis

Categorical variables were analyzed using the chi-squared test and continuous variables were analyzed using the Student's *t*-test. Kaplan–Meier methods estimated recurrent stroke and mortality risk. Differences were considered statistically significant at $p < 0.05$. All analyses were carried out with the SPSS package, version 16.0 (SPSS, Chicago, USA).

3. Results

3.1. Demographics and clinical presentation

One hundred and one MMD patients including 58 females and 43 males were retrospectively analyzed. The ratio of female to male patients was 1.3:1. The mean age at symptom onset was 43.3 (range, 18–64) years. Figure 1 shows the age distribution of the adult patients; the peak detection rate occurred at 40–44 years. In our patients, cerebral hemorrhage was the most common type of stroke. Ninety (89.1%) patients had intracranial hemorrhage, while only six (5.9%) patients presented with ischemic stroke and five (4.9%) presented with transient ischemic attack (TIA). Three-dimensional CTA was performed on all 90 patients with hemorrhage and DSA was performed in 65 patients (64.3%). Out of 11 patients with ischemic stroke or TIA, four patients accepted MRA, and seven accepted CTA. DSA was performed in eight patients. Out of 90 patients with hemorrhagic stroke, thirty-three (36.7%) patients had intraventricular hemorrhage. Thirty (33.3%) patients had intraparenchymal, intraventricular hemorrhage and subarachnoid hemorrhage in combination. Sixteen (17.8%) had isolated intraparenchymal and eleven (12.2%) had isolated subarachnoid hemorrhage. Additional findings on CTA and DSA included eight (7.9%) patients with intracranial aneurysms. All patients who had aneurysms presented with intracranial bleeding. Out of these eight patients, six had single aneurysms and two patients had multiple aneurysms (two or more). Out of eight patients with aneurysms, five patients presented with rupture of the aneurysm. In-hospital mortality was 10% (nine out of 90 hemorrhagic patients died) after initial bleeding (Table 1).

3.2. Treatment

Table 1 lists MMD clinical signs and surgical management of the 101 patients included in this study. Ten patients underwent cerebral revascularization and four of them underwent indirect revascularization: EMS (three patients), and EDAMS (one patient). One patient underwent direct STA–MCA bypass revascularization. Five patients underwent both indirect revascularization (EDAMS) and direct revascularization (STA–MCA). Among eight patients with aneurysms, three patients underwent surgery or embolization for associated aneurysms: two underwent coil embolization, and one underwent surgical clipping. Another five patients refused treatment in view of their poor neurological condition and financial constraints. Twelve patients accepted evacuation of intracranial hematoma, eight patients accepted hydrocephalus shunt, and four patients accepted both treatments.

3.3. Follow-up

Among the 92 patients who were discharged, follow-up was available for 84 patients, while eight patients failed to participate. The follow-up lasted from 6 to 62 months (median, 26.5 months). Out of 11 patients with ischemic stroke or TIA, nine patients accepted follow-up. Out of 81 patients with hemorrhagic stroke, 75 patients participated in follow-up. Five patients (including one patient who underwent revascularization procedures) had intracranial hemorrhage and perished soon thereafter. Seventy-nine survivors had no subsequent strokes during follow-up (Table 2).

The Kaplan–Meier estimate of recurrent stroke and death risk after the first event was about 5.5% in the following 2 years for all patients. The 5-year Kaplan–Meier risk of recurrent stroke and death risk was about 10% after the first event for all patients (Fig. 2). In the drug-treated group, the 5-year risk of recurrent stroke and death was 8% after the initial symptom. In the revascularization group, the 5-year risk of recurrent stroke and death was 25%, on the other hand, this difference between the surgical and drug-treated groups after the first symptom was not significant ($p > 0.05$) (Fig. 3). Similarly, no difference in mRS between the two groups was detected at discharge ($p > 0.05$). However, at the last follow up visit, in the revascularization group, the mRS was less than that in the drug-treated group ($p < 0.05$) whereas the mortality incidence in both groups was not different ($p > 0.05$) in the follow up period (Table 2).