Moyamoya like arteriopathy: Neurosonological suspicion and prognosis in adult asymptomatic patients

Giovanni Malferrari, Marialuisa Zedde, Gianni De Berti, Massimo Maggi, Norina Marcello

Neurology Unit, Department of Neuromotor Physiology, Azienda Ospedaliera ASMN, Istituto di Ricovero e Cura a Carattere Scientifico, Viale Risorgimento 80, 42100 Reggio Emilia, Italy
Neuroradiology Unit, Department of Radiology, Azienda Ospedaliera ASMN, Istituto di Ricovero e Cura a Carattere Scientifico, Viale Risorgimento 80, 42100 Reggio Emilia, Italy

KEYWORDS
Moyamoya; Transcranial; TCCS; Intracranial stenosis; MCA; Asymptomatic

Summary
Introduction: The epidemiology and the prognosis of asymptomatic moyamoya arteriopathy is virtually unknown, mainly in white western population, while symptomatic moyamoya arteriopathy is a more known disease, both in children and in adult people. We are presenting a single centre case series of six asymptomatic adult people with a neurosonological (Transcranial Colour Coded Sonography – TCCS) suspicion of this type of cerebral arteriopathy, confirmed by Digital Subtraction Angiography (DSA).

Patients and methods: During a time period of three years we collected a series of six patients (5 female and 1 male, mean age 29.16 ± 8.45 years) with a neurosonological suspicion and a neuroradiological diagnostic confirmation of moyamoya type arteriopathy. All patients underwent TCCS, brain magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) and DSA, besides the differential diagnosis of immunological or infectious etiology. The mean follow-up was 1.8 years.

Results and discussion: All patients but one had a bilateral internal carotid artery (ICA) stenosis at terminus and M1 middle cerebral artery (MCA) multiple stenoses. There is only one young patient with an atypical unilateral pathway and narrowing of extracranial ICA with prominent posterior cerebral artery (PCA) compensation. No clinical events occurred during the follow-up and also brain MRI failed to find new ischemic lesions, compared with the baseline examination. Conclusions: Asymptomatic cerebral moyamoya arteriopathy is an infrequent but underestimated condition in young white people. More prognostic informations are needed in order to define the natural course and propose the treatment.

© 2012 Elsevier GmbH. Open access under CC BY-NC-ND license.
Introduction

Moyamoya syndrome is a cerebrovascular disease that is associated to a predisposition to stroke because of the presence of multiple progressive stenosis of the intracranial ICAs and their proximal branches. It is a distinguishing feature of the disease the compensatory development of collateral circulation, determining the growth of a widespread network of small vessels at the terminus of the ICA, on the cortical surface, leptomeninges, and anastomotic branches of the ECA. The moyamoya syndrome includes patients with the characteristic moyamoya vasculopathy and well recognized associated conditions, whereas moyamoya disease concerns patients without known associated risk factors. The pathognomonic arteriographic findings are bilateral in moyamoya disease, with a variable severity between sides. Unilateral findings are indicative of the moyamoya syndrome, even without other associated risk factors [1].

It is more frequent in Asian populations and in children, mainly in Japan, where it is the most common pediatric cerebrovascular disease with a prevalence of about 3 cases per 100,000 children [2], but an adult form is also known and few cases are described in white population. In Europe the incidence of moyamoya among all ages is about 1/10th of that observed in Japan [3]. Therefore several data about the natural history of moyamoya disease concern Asian children [1]. The disease tends to be progressive, both in children and in adult patients. The progression of the vascular involvement usually means the increasing severity of stenosis to occlusion of large intracranial arteries and the increasing number of involved vessel segments, with a parallel development of the collateral circulation. It is believed that the rate of disease progression is high, even among asymptomatic patients, and that medical therapy alone is not sufficient to stop or slow it [4]. Current estimation is similar to the previous one that up to two thirds of patients with moyamoya have symptomatic progression over a 5-year period, and the outcome is reported poor without treatment [4–6].

The natural course of the moyamoya disease in European adult asymptomatic people is not so clear in the literature, because of the small sample of the available studies, and also in neurosurgical studies the subgroup of asymptomatic people is not numerous. Therefore it is not automatically right that in this subpopulation the outcome of surgically untreated patients is poor.

Therefore several data are lacking for asymptomatic vs symptomatic patients, European vs Asian patients and adults vs children patients. The lesser-known group concerns the asymptomatic European adult patient. We are presenting a single center case series of 6 European adult people with asymptomatic moyamoya disease, suspected through TCCS and confirmed by DSA, followed up in medical treatment.

Materials and methods

During a time period of three years we collected a series of six patients (5 female and 1 male, mean age 29.16 ± 8.45 years) with a neurosonological suspicion and a neuroradiological diagnostic confirmation of moyamoya type arteriopathy. All patients underwent neurosonological examination for episodic not related symptoms, like dizziness, or for a screening purpose in a family history of cerebrovascular atherosclerotic accidents. Besides the neurosonological examination with ultrasound study of the cerebroafferent vessels and of the intracranial arteries by TCCS, all patients underwent brain MRI and MRA and blood sampling and other investigations for differential diagnosis of immunological or infectious etiology.

Diagnosis was made according to the approved criteria [Research Committee on Spontaneous Occlusion of the Circle of Willis (moyamoya disease) in Japan] [7].

TCCS was performed as a basal evaluation and with contrast agents for the evaluation of intracranial vessels in Power Modulation or Pulse Inversion. Ultrasound perfusional study was also performed but the data were not analyzed, because of the bilateral involvement in most patients and the lesser reliability of PCA territory for a comparison, due to the collateral circulation.

MRI and DSA were analyzed according to the Ministry of Health and Wellness of Japan criteria [7].

The mean follow-up was 1.8 years and it was both clinical and neurosonological—neuroradiological (with MRI). All patients were followed-up in at least 3 control visits, at 3 months from the diagnosis, at 6 months and at 12–18 months.

Results

The main features of the six patients are illustrated in Table 1.

All patients had a bilateral involvement in the intracranial circulation and all but one had a diagnosis of moyamoya disease/phenomenon, because of the absence of the well-known risk factors and associated conditions; one patient had a unilateral involvement, and therefore the diagnosis was a moyamoya syndrome. There is an evident prevalence of the female sex (female to male ratio 5). TCCS study was performed by an experienced neurosonologist both without and with ultrasound contrast agents (SonoVue®) in all patients and no side effects from the procedure were reported.

Neuroradiological examination, first brain MRI and intracranial MRA, and second DSA, were performed because of the suspicion of moyamoya arteriopathy and confirmed it. There was not any brain tissue abnormality suggesting acute cerebrovascular event in all examined patients, nor in basal MRI study and in control examinations. Both neurosonological findings and MRI findings did not change in the follow-up examination, therefore a control DSA was not performed.

TCCS studies were analyzed mainly considering the Doppler waveform, because of the existing classification of the MCA flow patterns (see Appendix A), made to classify TCD findings [8]. All patients with bilateral involvement but one had the same flow pattern in the MCA on both sides and a similar situation was reported for the DSA classification [9] (see Appendix B) but not in the same patients.

Both neurosonological and MRA findings were unchanged in the follow up examinations and no patients reported focal neurological events of vascular origin during the follow-up.

In Fig. 1 it is showed an example of the findings from the three techniques (TCCS, MRA, DSA) in two patients of our series. 
Table 1  Main features of followed-up patients.

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Sex a</th>
<th>Age at the diagnosis (years)</th>
<th>Affected side</th>
<th>TCCS right side b</th>
<th>TCCS left side b</th>
<th>DSA stage right side c</th>
<th>DSA stage left side c</th>
<th>Cerebrovascular events</th>
<th>Length of follow-up (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>18</td>
<td>Left</td>
<td>—</td>
<td>—</td>
<td>Stage 4</td>
<td>Stage 4</td>
<td>None</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>41</td>
<td>Both</td>
<td>High—low flow pattern</td>
<td>High—low flow pattern</td>
<td>Stage 3</td>
<td>Stage 3</td>
<td>None</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>31</td>
<td>Both</td>
<td>High—high flow pattern</td>
<td>High—high flow pattern</td>
<td>Stage 3</td>
<td>Stage 3</td>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>28</td>
<td>Both</td>
<td>High—low flow pattern</td>
<td>High—low flow pattern</td>
<td>Stage 4</td>
<td>Stage 4</td>
<td>None</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>25</td>
<td>Both</td>
<td>High—low flow pattern</td>
<td>High—low flow pattern</td>
<td>Stage 3</td>
<td>Stage 3</td>
<td>None</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>32</td>
<td>Both</td>
<td>High—low flow pattern</td>
<td>High—low flow pattern</td>
<td>Stage 4</td>
<td>Stage 5</td>
<td>None</td>
<td>2</td>
</tr>
</tbody>
</table>

a  F is for female sex and M is for male sex.

b  TCCS data were presented according to the flow patterns detailed in Appendix A; only Doppler waveforms were used for this classification.

c  TCCS data were presented according to the flow patterns detailed in Appendix B.

Discussion

For the reasons detailed in the introduction, there are few data about the natural course of the moyamoya disease in asymptomatic patients, mainly in adult people, both in Asian and particularly in European population. The lack of reliable informations is even more evident for asymptomatic patients, particularly for the adult form of the disease, because the introduction of noninvasive diagnostic tools made possible the sporadical identification of asymptomatic subjects. In a Japanese questionnaire survey, made in 88 neurosurgical institutes in 1994, to define clinical features and outcome of asymptomatic moyamoya disease [10], only thirty three asymptomatic moyamoya disease patients were collected (11 male, 22 female) and divided into 2 groups: patients without any symptoms (group 1, mainly adult people), and patients without any symptoms except headache (group 2). In this survey the natural course of asymptomatic moyamoya disease seemed benign and the need of a dedicated prospective study about this item was proposed.

But in the next years the non-invasive screening led to a change in the known epidemiological data, also in the Japanese population, as shown in a more recent all-inclusive survey of moyamoya disease in Hokkaido island.

Figure 1  Example of diagnostic results for two patients of our series (1 TCCS, 2 MRA, 3 DSA). In the row 'a' patients with high low flow condition is illustrated; in the row 'b' a patient with low low flow condition is showed.
(population 5.63 million) [11], that analyzed data from 267 newly registered patients with moyamoya disease from 2002 to 2006. Overall the prevalence of the disease and the age at onset were reported higher than those previously known. The highest peak of onset age was older than those reported previously. In addition, 17.8% of patients were asymptomatic at onset in all decades.

In European population the moyamoya disease has also a lesser prevalence, therefore large epidemiological data are lacking, mainly about asymptomatic people. The limited existing European studies mostly deal with a mixed cohort of MMD and angiographic syndromes caused by other conditions, as in Khan’s study [12] about surgical revascularization (15 of 23 patients with moyamoya angioopathy had idiopathic moyamoya disease). One of the largest European cohort was recently published, but all 21 adult patients were symptomatic for ischemic cerebrovascular events at the time of diagnosis [13]. There are few data in the literature also about the natural course of the disease in the white American population, and mainly in symptomatic people. In a retrospective study about the moyamoya phenomenon in these adult population, by review of angiographic records, only 3 of 34 patients were asymptomatic [14]. It is interesting to note that these three patients were free of events at the follow-up (5–8 years), but in symptomatic patients the recurrences of ischemic and hemorrhagic events was very high with the medical treatment.

Conclusions

Moyamoya disease is a condition lesser rare than otherwise thought, and it is present also in adult caucasian people with both symptomatic and asymptomatic form. The subgroup of asymptomatic adult caucasian people is very small in the literature, because the diagnostic suspicion is casual, therefore few informations are available on the natural course of this disorder. The smallest series in the literature raised the question about the especially benign course of this form and our series seems to confirm this impression.

Appendix A. Transcranial Doppler evaluation

Takase et al. [8] classified the CBF velocity patterns into 3 types:

1) the high–high flow pattern, commonly seen in younger patients, in whom high flow velocities exist with high flow, but with moderate grade stenosis in the ICA or MCA, in the absence of proper collateralization;
2) the high–low flow pattern, in which higher-grade stenoses are associated with high velocity but lower overall flow;
3) the low–low flow pattern, in which velocity and flow are low secondary to the highest degree of stenosis.

Appendix B. DSA

Suzuki and Takaku [9] have described 6 stages of moyamoya progression:

1) narrowing of the CA termination;
2) dilation of the proximal portions of the ACA and MCA with initial basal moyamoya blush;
3) proximal portions of the ACA and MCA are no longer visualized; distal branches are still present due to collateral vessels from the PCA and intensification of the moyamoya blush;
4) minimization of the basal moyamoya network together with progressive occlusion of the ICA, which reaches the origin of the PCA;
5) further reduction of moyamoya vessels, with complete disappearance of the main arteries arising from the CA, continuous decrease of moyamoya collateral vessels that are more limited to the siphon area, and increased collateral supply from the ECA; and
6) disappearance of the moyamoya blush together with the blood supply from the ICA.

References