

Moyamoya disease in childhood: a familial case report

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Abstract. Moyamoya is an obstructive cerebrovascular disease characterized by a cerebral angiographic picture of stenosis or occlusion of main cerebral arteries with an abnormal vascular network at the base of the brain. No definitive cause has been found for this disease and opinion is still divided between a congenital and an acquired etiology. Hemiplegia of sudden onset and epileptic seizures are the prevailing presentation in childhood, while subarachnoid bleeding occurs more frequently in adults. We report a new case of childhood moyamoya with clinical onset of the neurological symptoms within the 3rd year of life; during the child's illness the maternal grandmother presented with moyamoya disease too. Antiaggregating and calcium-antagonist drugs seem effective in preventing further vascular accidents, while a surgical approach is not possible. Computed tomography, single positron emission computed tomography, and magnetic resonance imaging are very useful in the diagnosis of this rare disease.

Key words: Moyamoya disease – Children – Cerebral angiography – MRI – Seizures

Introduction

Moyamoya disease is a rare cerebrovascular disorder of unknown etiology consisting of stenosis or occlusion of main cerebral arteries which causes an abnormal vascular network at the base of the brain. The Japanese term “moyamoya” (“something hazy, like a puff of smoke drifting in the air”) describes the angiographic appearances [13, 23]. The vascular abnormalities are bilateral in the disease, while a unilateral appearance (known as the moyamoya phenomenon) can occur in other conditions such as neurofibromatosis, tuberous sclerosis, tuberculous meningitis, etc. [8]. The disease commonly presents with strokes in childhood, while in adults subarachnoid

and intracranial hemorrhage is the prevailing presentation [8]. About 200 childhood cases have been reported (two-third in Japan) with a male-female ratio of 2:3 [2], in Italy there are less than ten. We discuss here the case of a child with clinical onset of the neurological symptoms in the 3rd year of life.

Case report

The patient is a boy aged 3 years and 2 months. The family history revealed febrile convulsions in the mother and transient ischemic attacks in the maternal grandmother. The child's past history was unremarkable except for a febrile convulsion at 15 months. The child was admitted at the age of 26 months because of a sudden right hemiparesis; 3 days before hospitalization he had suffered vomiting and partial seizures. On admission, cranial computed tomography (CT) revealed two cortical-subcortical hypodense zones in the left temporoparietal-occipital and right parietal areas, both without contrast enhancement. Magnetic resonance imaging (MRI) of the brain (Fig. 1) showed cerebral infarction with cortical-subcortical atrophy in the right parietal area and cortical atrophy in the left parietal area. The striate and perforating arteries and the medullary vessels were markedly hypertrophic. EEG showed a slow-wave pattern localized in the right occipital-temporal and left frontal regions. Blood biochemistry showed no abnormalities. Lumbar puncture yielded normal spinal fluid under normal pressure.

Subsequently the patient's neurologic status improved. EEG and CT scan showed only abnormalities in the right area. Two weeks later pharyngitis with fever developed and the patient suffered from two clonic partial seizures affecting his left face, so he was treated with phenobarbital. EEG was unchanged. Fifteen days later he presented left-sided status epilepticus, followed by a residual left hemiparesis and disturbance of cranial nerve VII and aphasia. CT scanning showed the reappearance of cortical abnormalities in the left temporoparietal-occipital area and revealed recent cortico-subcortical lesions in the right temporoparietal region, near to the territory of previous parietal posterior cerebral infarction. CT scanning also revealed dilatation of the supratentorial ventricles and enlarged frontal subarachnoid space. Single positron emission computed tomography (SPECT) with ^{99m}Tc HmPAO showed diffuse low perfusion in the bilateral frontoparietal, right temporoparietal and left parieto-occipital regions. EEG revealed a diffuse increase of slow frequencies and high voltage sharps in the right parietal rolandic area. Upon admission, the patient's hemiparesis began to

improve and reached an almost complete neurologic recovery except for persisting aphasia.

Because clinical, neuroradiological, and EEG findings suggested the diagnosis of moyamoya disease, cerebral angiography was performed.

Angiographic study (Fig. 2) showed stenosis of both carotid siphons distal to the origin of the ophthalmic arteries. Above the stenosis there was a marked collateral circulation network mainly

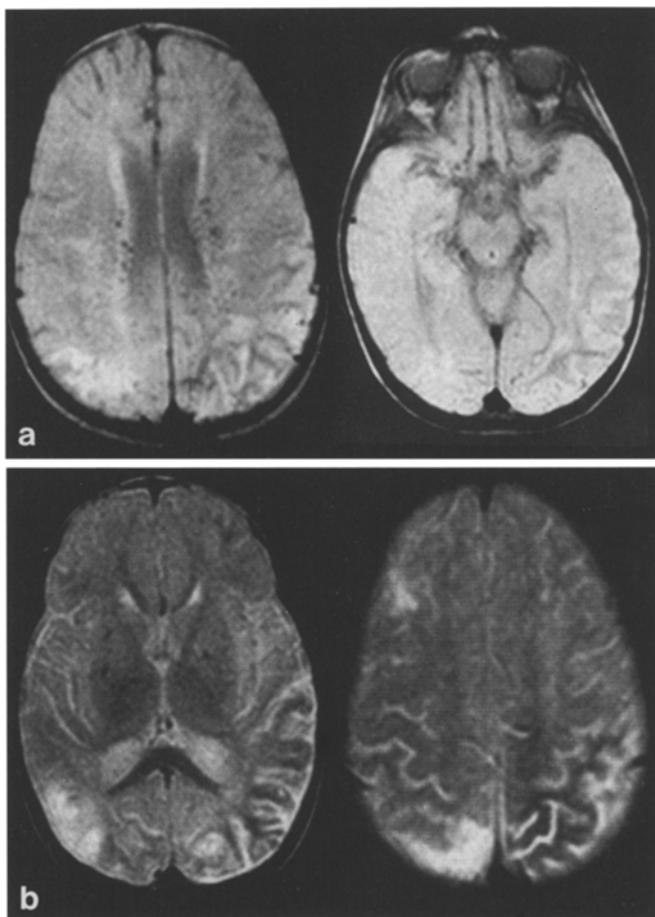


Fig. 1 a, b. Magnetic resonance imaging shows cerebral infarction with cortical-subcortical atrophy in the right parietal area and cortical atrophy in the left parietal area

composed of near perforating arteries and others arising from the posterior choroidal arteries. A right carotid angiogram did not visualize the origin of the anterior and middle cerebral arteries, while in the left carotid angiogram the same arteries were markedly stenosed and opacified only for the first 2–3 cm. There was a dilated external carotid network.

Subsequently, the child presented with another right-sided status epilepticus, with a residual hemiparesis. In the mean-while a therapy was started with antiaggregating and calcium-antagonist drugs. Phenobarbital was stopped and carbamazepine was initiated. The patient began physical therapy. After a few days the right hemiparesis improved, while aphasia and left motor disturbance persisted.

Today, after a 14-month follow-up, the left hemiparesis has improved, but the aphasia has persisted. The child's abilities are underdeveloped for his age; his IQ (Brunet-Lezine scale) is 62. He has no more seizures. EEG is normal. MRI shows cerebral infarction in fronto-temporoparietal-occipital cortical-subcortical areas of both the hemispheres, and dilatation of the lateral ventricles and subarachnoid space.

Discussion

Reports of moyamoya in infancy are rare: in Italy (Table 1) they are very few [4], with an onset most frequently marked by convulsions and episodes of sudden hemiplegia in patients aged less than 2 years (6 out of 9 cases); the clinical course shows irreversible neurological deficits and intellectual regression.

The vascular abnormalities are bilateral in the disease, while a unilateral appearance (known as the moyamoya phenomenon) can occur in other conditions, such as neurofibromatosis, tuberous sclerosis, etc. Our patient suffers from moyamoya disease, not the moyamoya phenomenon.

It has been reported in uncontrolled studies [8] that moyamoya disease is often preceded by a prodrome such as an upper respiratory tract infection, or a seizure or a fever of unknown etiology. Our patient suffered vomiting and partial seizures 3 days before the hospitalization.

The onset with neurological deficits due to cerebral infarction, followed by repeated episodes of cerebral infarction, suggests the pattern of stage V moyamoya disease according to Suzuki and Takaku [23]. This type is unusual in children and corresponds to the so-called

Table 1. Symptoms and clinical data in Italian cases of childhood moyamoya disease

Authors	Year	n	Sex	Age	Symptoms	Follow-up
Galligioni et al. [7]	1971	1	F	4 years	Convulsion, hemiparesis	Mental and motor disturbance
Lanzi et al. [15]	1974	2	F	8 months	Convulsion, hemiparesis	Motor disturbance
Benedetti et al. [3]	1977	3	M	11 months	Convulsion, hemiparesis	Motor disturbance
Carella et al. [4]	1977	4	M	8 years	Convulsion, hemiparesis	Not reported
Piattella et al. [18]	1981	5	F	6 months	Convulsion, hemiparesis	Recurrent episodes of motor disturbance
Piattella et al. [18]	1981	6	M	2 years	Convulsion, hemiparesis	Recurrent episodes of motor disturbance
Di Rocco et al. [5]	1984	7	M	13 months	Not reported	Not reported
Di Rocco et al. [5]	1984	8	M	18 months	Not reported	Not reported
Battistella et al. [2]	1987	9	F	5 years	Hemiparesis, headache	Normal

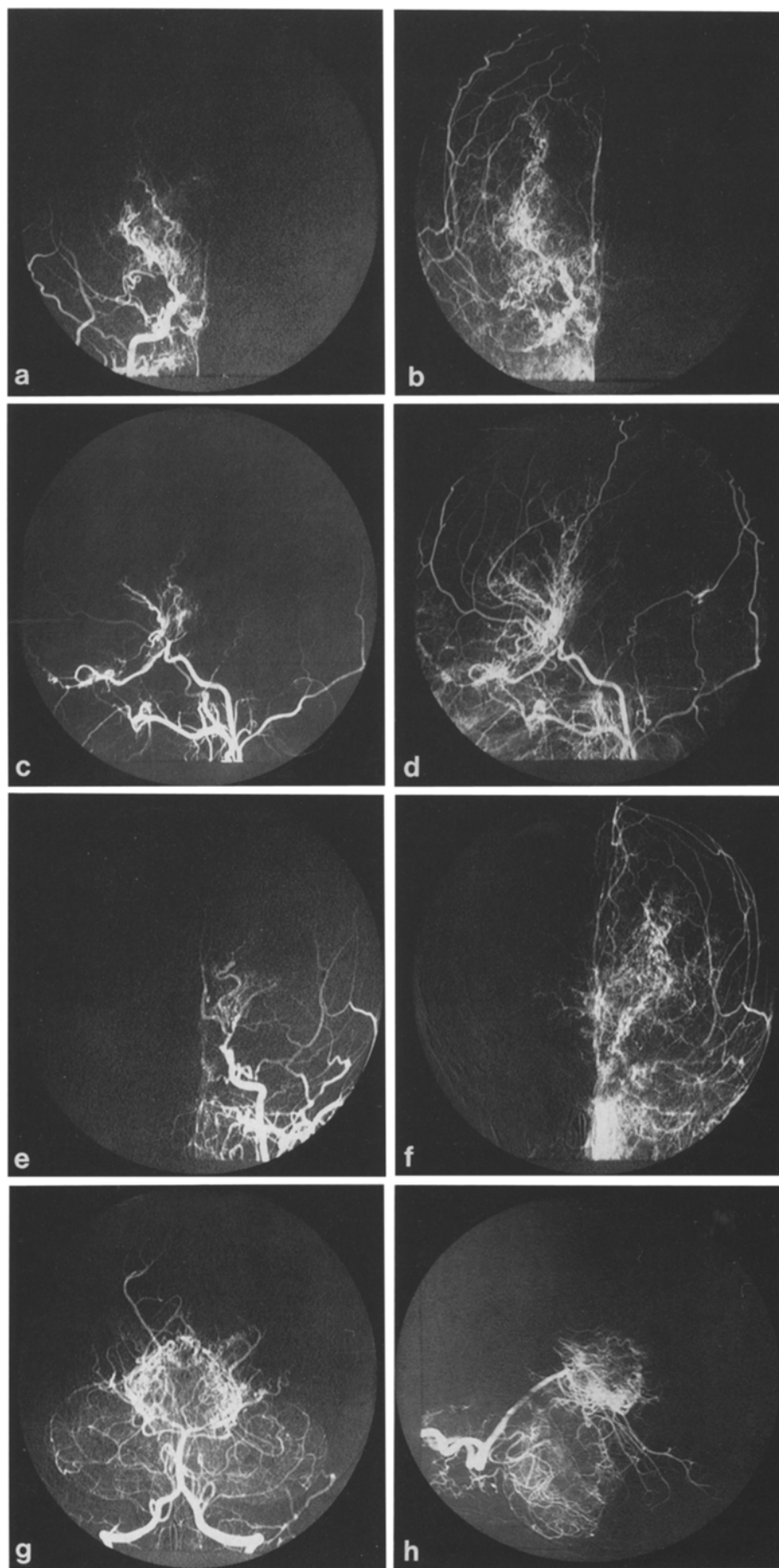


Fig. 2 a–h. Bilateral carotid angiograms showed stenosis of both carotid siphons distal to the origin of the ophthalmic arteries. The right carotid angiogram (a–d) revealed no origin of the anterior and middle cerebral arteries; in the left carotid angiogram (e–f) the same arteries were markedly stenosed and opacified only for the first 2–3 cm

adult moyamoya disease that is often observed in patients older than 20 years of age. In Suzuki and Takaku's series of 81 childhood patients there was only one with type V disease, and this presented in the patient when he was almost adult [23].

Onset under the age of 4 years, seizures, and cerebral infarctions are risk factors [8] suggesting irreversible neurological deficits and intellectual regression, as demonstrated in our patient after a 14-month follow-up.

The medical treatment of moyamoya disease with antibodies, low molecular-weight dextran and steroids is not very effective [8]. In our patient, pharmacological therapy with antiaggregating and calcium-antagonist drugs was carried out and seems to be effective in preventing further vascular accidents. Antiaggregating drugs seem useful because of the increased platelet aggregability in moyamoya disease. As for calcium-antagonist drugs, there is a report of two children [5] with moyamoya disease treated with verapamil which improved their acute neurological deficits [16]. Subsequently other authors have stressed the efficacy of flunarizine in the treatment of ischemic attacks in moyamoya disease [17].

Many reports have described the promising effects of revascularization procedures for the prevention of ischemic cerebral attacks in moyamoya disease [21]. However, it is still a matter of debate whether such procedures prevent progression of the disease or only stabilize it temporarily. Anyway, we ruled out the possibility of a surgical approach for our patient because of the severity of the case: our patient's condition fits the criteria of stage V moyamoya disease according to the angiographic classification described by Suzuki and Takaku [23].

No definite cause has been found for moyamoya disease; opinion is still divided between a congenital and an acquired etiology, in particular infection [8]. A primary malformation of blood vessels has been suggested by Galligioni et al. [7]. The association with a history of trauma, infection, brain tumor, or radiation suggests there may also be an acquired form. Recurrence of moyamoya within the same family seems a point in favor of congenital malformation. Kitahara et al. [12] stressed the hereditary component in the pathogenesis of the disease as a cause of the relatively high familial incidence (7%) found in his totally Japanese series. Case reports found in the literature that deal with familial cases are summarized in Table 2.

In the present case the family history is very interesting: during the child's illness, the maternal grandmother, living together with the patient, experienced some transient ischemic attacks in the same time period. She underwent cerebral angiography that showed the occlusion at the origin of the right internal carotid artery, a high grade of stenosis of the left internal carotid artery, and moyamoya collateral circulation. Our data support a familial congenital disease of possible hereditary origin, but an infectious cause can not be ruled out, because of the presence of the illness in the child and in his grandmother at the same time.

In conclusion, the reported case confirms that the prognosis is poor if the patient is under 4 years of age at onset and seizures and cerebral infarctions appear. We

Table 2. Familial cases of moyamoya disease (from the literature)

Authors	Year	Reported cases
Austin and Stears [1]	1971	Two (or three) brothers
Praud et al. [19]	1972	Two brothers
Sogaard and Jørgensen [22]	1975	Three patients in a family
Kudo [14]	1975	Seven instances of familial occurrence
Richman et al. [20]	1977	Two adults (a man and his niece)
Fujiwara et al. [6]	1977	Two cases (a mother and her child)
Kitahara et al. [12]	1979	Three familial cases
Yamada et al. [27]	1980	Two identical twin girls
Vinals et al. [25]	1986	A familial presentation
Kawamura et al. [11]	1987	Two twin girls
Ikeda et al. [9]	1990	Two cases (a mother and her daughter)
Usuki et al. [24]	1991	One familial case
Iwamoto et al. [10]	1991	Three patients in a family

stress the importance of the genetic factor in the pathogenesis of the disease and the effectiveness of pharmacological therapy in our patient. Finally, our data underline that CT, SPECT and especially MRI [26], are very useful to reach a suspected diagnosis of moyamoya disease, which must be confirmed by cerebral angiography.

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