CASE REPORT

Postpneumococcal Moyamoya syndrome case report and review of the postinfective cases

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SUMMARY

Our aim was to describe a patient who experienced a postpneumococcal Moyamoya syndrome (MMS), with a great involvement of the posterior cerebral circulation, and to review the MMS postinfective cases. A 55-year-old Pakistani man with a history of pneumococcal meningitis 3 months before developed acute headache, left otalgia and body paresthesiae. Brain CT showed a right occipital ischaemic lesion. Seven days later, he developed acute left haemianopsia, haemiplegia, haemineglect and 'frontal' cognitive and behavioural symptoms. A second brain CT and MRI disclosed an increase in the occipital lesion and the appearance of a further one in the right frontal lobe. Cerebral CT and MRI-angiography were consistent with Moyamoya vessel alterations. Treatment with antiplatelets, methylprednisolone, followed by prednisone tapering, and motor rehabilitation began. Six months later, no relapses had occurred. Our case represents a delayed manifestation of postmeningitis vasculopathy. Meningitis may represent a risk factor for developing a disabling cerebrovascular disease like MMS.

BACKGROUND

Moyamoya disease (MMD) is a chronic idiopathic cerebrovascular disease characterised by the bilateral steno-occlusive angiopathy of the intracranial vascular networks and concurrent generation of compensatory new irregular perforating vessels, named 'moyamoya vessels'.

In addition to the idiopathic form, MMD-like features have been described in a variety of conditions, including autoimmune or haematological disorders, metabolic diseases, genetic/chromosomal disorders, drug toxicity, neoplasms, cranial trauma and cranial irradiation,¹ thereby giving rise to the concept of Moyamoya syndrome (MMS).

MMS has occasionally been reported to also occur after bacterial meningitis. Acute bacterial meningitis may be complicated by alterations of the vessel systems. Typical cerebrovascular complications are ischaemia and thrombosis, particularly related to arterial narrowing of the supraclinoid portion of the internal carotid artery with vessel wall irregularities, focal dilations and thrombo-occlusions. These meningitis-related vascular events are due to vascular inflammation of the immune response against the invading pathogen, and generally occur within the first 2 weeks after bacterial infections. Delayed postinfective vasculitis is less frequently reported.

We describe a case of postpneumococcal meningitis complicated by delayed MMS, and review the postinfective cases in the literature.

CASE PRESENTATION

A 55-year-old Pakistani man with a history of pneumococcal meningitis 3 months before, without reliques, was admitted in August 2010 for acute bilateral headache, left otalgia and left body paresthesiae. A brain CT scan (GE Medical Systems, U.S. A64 slices) showed a right occipital cortical-subcortical hypodensity. No cerebrovascular risk factors were documented in the medical history.

INVESTIGATIONS

Laboratory tests, including coagulative screening, demonstrated only transitory elevation of inflammatory indexes. Autoantibody levels and cerebrospinal fluid (CSF) analysis including infective searches were negative. Transthoracic ECG, blood pressure monitoring, 24 h Holter-ECG monitor, supra-aortic tract and transcranial Eco-Doppler and venous and arterial Eco-Doppler of the legs were normal.

Seven days later, he developed acute left haemiplegia. Neurological examination showed left haemianopsia, haemiplegia, haemineglect and a frontal syndrome. Another CT scan showed an extension of the right occipital hypodensity and a second hypodense cortical-subcortical area in the right

Figure 1 CT scan: right frontal and occipital cortical-subcortical hypodensities in different vascular territories.

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Figure 2 CT angiography, VR reconstructions. Intradural vertebral-basilar system with progressive rarefaction then disappearance.

frontal lobe, both of ischaemic nature, in different vascular territories (figure 1). The patient underwent extra-intracranial CT angiography (CTA) (contrast agent: Guerbet, Xenetix 350) to disclose the involvement of different vascular territories. CTA (figures 2–6) revealed bilaterally steno-occlusive angiopathy in the proximal ramifications of the Willis circle, namely in the supraclinoid segment of the carotid siphons, extending to the A1 and M1 segments of the anterior and middle cerebral arteries, also involving the intradural vertebral–basilar system and an abnormal vascular network in the proximal M1 segment of the right middle cerebral artery, consistent with an over-representation of lenticulostriates perforating arteries because of collateralisation (puff of smoke). The extracranial vessels were normal (figures 7–10).

A brain MRI (figures 1 and 2) study confirmed the neuroradiological findings and their ischaemic nature. A brain MR Angiography (MRA; figures 3 and 4) study confirmed the bilateral steno-occlusive angiopathy, the vertebral–basilar system involvement and the abnormal vascular network (Moyamoya-like vessels). It wasn't possible to realise an angiogram due to the bad condition of the patient and the absence of compliance and of the consent.

Figure 3 VR reconstructions, supraclinoid segments of the carotid siphons with tapered aspect; M1-segments of the middle cerebral arteries with stenosis and stretching; disappearance of A1 segments of the anterior cerebral arteries.

Figure 4 CT angiography, coronal MIP reconstructions: an abnormal vascular network in the proximal M1 segment of right middle cerebral artery (puff of smoke).

Figure 5 CT angiography, axial MIP reconstructions: supraclinoid segments of the carotid siphons with tapered aspect; M1-segments of the middle cerebral arteries with stenosis and stretching; disappearance of A1 segments of the anterior cerebral arteries.

Figure 6 MR angiography, coronal reconstructions: an abnormal vascular network in the proximal M1 segment of right middle cerebral artery (puff of smoke).

Neuropsychological tests underlined serious left special neglect, attention and praxis function deficits. According to clinical and radiological findings, previous meningitis and the absence of any other symptoms demonstrating the cause of strokes despite an extensive search, we concluded that it was postinfective MMS.

DIFFERENTIAL DIAGNOSIS

The absence of any other symptoms demonstrating the cause of strokes despite an extensive search supported our diagnosis. We considered in differential diagnosis a chronic bilateral atherosclerosis, but this hypothesis is unlikely for the complete absence of anamnestic vascular risk factors (ie, diabetes, dyslipidaemia, hypertension, smoke cigarette use and coronaropathy artery sign), as well as a normal arterial investigation of supra-aortic extracranial vessels documented both baseline and on admission. Moreover, we have ruled out active infections of the central nervous system, past infective diseases such as *Mycobacterium tuberculosis*, β -haemolytic group A

Figure 7 MR angiography axial reconstructions: supraclinoid segments of the carotid siphons with tapered aspect; M1-segments of the middle cerebral arteries with stenosis and stretching; disappearance of A1 segments of the anterior cerebral arteries.

Figure 8 DWI MRI: right frontal and occipital cortical-subcortical hypodensities in different vascular territories.

Figure 9 CT angiography, coronal MIP reconstructions. Intradural vertebral-basilar system with progressive rarefaction then disappearance.

Figure 10 DWI RMI: right frontal and occipital cortical-subcortical hypodensities in different vascular territories.

Streptococcus, Syphilis, HIV, *Mycoplasma pneumoniae* and other causes of MMS as Sjogren's syndrome, sickle cell anaemia, haemolytic anaemia, aplastic anaemia, lupus anticoagulant, glycogen storage disease, hyperlipoproteinaemia, hyperthyroidism, neurofibromatosis, Down's syndrome, tuberous sclerosis, retinitis pigmentosa, fibromuscular dysplasia, neoplasms, past drug toxicity, cranial trauma and irradiation.

TREATMENT

Therapy with oral acetyl salicylic acid 100 mg daily and subcutaneous heparin 4000 IU daily was started. Moreover, the patient was treated with intravenous methylprednisolone (1 g daily for 5 days), followed by prednisone tapering starting at 50 mg daily. A motor and cognitive rehabilitation treatment was started,

whereas no surgical therapy was indicated because of the severe anatomic condition of the cerebral vessels.

OUTCOME AND FOLLOW-UP

Six months later, no relapses had occurred. He had motor improvement, but the frontal syndrome persisted. The patient did not assent to an angiogram after the treatment.

DISCUSSION

Our case represents a delayed manifestation of postmeningitis vasculopathy, diagnosed as MMS, as suggested by the clinical–radiological MMD-like vessel changes, with an anamnestic history of streptococcal meningitis, without new CSF bacterial localisation, and a great involvement of the posterior cerebral circulation.

The absence of any other symptoms demonstrated the causes of strokes and MMS, despite an extensive search, supporting our diagnosis.

MMD is a chronic idiopathic cerebrovascular disease characterised by bilateral steno-occlusive angiopathy of the intracranial vascular networks, with new irregular perforating vessels ('moyamoya vessels') to supply blood flow to the ischaemic regions. Occlusions of the terminal portion of the internal carotid arteries (ICAs) and proximal portion of the middle cerebral arteries (MCAs) and anterior cerebral arteries (ACAs) are typical. Posterior circulation involvement is rare.

MMD-like features have been described in several conditions, giving rise to the concept of MMS. MMS vessel alterations have been found after infective meningitis in autoimmune or haematological disorders (Sjogren's syndrome, sickle cell anaemia, haemolytic anaemia, aplastic anaemia and lupus anticoagulant), metabolic diseases (glycogen storage disease type 1, hyperlipoproteinemia type 2A, hyperthyroidism and pseudoxanthoma elasticum), genetic/chromosomal disorders (neurofibromatosis, Down's syndrome, tuberous sclerosis, retinitis pigmentosa and fibromuscular dysplasia), drugs (phenobarbital and oral contraceptives), neoplasms (craniopharyngioma and Wilm's tumour), cranial trauma and cranial irradiation.¹

Concerning postinfective aetiology, postmeningitis Moyamoya syndrome is rare; to our knowledge, 14 cases have been reported (table 1).

The infectious agents involved are *Streptococcus pneumoniae*,^{2–3} β -haemolytic group A *Streptococcus*,⁴ *Mycobacterium*

Table 1 Review of the postinfective cases

References	Infective agents	Age (range) and sex	Symptoms (from 2 weeks to 30 years)	Therapy
Czartoski <i>et al</i> ²	<i>Streptococcus pneumoniae</i>	► 2–65 years old	► Intracranial bleeding	► Intravenous methylprednisolone
Pugin <i>et al</i> ³		► F:M=8:6	► TIA	(1 g daily for 3–5 days), followed
Javier <i>et al</i> ⁴	β -Haemolytic group A <i>Streptococcus</i>		► Brain infarction	by slow prednisone tapering,
Stoeter <i>et al</i> ⁵	<i>Mycobacterium tuberculosis</i>		► Epileptic seizure	$\pm$ cyclophosphamide (950 mg)
Kitahara <i>et al</i> ⁶			► Refractory migraine-like headache	► ASA, ticlopidine, warfarin
Kashiwagi <i>et al</i> ⁷			► Movement disorders (chorea, dystonia)	► Neurorehabilitation programme
Nakayama <i>et al</i> ⁸				
Palacio <i>et al</i> ⁹	<i>Neisseria meningitidis</i> + <i>Haemophilus influenzae</i>			
Kerr <i>et al</i> ¹⁰				
Sophia <i>et al</i> '07	HIV			
Galati <i>et al</i> ¹²				
Hsiung <i>et al</i> ¹³				
Morgello <i>et al</i> ¹⁴	Syphilis with HIV infection			
Greco <i>et al</i> ¹⁵	<i>Mycoplasma pneumoniae</i>			

tuberculosis,^{5–8} *Neisseria meningitidis* with *Haemophilus influenzae*,^{9–10} HIV,^{11–13} syphilis with HIV infection and¹⁴ *Mycoplasma pneumoniae*.¹⁵ Symptoms may appear after some weeks or many years after the infection, with intracranial bleeding, transient ischemic attack (TIA) transient ischaemic attack, brain infarction, epileptic seizure, refractory migraine-like headache and movement disorders, such as chorea and dystonia.

The pathogenesis of this type of postinfectious vasculopathy is unknown. Several mechanisms have been proposed: inflammatory infiltration (vasculitis) due to the infective agent¹¹ with reactive vasospasm and residual organic stenosis,¹⁶ or an autoimmune process.² Moreover, host susceptibility to autoimmune disease may be considered.¹⁷

Concerning the therapy, no guidelines are available; the few cases of the literature reported intravenous methylprednisolone (1 g daily for 3–5 days), with or without cyclophosphamide (950 mg), followed by slow prednisone tapering. Furthermore, aspirin, antiplatelet agents and neurorehabilitation programmes have been used.

The course may be monophasic or relapsing, with or without recovery. The high relapsing risk during the tapering period enhances the immunity pathogenesis and suggests slow steroid tapering. Prognosis may be poor with early exitus.

Learning points

- Our observation documents a case of Moyamoya syndrome (MMS) as a delayed manifestation of postmeningitis vasculopathy without relapses at 6 months. This diagnosis may be considered when suggested by the clinical–radiological Moyamoya disease-like vessel changes, with an anamnestic history of infective meningitis, without new cerebrospinal fluid bacterial localisation.
- MMS should be considered a cause of stroke in patients with previous meningitis; this entity is rare.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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