CASE REPORT

Is congenital melanocytic naevus a link between Hirayama disease and moyamoya pattern: a new syndrome or a co-incidence?

Inder Puri, Deepti Vibha, Kameshwar Prasad, Rohit Bhatia

Department of Neurology, All India Institute of Medical Sciences, New Delhi, India

Correspondence to

Dr Deepti Vibha,
deeptivibha@yahoo.com

Accepted 16 December 2015

SUMMARY

A 22-year-old man presented with a history of progressive weakness and wasting of the right hand and forearm for 12 months followed by similar symptoms in the left upper limb for the past 5 months. He also gave a history of episodes of loss of consciousness for the past 5 years with a frequency of one per 3 months. On examination, there were melanocytic naevi—one large lesion in the nape of the neck and multiple satellite lesions. On investigation, the cervical cord MRI was normal. The brain MRI and angiography showed a moyamoya pattern. Thus, this patient had congenital melanocytic naevi with Hirayama disease and moyamoya pattern. He was treated with extracranial–intracranial bypass for moyamoya disease. During 6-month follow-up, he has been stable. Although moyamoya syndrome has been associated with several systemic diseases and conditions, the coexistence of a moyamoya pattern with Hirayama disease and melanocytic naevi has not been described so far.

coarctation of the aorta, fibromuscular dysplasia and tuberculosis.

The coexistence of congenital melanocytic naevi (CMN) made our case further intriguing, from a mere co-incidence to a probably undescribed syndrome. However, the coexistence of both these rare Asian syndromes has not been described so far. This may be a lead towards an underlying common pathogenesis/genetic basis in the form of cytopathy/vasculopathy.

CASE PRESENTATION

A 22-year-old man presented with progressive weakness and wasting of the right hand and forearm for the past 12 months. He had difficulty in performing fine work, and had thinning of the dorsum of the hand, with tremors. Five months after the initial symptoms had begun, similar symptoms appeared in the left upper limb.

He also had an associated history of three episodes of loss of consciousness during micturition. There was no witness for these episodes and the last episode was 1 year earlier; he had never been evaluated for this medical problem.

On general examination, vitals were normal. We observed hyperpigmented skin lesions, melanocytic naevi, one large lesion in the nape of the neck (figure 1A) and multiple satellite lesions all over the body. These had been present since birth, and the patient had never sought medical advice for them. Neurological examination showed wasting and weakness in the thenar, hypothenar and forearm muscles of both upper limbs (figure 1B). Deep tendon jerks, and sensory and cerebellar function, were normal.

INVESTIGATIONS

For the work up of these presenting symptoms, mainly distal upper limb lower motor neuron type of weakness, the patient underwent MRI of the cervical spine (figure 1C,D), which did not show any evidence of significant signal alteration or cord compression or thinning in the flexion/extension.

Since there were melanocytic naevi, a skin biopsy was planned. As the patient had a history of recurrent episodes of loss of consciousness, the treating team also decided to carry out MRI of the brain after excluding routine causes. The skin biopsy showed normal melanocytes, with normal cytoplasm and nuclei (figure 1E,F). MRI of the brain revealed focal area of T2 weighted and fluid-attenuated inversion recovery hyperintensity

BACKGROUND

Moyamoya disease and Hirayama disease are rare ailments with a predilection for the Asian population. While Hirayama disease was first described as 'juvenile muscular atrophy of the unilateral upper extremity',¹ the complexity has only grown more with terms such as benign juvenile brachial spinal muscular atrophy, juvenile asymmetric segmental spinal muscular atrophy, juvenile muscular atrophy of the distal upper extremity, monomelic amyotrophy and oblique amyotrophy.² This only goes to show that the exact pathogenesis of the disease is still elusive. The postulated mechanisms range from a degenerative motor neuron disease variant, traumatic injury of the cervical spinal cord and prolonged survival of acute anterior poliomyelitis, to genetic or flexion-induced cervical myelopathy leading to ischaemic changes in the anterior horn of the cervical cord.

Moyamoya disease is a rare cerebral steno-occlusive disease characterised by progressive occlusion of the terminal segments of the internal carotid arteries (ICAs), with compensatory development of tortuous, dilated collateral networks.³

The term moyamoya syndrome is used when there is an underlying association such as sickle cell anaemia, Down syndrome, Marfan syndrome, tuberous sclerosis, Turner syndrome, von Recklinghausen disease, atherosclerotic disease,

CrossMark

To cite: Puri I, Vibha D, Prasad K, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-212894

Figure 1 (A) Presence of large congenital nevi on the nape of the neck, (B) wasting of intrinsic muscles of the hand and forearm, (C) and (D) are T2-weighted sagittal images of the MRI cervical cord in flexion and extension position, respectively, with mild attenuation of the cerebrospinal fluid spaces, without any significant cord compression or atrophy, (E) and (F) histopathology of the skin lesion in $\times 4$ and $\times 10$ magnification, and H&E stain showing normal dermal architecture with normal cytoplasm and nucleus of the melanocytes.

in the left frontal high subcortical white matter and centrum semiovale (figure 2A,B). These features were suggestive of chronic watershed infarcts in the middle cerebral artery (MCA)/anterior cerebral artery territory. There was also note made of multiple small tortuous flow voids in the basal cisterns. To explore these findings further, a digital subtraction angiography (DSA) was performed, which showed a moyamoya pattern. The left ICA was occluded beyond the origin of the ophthalmic artery with attenuation of its calibre. The left MCA was reformed through collaterals from the left internal maxillary artery (figure 2C). The right ICA was attenuated in calibre from the carotid bulb, with poor filling of the right MCA (figure 2D). Multiple moyamoya collaterals were seen at the base of the brain.

DIFFERENTIAL DIAGNOSIS

The clinical presentation of the patient was usual for Hirayama disease. The presence of coexisting CMN and unusual findings on brain MRI prompted us to further investigate beyond the cervical cord MRI. The brain MRI suggested an anterior watershed infarct. Since there were no conventional vascular risk factors for stroke in this young man, he underwent DSA, which revealed a moyamoya pattern. We searched the literature for differentials of syndromes of all three disease components of this patient, but even two components had not so far been reported

in a single syndrome. Although the symptoms of Hirayama disease are not amenable to proven successful medical or surgical therapy, there was a potential danger of progression of the moyamoya disease.

TREATMENT

As the patient was symptomatic in the form of a micturition syncope, and found to have a moyamoya pattern, he was referred to neurosurgery, where he underwent a successful external carotid-internal carotid (EC-IC) bypass. He was treated with left superficial temporal artery to MCA bypass and encephalomyosynangiosis.

OUTCOME AND FOLLOW-UP

Our patient underwent an indirect revascularisation procedure with good short-term follow-up. The outcome of the surgical procedure was successful and the patient had not had any episodes of syncope at 6 months of follow-up. No new melanocytic lesions had appeared and neither size nor colour had changed in any lesion. The wasting of the right hand was static but a minimal increase in left hand wasting was noted. We plan to follow-up the patient every 6 months to observe for any progression. The patient has been counselled to report earlier in case of any event.

Figure 2 (A) and (B) Focal area of T2 weighted and fluid-attenuated inversion recovery MRI of the brain, respectively, showing hyperintensity in the left frontal high subcortical white matter and centrum semiovale, (C) left internal carotid artery (ICA) is occluded beyond origin of the ophthalmic with attenuation of its calibre. Left middle cerebral artery (MCA) is reformed through collaterals from the left internal maxillary artery, with poor opacification. (D) Right ICA is attenuated in calibre from the carotid bulb, with poor filling of the right MCA.

DISCUSSION

The diagnostic criteria of Hirayama disease includes the following: (1) chronic weakness and atrophy of the distal upper limb (s), (2) insidious onset in the second or third decade of life and (3) absence of substantial sensory deficits, reflex abnormalities, and cranial nerve, pyramidal tract, lower limb, sphincter, or cerebellum involvement; no history of poliomyelitis, toxin exposure, or periodic paralysis; and no evidence of an underlying disease causing peripheral neuropathy of an axonal motor type shown at biochemical and neurophysiological work up, which occurs mainly in people in their early 20s, with a significant male predominance. The presenting features of our patient were consistent with Hirayama disease. So far, there have been no published reports regarding genetics information that may be related to Hirayama disease.⁴ Chronic microcirculatory disturbances during strenuous physical activities, elevated serum total immunoglobulin E level (hyperIgEaemia) and dynamic flexion myelopathy, have all been postulated in the pathophysiology of Hirayama disease.² The forward movement of the dural canal in flexion and no dural folding in extension are considered to be important factors for diagnosis on neuroimaging. However, they might not be present in all cases of Hirayama disease. None of these circumstances were found on evaluation in our patient.

The patient had associated CMN syndrome, which is characterised by pigmentary skin lesions at birth. Less commonly, CMN is associated with malignant melanoma, but the risk appears to be low, ranging from 1% to 2% for all individuals, but rising to 10–15% in those with very large naevi (>40 cm).

Small subsets of patients with CMN have abnormalities of the central nervous system (CNS), known as ‘Neurocutaneous melanosis’ or ‘Neuromelanosis’, which may be symptomatic, but with no hint in the presented case. Our patient had CNS involvement other than neuromelanosis, so it is possible that it had a different spectrum and pathology.

A moyamoya pattern has never been reported in association with CMN and/or Hirayama disease. The characteristic findings of a moyamoya pattern on MR angiography are stenosis of the supraclinoid ICA and moyamoya vessels, with signal intensity voids in the basal ganglia, and collaterals around and distal to stenotic segments. Genetic linkage studies have revealed putative chromosomal locations linked to moyamoya disease.⁵ The treatment is surgical: direct revascularisation, in which a scalp artery or other extracranial vessel is sewn directly to a cortical artery in an effort to provide immediate increase in cerebral blood flow (CBF), and indirect revascularisation (encephaloduroarteriosynangiosis, encephaloduroarteriomyosynangiosis and multiple burr holes), in which vascularised tissues are applied to the cortical surface in an effort to promote angiogenesis and to improve CBF over time.

In conclusion, the coexistence of Hirayama disease and CMN with a moyamoya pattern remains speculative. It will be worthwhile to report this case so that further observation on coexistence of this cutaneous manifestation with moyamoya and/or Hirayama disease may provide clues for an unknown neurocutaneous syndrome and also help in understanding the pathogenesis of Hirayama disease and the vasculopathy of moyamoya disease. The co-occurrence of rare diseases in a patient may hint more towards a correlation than a co-incidence.

Learning points

- Cases of Hirayama and moyamoya disease should be screened for melanocytic naevi.
- Since the pathogenesis of Hirayama is still unclear, co-occurrence with Moyamoya could point out towards a vascular ischaemia/vasculopathy that is unrelated to flexion myelopathy.
- Evaluation of unexplained syncope should include brain imaging.

Acknowledgements The authors would like to thank the patient who kindly consented for the pictures and also contacted us for follow-up.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Hirayama K, Tsubaki T, Toyokura Y, *et al.* Juvenile muscular atrophy of unilateral upper extremity. *Neurology* 1963;13:373–80.
- 2 Huang YL, Chen CJ. Hirayama disease. *Neuroimaging Clin N Am* 2011;21:939–50.
- 3 Garg A. Vascular brain pathologies. *Neuroimaging Clin N Am* 2011;21:897–926.
- 4 Misra UK, Kalita J, Mishra VN, *et al.* A clinical, magnetic resonance imaging, and survival motor neuron gene deletion study of Hirayama disease. *Arch Neurol* 2005;62:120–3.
- 5 Phi JH, Wang KC, Lee JY, *et al.* Moyamoya Syndrome: A Window of Moyamoya Disease. *J Korean Neurosurg Soc* 2015;57:408–14.

Copyright 2016 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow