SHORT REPORT

Carotid Rete Mirabile and Pseudoxanthoma Elasticum: An Accidental Association?

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Abstract We report the case of a young female patient with a transient amaurosis due to a carotid rete mirabile (CRM), a rare congenital carotid malformation, and pseudoxanthoma elasticum (PXE), an inherited autosomal recessive systemic metabolic disorder characterised by fragmentation and mineralisation of elastic fibres in connective tissues (skin, eyes) and the vascular system. CRM is a rare form of intracranial carotid malformation whose association with PXE (6 cases at present) would appear not to be accidental. This observation suggests a new link between congenital arterial remodelling and the PXE.

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Pseudoxanthoma elasticum (PXE; OMIM 264800) is a rare (1/25,000–1/50,000) inherited (autosomal recessive) multisystem disorder of connective tissue, characterised by fragmentation and progressive mineralisation of elastic fibres (elastorrhexis) in the skin, Bruch’s membrane of the retina and the vascular system.1 PXE is linked to a defect of the ABCC6 gene encoding for an adenosine triphosphate (ATP)-binding cassette membrane transporter in the liver and the kidney. The cerebral arterial malformations frequently reported in PXE are fusiform cervical aneurysms, pontine arteriovenous malformations, bilateral calcified common carotid aneurysms, aneurysm of the anterior spinal artery and, in a few cases, carotid rete mirabile (CRM).2 CRM is defined by an arterial network occurring in the cavernous part of the internal carotid artery (ICA) most often supplied by external carotid artery (ECA) branches, in particular branches of the maxillary artery. An association between cerebrovascular malformations and PXE is currently considered accidental. We report a new case of carotid malformation in a young female patient with PXE, who also displayed coronary narrowing.

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Report

A 38-year-old woman complained of two brief and spontaneously regressive episodes (<2 min) of amaurosis of the right eye without other symptoms. She had undergone coronary bypass surgery when she was 10 years old for unexplained congenital narrowing of her coronary arteries responsible for chronic myocardial ischaemia. She was diagnosed with PXE at age 12 years, with characteristic skin involvement (Fig. 1). Ophthalmologic examination revealed the previously identified angioid streaks without haemorrhage and progression in these lesions. The patient had the ABCC6 gene mutations p.Arg1141X and c.IVS21 G > T.

Colour Doppler imaging scans revealed regular and extended hypoplastic (luminal diameter 2.0–2.5 mm) post-bulbar extracranial segment of the ICAs. Both ICAs and ECAs were patent, with limited asymmetry of the peak systolic velocities (left ICA: 74 cm s\(^{-1}\), right ICA: 65 cm s\(^{-1}\)) and Pourcelot’s resistance index being within the normal range (left ICA: 0.77, right ICA: 0.73). The right vertebral V4 segment presented 50% higher flow compared with the left. Contrast-enhanced magnetic resonance imaging confirmed a hypoplastic aspect of the extracranial part of both ICAs with hyperplastic and tortuous vertebral arteries (Fig. 2). The time-of-flight scans revealed the absence of the intracavernous segments of both ICAs, replaced by an abnormal arterial network consisting of multiple small serpiginous vessels (Fig. 3). This arterial network reconnected in the supra-cavernous segment to form normal-sized intracranial ICAs anastomosed with ECAs via the maxillary artery. The supra-cavernous segment of both ICAs showed normal and patent branching of the main intracranial vessels. Both vertebrobasilar and posterior cerebral arteries were extensively developed, with large posterior communicating cerebral arteries. No ischaemic lesions or haemorrhages were observed. The diagnosis of bilateral agenesis of the ICAs with CRM was suggested and was thought to be responsible for the amaurosis episodes. Anti-platelet therapy was started to prevent further cerebrovascular events.

Discussion

CRM represents a distinct anatomical vascular entity classically observed in lower mammals (cats, sheep and pigs) but very rarely in humans. A CRM is defined as an arterial network occurring in the cavernous part of the

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Figure 1  Typical cervical skin lesions in the patient with pseudoxanthoma elasticum with yellowish papules and “peau d’orange” aspects.

Figure 2  Magnetic Resonance Angiography. MIP images of the CE-MRA showing the bilateral carotid rete mirabile with the hypoplastic aspect of the internal carotids and hypertrophied tortuous vertebral arteries. Note the external-internal anastomosis via the maxillary artery.

Figure 3  MIP image (TOF) focussing on the Willis circle confirms the absence of intracavernous segments of both ICAs replaced by an abnormal network of multiple small serpiginous vessels.
ICA, most often supplied by ECA branches, such as the maxillary artery. Some CRMs are occasionally discovered when investigating transient or permanent ischaemic stroke or haemorrhage, but mostly as incidental findings suggesting well-compensated cerebral perfusion by the carotid collateral network. The cerebrovascular manifestations in PXE are mainly represented by aneurysms or ischaemic lesions, leading to a higher incidence of ischaemic stroke. In humans, we found 32 reports of CRM (Medline search), five (16%) of which were associated with PXE. In all these reports, CRM was revealed by transient or permanent ischaemic symptoms (i.e., stroke), mostly in children and women. At present, a possible link between PXE and CRM is excluded, suggesting instead an accidental association between both conditions. Given the rarity of having both PXE and CRM, as in the present case, the probability of such an accidental association seems to us unlikely. An estimate of cases with both PXE and CRM yielded an expected number of approximately 14–28 cases in the world, which is within the range of the published cases in the literature, including ours. The fact that the arterial narrowing occurred simultaneously in two different arterial beds in our patient suggests a systemic mechanism. Thickening of the carotid intima–media layers and a reduction of the medium-sized and smaller arteries (e.g., radial artery) has been already reported in PXE. We speculate that these abnormalities could result from abnormal signalling involving ABCC6 during embryonic construction of the arterial wall structure, similar to that reported in the cardiovascular system of the zebrafish. Clinically, the CRM could favour transient episodes of functional impairment of the retinal perfusion. Finally, recommendations for the medical management of this abnormality are lacking and prevention of a thrombotic episode with anti-platelet therapy should be balanced with the higher risk of gastrointestinal bleeding reported in these patients.

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Conflict of Interest

None.

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References