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Case Report

Ischemic stroke with extensive vasculopathy in a patient with neurofibromatosis type 1☆,☆☆

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ABSTRACT

Neurofibromatosis type 1 is an autosomal dominant genetic disorder with multisystem manifestations including vascular abnormalities. The condition is also associated with an increased risk of both ischemic and hemorrhagic stroke. Here we report a case of a 60-year-old male with known neurofibromatosis who presented with right sided hemiparesis. Neuroimaging work-up revealed left internal carotid artery dissection and tandem occlusion of the left internal carotid artery and left middle cerebral artery. There was associated territorial ischemic infarction. The patient was found to have extensive intra and extra cranial vasculopathy including gross basilar dolichoectasia and a right-sided cervical internal carotid artery pseudoaneurysm. This case highlights the clinical significance of neurofibromatosis associated vasculopathy which can result in stroke.

Introduction

Neurofibromatosis type 1 (NF1), also known as von Recklinghausen disease, is an autosomal dominant multisystem genetic disorder with a prevalence of approximately 1 in 3000 [1]. It is one of the most common phakomatoses, a neurocutaneous disorder involving structures which arise from embryonic ectoderm such as the skin and central and peripheral nervous system. Classic features include café au lait spots, neurofibromas, optic nerve gliomas and iris hamartomas (Lisch nodules) [2]. As the condition involves inactivation of a tumor suppressor gene, it is also associated with particular neoplasms such as pheochromocytoma, carcinoid tumors and rhabdomyosarcoma. Mortality is most commonly associated with malignant tumors and cardiovascular or cerebrovascular complications [3].

NF1 also predisposes to vasculopathies. Such vasculopathies include moyamoya arteriopathy, vascular ectasia or stenoses, cerebral aneurysms, arteriovenous malformations, renal artery stenoses, and coarctation of the aorta [4]. Vascular ectasia may include dolichoectasia which refers to both the pathological dilatation and elongation of a vessel. Dolichoectasia occurs when the arterial wall weakens due to

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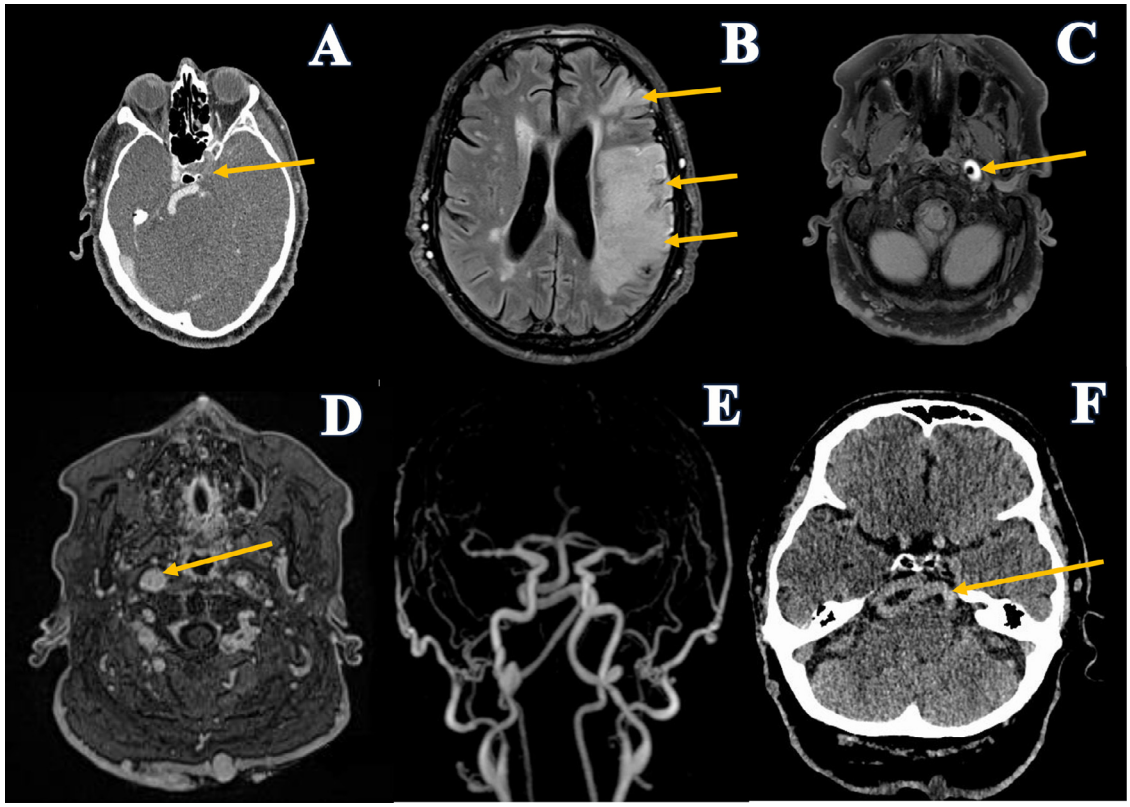

Fig. 1 – (A) Axial CTA showing cavernous left ICA occlusion. (B) Axial T2 FLAIR of left MCA territory infarction. (C) Axial T1-weighted image with left ICA dissection. (D) Axial T1 image showing pseudoaneurysm of the right ICA. (E) Coronal maximum intensity projection (MIP) magnetic resonance angiography representing generalized dolichoectasia. (F) Axial CT with basilar dolichoectasia.

deterioration of the vessel intima or media layer. It may be atherosclerotic, nonatherosclerotic or secondary to dissection. To classify as vertebrobasilar ectasia the basilar artery should be >4.5 mm in maximal diameter [5]. Smoker's criteria for vertebrobasilar dolichoectasia use the laterality, bifurcation height, and basilar artery diameter [6].

Dolichoectasia is an important imaging feature because it has a number of complications such as hemorrhagic or ischemic stroke, neurovascular compression syndrome, hydrocephalus, transient ischemic attack, and brainstem compression [7].

Cerebral aneurysm and pseudoaneurysm are also associated with NF1 and carry a risk of cerebral hemorrhagic stroke [4].

Case report

A 60-year-old gentleman with a known diagnosis of neurofibromatosis type 1 (NF1) presented with right sided hemiparesis, right sided facial palsy, and mixed aphasia. The stroke protocol pathway was initiated which included emergent CT head and CT angiography (CTA) with further assessment by MRI Brain and MR angiography (MRA).

Neuroimaging demonstrated acute left middle cerebral artery (MCA) territory infarction due to dissection of the left internal carotid artery (ICA) causing tandem occlusion of the left ICA and proximal M1 MCA (Figs. 1A-C). In addition, there was also an old right sided distal cervical ICA dissection with a large pseudoaneurysm (Fig. 1D).

Follow up imaging with MRI brain and MRA demonstrated features consistent with luxury reperfusion and laminar necrosis with hemorrhagic transformation in the left MCA territory.

CTA and MR Time of Flight imaging demonstrated widespread dolichoectasia (Fig. 1E). Of note, the basilar artery was particularly tortuous with a maximum diameter of 10 mm (Fig. 1F). Overall imaging features in keeping with widespread vasculopathy in association with NF1.

In this case the patient was unsuitable for thrombectomy and thrombolysis. Treatment with aspirin and high dose statin was commenced and the patient was managed in a specialist stroke unit.

Discussion

NF1 vasculopathy includes vascular stenosis or occlusions, aneurysms, arteriovenous fistulae and Moya-Moya like appearance [8]. This case demonstrates widespread vasculopathy associated with NF1 in the form of vertebrobasilar dolichoectasia, right internal carotid pseudoaneurysm

formation and acute left internal carotid dissection with tandem occlusion. The likely pathogenesis of NF1-associated vasculopathy is deficiency of neurofibromin, the protein product of the *NF1* gene which is important in maintaining integrity of the endothelial cell layer [9].

No specific guidelines for treatment of dolichoectasia exist at present and intervention is limited to symptomatic cases [10,11]. Similarly, no clear guidelines exist on treatment in the case of internal carotid pseudoaneurysms; however, options range from surgical or endovascular coiling or clipping to conservative management [12].

While no specific guidelines exist for treatment of cerebral vasculopathy in patients with NF1, further research in this area is recommended given the morbidity and mortality associated with these vascular abnormalities.

Author contributions

FD: study concept and design, first and subsequent drafts, literature review, neuroimaging discussion. AB: study concept and design, first and subsequent drafts, literature review, critical review of manuscript for intellectual content. EK: study concept and design, neuroimaging discussion, critical review of manuscript for intellectual content. SM: study concept and design, critical review of manuscript for intellectual content.

Patient consent

Written informed consent for this case report was obtained from the patient's next of kin.

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