Cranial nerve palsy in diabetes: ‘Hunt’ for the diagnosis

Abstract
A 55-year-old diabetic woman presenting with right sixth nerve palsy was diagnosed initially as having diabetic cranial neuropathy. Worsening headache and reported blurring of the right optic disc margin warranted further evaluation. CT scan of the brain was normal and a diagnosis of idiopathic intracranial hypertension was made. Her headache worsened and a partial pupil involving third nerve palsy evolved, at which point she was referred to our institution. Cranial MRI revealed features suggestive of Tolosa-Hunt syndrome and she responded dramatically to steroid therapy. While third nerve palsy is the most common cranial neuropathy in diabetic patients, sixth nerve palsy merits a wide array of differential diagnoses. A gadolinium-enhanced MRI of the brain is the preferred imaging modality for evaluating such patients, before branding them as having diabetic cranial neuropathy. Copyright © 2013 John Wiley & Sons.

Introduction
Neuropathy is an important complication of diabetes with a reported prevalence of around 50% for patients with 25 years of diabetes. While the vast majority of such patients have distal symmetrical neuropathy, some patients develop focal and multi-focal neuropathies, including cranial nerve palsies. It is important for the clinician to think about a wide variety of differential diagnoses in patients with diabetes presenting with cranial nerve palsy, as there are significant implications in treatment and prognosis depending on the cause. We report a case of an apparently straightforward diabetic cranial neuropathy but a ‘hunt’ for the diagnosis led to targeted treatment with prognostic implications.

Case report
A 55-year-old woman, with a two-year history of well-controlled type 2 diabetes, presented to her general practitioner with headache and clinical signs consistent with right sixth nerve palsy. A provisional diagnosis of diabetic cranial neuropathy was considered with plans for a conservative line of management. However, her headache progressively worsened and she was referred to a neurologist. Cranial unenhanced CT scan was unremarkable. The consulting neurologist made a provisional diagnosis of suspected idiopathic intracranial hypertension (IIH) due to reported blurring of the right disc margin. A cerebrospinal fluid analysis with opening pressure was not documented. Acetazolamide was prescribed with no remission from headaches, at which point she was referred to our institution.

Examination of her eyes revealed right sixth and pupil involving partial third nerve palsy. Optic fundi revealed blurring of the right disc margins. Visual acuity and fields were normal. The rest of the neurological examination was normal. Cranial gadolinium-enhanced MRI revealed a normal brain parenchyma. An enhancing soft tissue mass of size 1.5x1.3cm was seen involving the right orbital apex, superior orbital fissure and cavernous sinus (Figure 1a).

Vasculitic screen, tuberculosis, sarcoidosis and lymphoma work-up were negative. A diagnosis of Tolosa-Hunt syndrome was made. Steroid therapy (methyl prednisolone 0.75mg/kg/day) was instituted with dramatic resolution of headaches. Glycaemic control was optimised and steroid taper was instituted after two weeks. Her eye movements normalised by four weeks. A follow-up MRI of orbits after 12 weeks revealed complete resolution of the mass (Figure 1b). Follow up one year later showed no recurrence of the condition.

Discussion
Ophthalmoparesis in a diabetic patient is the result of microvascular
ischaemia and is often painful. Diabetic cranial neuropathies usually involve the third, fourth and sixth cranial nerves. The oculomotor nerve is more frequently affected in diabetes than its counterparts. In a large retrospective study of 8150 hospitalised diabetic subjects, isolated third nerve palsies accounted for the majority of patients with cranial nerve palsy, followed by seventh and sixth nerve in that order. Thus, sixth nerve palsy in a diabetic patient merits consideration of a wide variety of differential diagnoses before being labelled as ‘diabetic cranial neuropathy’. Unilateral or bilateral sixth nerve palsy in IIH is a non-localising effect of intracranial pressure. The involvement of oculomotor or trochlear nerves is seen only rarely in this condition. The hallmark of the disease is papilloedema, which is often striking. Diagnostic confusion arose in this patient because of the blurred nasal margins of the right disc. While papilloedema in IIH is almost always symmetrical, 10% of patients can present with unilateral findings and this can lead to an erroneous diagnosis. An unenhanced CT scan may miss important abnormalities of significance, as was seen in this patient. Gadolinium-enhanced MRI of the brain is the preferred test. Classical MRI features of IIH have been described in the literature. However, MRI done in our patient did not reveal any of these findings.

Tolosa-Hunt syndrome has been characterised by the Headache Classification Subcommittee of the International Headache Society as a syndrome of episodic orbital pain associated with paralysis of one or more ocular motor nerves (third, sixth or fourth) that usually resolves spontaneously but tends to relapse and remit. The aetiology is unknown and granulomatous inflammation of the cavernous sinus is the characteristic feature of the disease. This syndrome of painful ophthalmoplegia may be caused by any process exerting a mass effect on the cavernous sinus including tuberculosis (especially in developing countries), sarcoidosis or lymphoma. In addition, cases of Tolosa-Hunt syndrome have been reported in patients with systemic lupus erythematosus. Hence, it is imperative to screen for the above conditions before a diagnosis of Tolosa-Hunt syndrome is considered. The diagnosis in our patient became more apparent when third nerve palsy was additionally noted. Whether partial third nerve palsy was missed during the initial evaluation or this evolved later was not known to us. Enhancing soft tissue lesion within the cavernous sinus, increase in size and lateral bulging of the anterior cavernous sinus contour, internal carotid artery narrowing, extension towards the superior orbital fissure and orbital apex involvement are the imaging features of the syndrome. The differential diagnosis of headache syndromes and cranial nerve palsies in patients with diabetes can often be challenging. It has to be emphasised that a detailed history, thorough clinical examination and focused investigations are essential in the management of such patients. The importance of establishing the correct diagnosis in a given patient cannot be overemphasised. Although spontaneous remissions are known in Tolosa-Hunt syndrome, the clinical course and pain relief can be optimised with steroid therapy. A dramatic response to steroid therapy is the usual outcome, often within 24 hours, as was seen in our patient.

Declaration of interests
There are no conflicts of interest declared.

Patient consent
Informed patient consent has been obtained.

References