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Multiple cranial nerve palsies associated with type 2 diabetes mellitus

Singh N P, Garg S, Kumar S, Gulati S

ABSTRACT

Although isolated cranial nerve palsies are common in patients with diabetes mellitus, multiple simultaneous cranial neuropathies are rare. We report a 48-year-old man, a known case of diabetes mellitus, who presented with facial palsy, foot drop and painful ophthalmoplegia of the left eye. The initial differential diagnosis included diabetic polyneuropathy, septic cavernous sinus thrombosis, mucormycosis and the Tolosa Hunt syndrome. Magnetic resonance (MR) imaging findings were consistent with those of the Tolosa Hunt syndrome. The patient had a remarkable complete resolution of his ophthalmoplegia after four weeks of steroid treatment, with repeat MR imaging showing resolution of the initial changes.

Keywords: cranial nerve palsy, diabetes mellitus, diabetic neuropathy, ophthalmoplegia, Tolosa Hunt syndrome

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INTRODUCTION

Tolosa Hunt syndrome (THS) is relatively rare, with a reported incidence of 1-2 cases/million[1]. It represents only 2.9%-3.4% of cases of painful ophthalmoplegia. In a patient with diabetes mellitus, the causes of isolated cranial nerve palsies range from diabetic mononeuropathy to potentially fatal cavernous sinus thrombosis[2]. Although the association of THS with type 1 diabetes mellitus has been described[3], to the best of our knowledge, this is the first case of Tolosa Hunt syndrome in type 2 diabetes mellitus with documented past facial nerve palsy due to diabetic neuropathy.

CASE REPORT

A 48-year-old right-handed man, a known case of diabetes mellitus, presented with a ten-day history of pain in the left retro-orbital region associated with left facial paraesthesia, diplopia and left ptosis. He had a medical history of acute onset left infranuclear facial palsy and right foot drop eight months prior to the presentation. Investigation at that time revealed his diabetic status for the first time. Nerve conduction studies established diabetic neuropathy as a cause of his neurological deficits. Magnetic resonance (MR) imaging of the brain done at that time was essentially normal. He was put on oral hypoglycaemic drugs (glimepiride 2 mg and metformin SR 1,000 mg/day) with a fairly controlled diabetic status ever since. There was no fever, blurring of vision or redness of eye. He was a non-smoker and was not in habit of drinking alcohol.

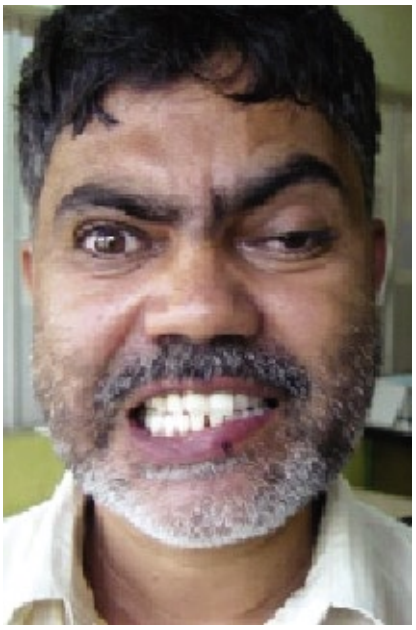


Fig. 1 Clinical photograph shows left ptosis and left infranuclear facial palsy. [Published with the patient's written consent].

On examination, he did not appear toxic and was afebrile. There was mild periorbital oedema, left ptosis (Fig. 1) and complete palsies of oculomotor, trochlear, and abducens nerves on the left side (Fig. 2).There was no nasal discharge of black pus, conjunctival chemosis or altered sensorium. The left pupil was fixed and dilated (Fig. 3). There was no orbital bruit. Visual acuity was 6/6 in both eyes

Nephrology Division
Maulana Azad Medical College
New Delhi 110002
India

Singh N P, MD, FIACM, MNAMS
Professor of Medicine and Head

Department of Medicine

Garg S, MBBS, MD
Junior Specialist

Kumar S, MBBS, MD
Postgraduate Student

Gulati S, MBBS, MD
Senior Resident

Correspondence to:
Dr Sachin Kumar
Tel: (91) 11 2323 2400/3400
Fax: (91) 11 2321 5510
Email: drkumarsachin@yahoo.com

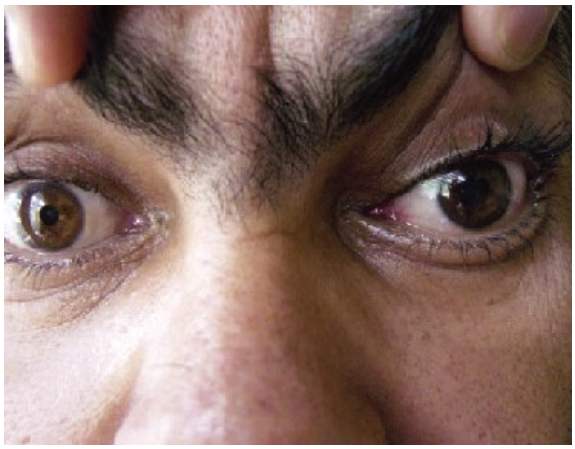


Fig. 2 Clinical photograph shows complete palsies of the left oculomotor, trochlear and abducens nerves.

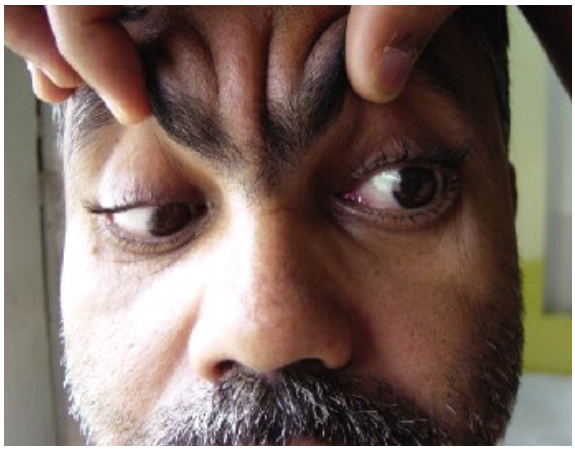
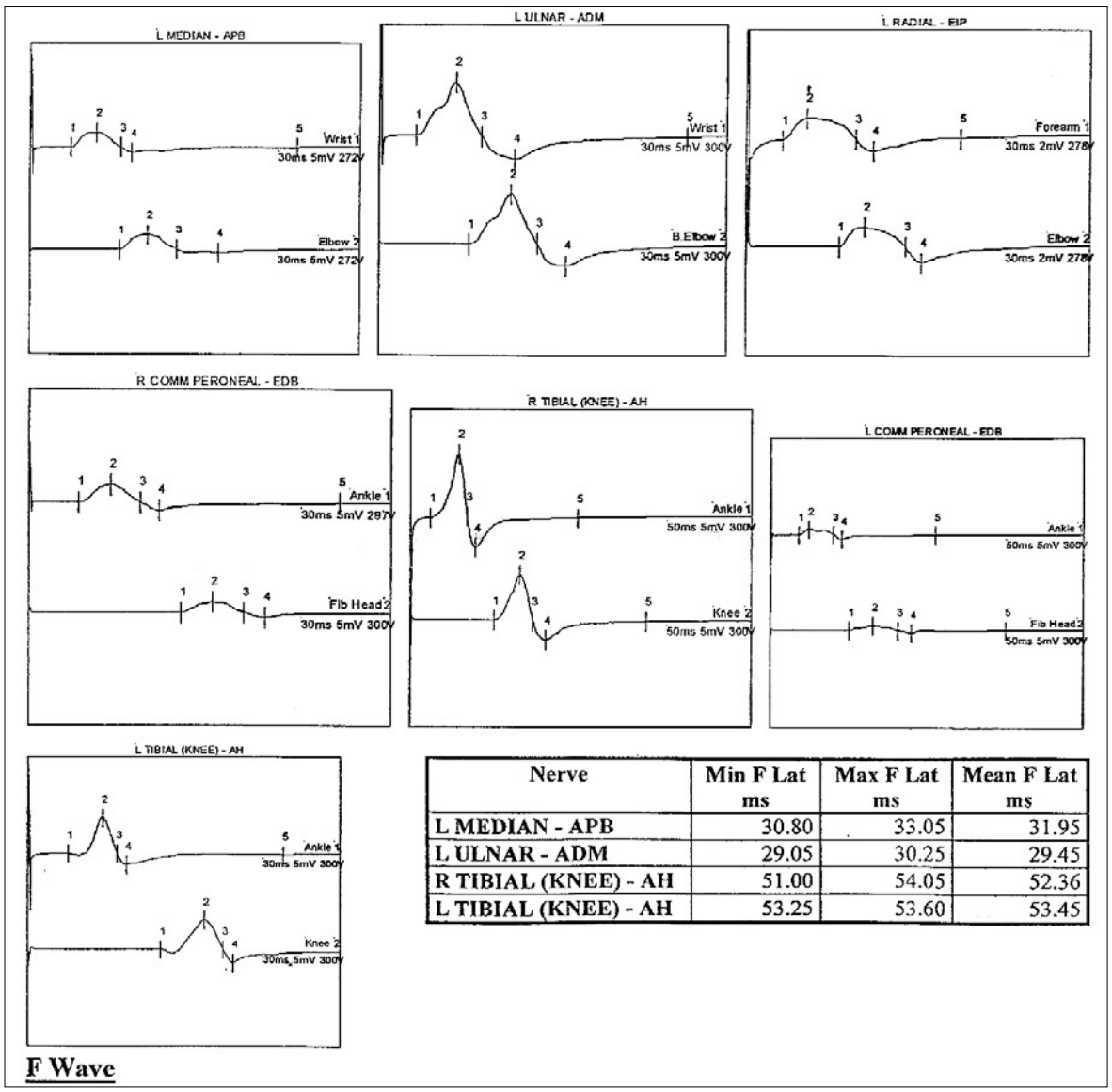


Fig. 3 Clinical photograph shows a fixed and dilated left pupil suggestive of complete (non pupil sparing) oculomotor nerve palsy.



Nerve	Min F Lat ms	Max F Lat ms	Mean F Lat ms
L MEDIAN - APB	30.80	33.05	31.95
L ULNAR - ADM	29.05	30.25	29.45
R TIBIAL (KNEE) - AH	51.00	54.05	52.36
L TIBIAL (KNEE) - AH	53.25	53.60	53.45

Fig. 4 Nerve conduction studies of common peroneal nerves show bilateral absence of F waves.

and visual fields were full. There was complete loss of touch, pain and temperature sensation in the distribution of the ophthalmic branch of left trigeminal nerve. The left corneal reflex was absent. Left infranuclear facial palsy (Fig. 1) was present. Mild right foot drop was also evident.

Fundoscopy revealed bilateral non-proliferative early diabetic retinopathy. The ankle jerks were absent. There was loss of vibratory sensation over the great toes and loss of all modalities of sensation including fine touch, pain and temperature up to the knee, suggesting bilateral symmetrical distal sensorimotor diabetic neuropathy. There were no trophic ulcers or deformities in the foot apart from the right foot drop. All the peripheral pulses were equally palpable.

His fasting blood glucose was 11.1 mmol/L with an HbA1c of 7.2% (9.9 mmol/L). A review of his past medical records showed poorly-controlled fasting blood sugar levels in the range of 8-10 mmol/L. The following investigations were normal or negative: complete blood count, blood urea, serum electrolytes, lipid profile, serum B12 level, liver function, thyroid function, serum Venereal Disease Research Laboratory (VDRL), serum angiotensin converting enzyme (ACE), prothrombin time, partial thromboplastin time, autoimmune profile including anti-neutrophil cytoplasmic antibodies, cardiolipin and phospholipid antibodies, chest radiograph, cerebrospinal fluid analysis and unenhanced computed tomography (CT) of the brain.Human immunodeficiency virus (HIV) antibody screening test was non-reactive. Erythrocyte sedimentation rate (ESR) was 33 mm/hr at initial presentation and 20 mm/hr 48 hrs after starting the therapy. Mantoux test was positive at 10 mm. The 24-hour urinary protein excretion rate was 600 mg/24 hour with a creatinine clearance of 96 ml/min.

Nerve conduction studies of common peroneal nerves revealed reduced sensory nerve action potentials (SNAP), poorly-formed amplitude and slow conduction velocities. Low amplitude motor responses and slight reduction of the amplitudes were also seen in the common peroneal nerves. Bilateral common peroneal F waves were absent (Fig. 4). Overall, these findings were consistent with diabetic neuropathy. Left blink reflex showed efferent pathway defect.

MR imaging of the brain revealed mild enlargement of the left cavernous sinus. The homogeneous soft tissue within the sinus appeared isointense on fluid attenuated inversion recovery (FLAIR) and T2-weighted images (Fig. 5). The abnormal tissue in the region of left cavernous sinus had a marked increase in signal intensity after intravenous gadolinium injection. This homogeneous contrast enhancement that extended to the orbital apex was highly suggestive of a non-specific inflammatory aetiology, consistent with the Tolosa Hunt syndrome (Figs. 6 & 7).

He received intravenous methylprednisolone 1 g daily for three days, then oral prednisolone 40 mg daily. There was a dramatic response, and the retro-orbital pain subsided completely within 48 hours of starting the therapy. There was also improvement in his ptosis. Follow-up after four weeks showed complete

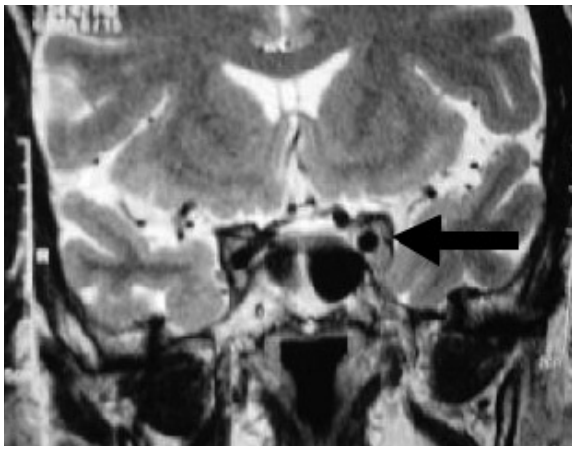


Fig. 5 Coronal T2-W MR image shows isointense homogeneous soft tissue (arrow) within the left cavernous sinus.

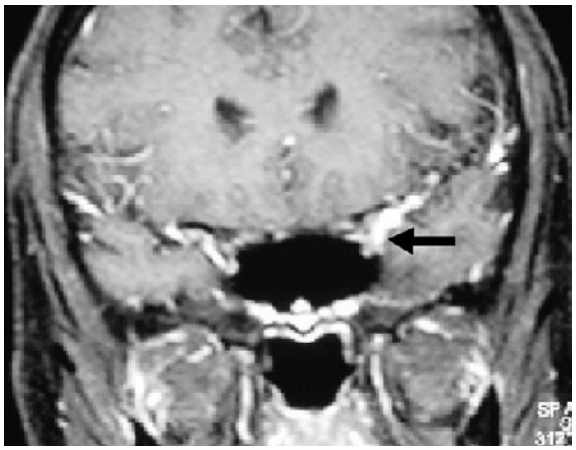


Fig. 6 Contrast-enhanced coronal T1-W MR image shows homogeneous enhancement in the region of the left cavernous sinus extending to the orbital apex, highly suggestive of a non-specific inflammatory aetiology, consistent with the Tolosa Hunt syndrome.

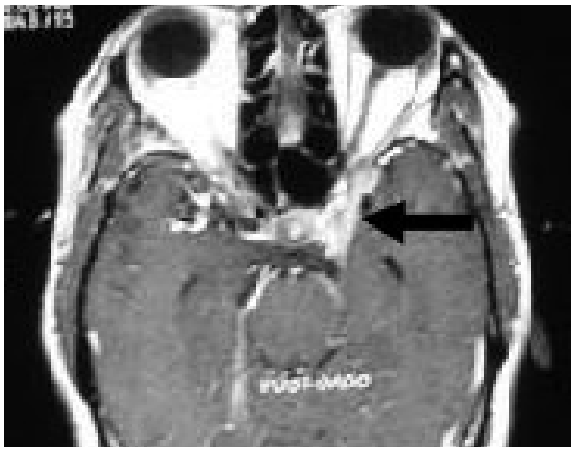


Fig. 7 Contrast-enhanced axial T1-W MR image shows homogeneous enhancement in the region of the left cavernous sinus extending to the orbital apex (arrow), highly suggestive of a non-specific inflammatory aetiology, consistent with the Tolosa Hunt syndrome.

resolution of his ptosis and ophthalmoplegia. Repeat MR imaging was essentially normal. However, his left facial palsy and mild foot drop still persisted.

DISCUSSION

THS is a complex of periorbital pain associated with ipsilateral ophthalmoplegia, oculosympathetic dysfunction, and sensory loss in the first division of the trigeminal nerve. The syndrome is essentially caused by idiopathic granulomatous inflammatory process. To date, however, no clear aetiology has been identified, and the diagnosis remains one of exclusion.

The International Headache Society defined the diagnostic criteria of THS in 1988 to include at least one episode of orbital pain for an average of eight weeks if untreated, with associated paresis of one or more of the third, fourth, and sixth cranial nerves, and exclusion of other causes by neuroimaging and (optional) carotid angiogram. The associated pain must be relieved within 72 hours after the initiation of corticosteroid therapy[4]. The differential diagnosis is quite broad (Table I).

The clinical course of THS is variable. Spontaneous remissions may occur, but recurrences have been reported in up to 39% of cases[5]. Considering the clinical presentation and laboratory findings in our case, the closest differential diagnoses were diabetic polyneuropathy, sarcoidosis and THS. Simultaneous involvement of multiple cranial nerves, especially trigeminal and pupillary involvement, excluded diabetic polyneuropathy. Normal ACE level, normal chest radiograph, a positive Mantoux and absence of any systemic involvement help to rule out sarcoidosis, although isolated cases of neurosarcoidosis presenting as cavernous sinus syndrome has been reported[6]. However, meningeal enhancement on MR imaging, a common finding in neurosarcoidosis was not present in our case[6]. In cases of painful ophthalmoplegia, the finding on MR imaging of cavernous sinus enlargement, with the herein described signal and extension characteristics and rapid resolution with corticosteroid treatment, is highly suggestive of THS[7]. We also excluded rare but potentially fatal complications seen in diabetic patients like mucormycosis and cavernous sinus thrombosis, especially the former in which steroid therapy is contraindicated.

Biopsy of the lesion would have been a gold standard ideal. However, the technical difficulty of cavernous sinus region biopsy precludes such a procedure. Nevertheless, the subsequent clinical improvement after a trial of steroids and resolution on MR imaging reinforces our management strategy. This highlights the importance of ruling out local pathologies apart from diabetic polyneuropathy in the appropriate clinical settings. The case presented exemplifies how careful use of laboratory tests and the clinical examination can guide the clinician through a vast array of aetiologies responsible for painful ophthalmoplegia. The aetiological differential diagnosis of painful ophthalmoplegia is extensive and include vascular, neoplastic, inflammatory and infectious conditions. A careful evaluation of painful ophthalmoplegia can lead to prompt recognition of serious disorders that, if left untreated, can be associated with significant morbidity or mortality. Inflammatory conditions such as THS are highly responsive to corticosteroids, but should be diagnoses of exclusion.

Table I. Differential diagnosis of the Tolosa Hunt syndrome.

Trauma
Vascular
• Carotid artery aneurysm
• Carotid-cavernous fistula
• Carotid-cavernous thrombosis
Neoplasm
Primary intracranial
• Pituitary adenoma
• Meningioma
• Neurofibroma
• Gasserian ganglion neuroma
Metastatic
• Nasopharyngeal
• Lymphoma
• Carcinomatous metastases
Inflammatory/infectious
• Bacterial: sinusitis, mucocoele, periositis
• Viral: Herpes zoster
• Fungal: Mucormycosis
• Spirochetal: Syphilis
• Mycobacterial
• Sarcoidosis
• Wegener's granulomatosis
Diabetic ophthalmoplegia
Migraine

REFERENCES

1. Iaconetta G, Stella L, Esposito M, Cappabianca P. Tolosa-Hunt syndrome extending in the cerebello-pontine angle. Cephalalgia 2005; 25:746-50.
2. Cheng AC, Sinha AK, Kevau IH. Superior orbital fissure syndrome in a latent type 2 diabetic patient. PNG Med J 1999; 42:10-12.
3. Cesareo R, Reda G, Verallo O. [Tolosa Hunt syndrome and autoimmune polyglandular syndrome. A rare case report.] Minerva Endocrinol.1995; 20:149-52. Italian.
4. Hunt WE, Brightman RP. The Tolosa-Hunt syndrome: a problem in differential diagnosis. Acta Neurochir 1988; 42:248-52.
5. Hannerz J. Recurrent Tolosa-Hunt syndrome: a report of ten new cases. Cephalalgia 1999; 19 Suppl:33-5.
6. Zarei M, Anderson JR, Higgins JN, Manford MR. Cavernous sinus syndrome as the only manifestation of sarcoidosis. J Postgrad Med 2002; 48:119-21.
7. Pascual J, Cerezal L, Canga A, et al. Tolosa-Hunt syndrome: focus on MRI diagnosis. Cephalalgia 1999; 19 Suppl:36-8.