Tolosa-Hunt syndrome as initial presentation of Systemic Lupus Erythematosus

Kang-Po Lee[1], Pi-Shan Sung[1,2], Wan-Ju Annabelle Lee[3,4]

Abstract

Purpose: Case presentation of newly diagnosed systemic lupus erythematosus (SLE) presenting initially as Tolosa-Hunt syndrome (THS).

Study Design: Retrospective clinical case.

Method: Case report.

Results: A healthy young man developed acute binocular diplopia within 2 days without other neurological deficits. Bilateral 6th cranial nerve palsy was observed with general reduction in the visual field test. Emergent brain magnetic resonance image (MRI) was performed, which revealed severe inflammation in the cavernous sinus, superior orbital fissure, and apex of the orbit. No cavernous thrombosis or intracranial lesion was shown in the MRI. THS was diagnosed and the patient's CN 6 palsy recovered quickly after corticosteroid treatment. However, severe anaemia was discovered during admission (Hb=6.0), so the patient was evaluated by profound laboratory tests, which revealed SLE.

Conclusion: With painful ophthalmoplegia, cavernous sinus syndrome is highly suspected. THS is one of the differential diagnoses for cavernous sinus syndrome. THS is a rare disease, recognized by the National Organization for Rare Disorders, and characterized by inflammatory changes in the cavernous sinus, superior orbital fissure and/or orbital apex under image study. The inflammatory changes are mostly idiopathic, but secondary causes such as sarcoidosis or other autoimmune diseases need to be ruled out. Physicians should be aware of possible underlying conditions, such as immunosuppressed status as in SLE, as the true cause of THS.

Keywords: Tolosa-Hunt syndrome, diplopia, brain MRI, painful ophthalmoplegia, haemolytic anaemia, SLE.

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From the [1]Department of Neurology, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan; [2]Institute of Clinical Medicine, College of Medicine, National Cheng Kung University, Tainan, Taiwan; [3]Department of Ophthalmology, Chi Mei Medical Center, Tainan, Taiwan; [4]Institute of Clinical Pharmacy and Pharmaceutical Sciences, College of Medicine, National Cheng Kung University, Tainan, Taiwan.

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Correspondence to: Wan-Ju Annabelle Lee, MD, PhD.
E-mail: wanjuleetw@gmail.com

INTRODUCTION

THS is also known as "painful ophthalmoplegia syndrome". It is caused by nonspecific inflammation of the cavernous sinus or superior orbital fissure. The diagnostic criteria were refined in 2004 by the International Headache Society, such that granuloma, demonstrated by MRI or biopsy is required for diagnosis[1,2]. Ophthalmoplegia occurs when the III, IV, and VI cranial nerves are compressed by granulomatous inflammation. Constant orbital pain is caused by the inflammation within the cavernous sinus or along the superior orbital fissure. Forehead paresis is due to involvement of the superior division of the trigeminal nerve (CN V1). Pupillary dysfunction may present, due to the involvement of sympathetic nerve fibres from the internal carotid artery

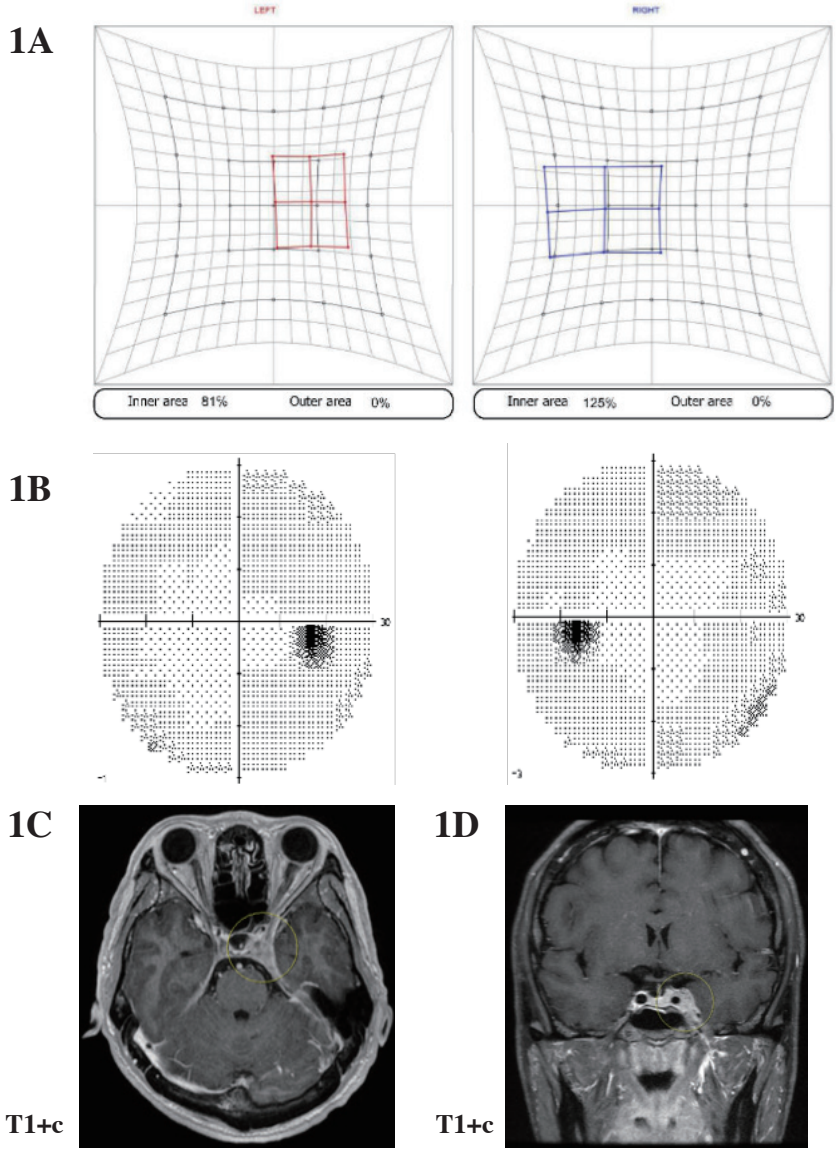

Figure 1. 1A: Hess chart revealed bilateral 6th cranial nerve palsies.
1B: Visual field showed general reduction without obvious scotoma or visual field defects.
1C-1D: Inflammation involving left orbital apex, along left cavernous sinus, left Meckel cave, and in left foramen ovale (yellow circles).

or parasympathetic fibres surrounded by the oculomotor nerve[3]. Autoimmune haemolytic anaemia (AIHA) due to systemic lupus erythematosus (SLE) is a rare cause of anaemia, possibly due to autoantibodies, T lymphocytes, and deregulation of the cytokine network which can affect bone marrow erythropoiesis[4,5]. Here, we describe a case with no underlying disease, diagnosed by painful ophthalmoplegia as THS, and later diagnosed as AIHA with SLE. The simultaneous occurrence of the 3 conditions may give clues for further surveys of the currently unknown aetiology of THS.

CASE PRESENTATION

A 33-year-old male suffered from sudden onset of blurred and double vision while working in the office. His medical histories were unremarkable without recent trauma, travel, or weight loss. He had suffered intermittent headache for 1 year without other neurological symptoms. Left retro-orbital pain sometimes accompanied the headache. One month prior, he had experienced intermittent left temporal and vertex throbbing pain. On the day he developed acute diplopia he also felt bilateral retro-orbital pain upon touching the peri-orbital area. When he presented in the ophthalmic clinic, his best corrected visual acuity was 20/25 bilaterally. Normal intraocular pressures, normal anterior chamber and fundus were observed in both eyes. Corneal reflex and colour sense were normal in both eyes, too. The pupils were well refractive to light without relative afferent pupil defect. External examination revealed limited adduction of both eyes. Hess chart revealed severe limitation of the bilateral lateral rectus muscles (Fig1A). Visual field examination showed general signal reduction without obvious scotoma or defects (Fig1B). The remainder of the neurologic examination results were normal.

Admission laboratory examinations showed macrocytic anaemia (Hb 6.0, MCV 104.8). Jaundice was noted with mild icteric sclera. Lumbar puncture was performed immediately, which revealed neither infection nor elevated intracranial pressure. The brain MRI indicated prominent inflammation from the left orbital apex, along the left cavernous sinus, left Meckel cave, and in the left foramen ovale (Fig1C-1D). Under the impression of THS, he received intravenous corticosteroid treatment (methylprednisolone 1g/day) for 3 days and tapered gradually. The extraocular symptoms and binocular diplopia improved soon after corticosteroid treatment.

The following studies revealed hyperbilirubinemia (Bilirubin-Total 2.6 & Bilirubin-Direct 0.3), with normal liver function (AST/ALT/Alk-P/GGT 30/15/65/17). Further survey revealed positive ANA (1:160 speckled type), Cardiolipin-Ab (aCL) (IgG) (42.8 GPL-U/mL) and positive AntiDNA (17.0IU/mL), low C3/C4 level (50.1/2.2 mg/dL). Persistent positive Anti-dsDNA and aCL were noted. Systemic lupus erythematosus and antiphospholipid antibody syndrome (APS) were diagnosed later in the rheumatologic outpatient clinic, according to 2019 EULAR/ACR criteria, with a total score of 10 (Autoimmune hemolysis: 4, aCL: 2, low C3 and C4: 4).

One month after pulse therapy, the patient had had no recurrence of diplopia. Nevertheless, the patient was prescribed oral quinine and low-dose corticosteroid due to SLE. Six months later, the follow-up brain MRI showed evidence of chronic cavernous sinus thrombosis, possibly due to antiphospholipid antibody syndrome; therefore lifelong anti-coagulant was given. Diplopia was not observed again during 9 months of regular follow-up.

DISCUSSION

Painful ophthalmoplegia is an awkward situation that challenges not only the patient but also their physician. Often, the patient may have underlying diseases such as hypertension or diabetes mellitus or other vascular risk factors. It may involve the extraocular muscles, the isolated nerves, the orbital apex or the cavernous sinus. There is a variety of aetiologies ranging from vascular (microvascular as DM/HTN, giant cell arteritis, aneurysm such as posterior communicating artery (pCOM) aneurysm, carotid-cavernous fistula and cavernous sinus thrombosis), neoplastic (nasopharyngeal cancer involving the cavernous sinus, metastases to the dura), and inflammatory (THS, SLE, sarcoidosis, orbital pseudo-tumour) to trauma related conditions (orbital floor fracture and concussion).

THS is characterized clinically by extraocular muscle paralysis with retro-orbital pain and granuloma-like lesion involving the cavernous sinus and/or orbital sinus under MRI[6]. The underlying pathogenesis remains

unknown but current focus is on non-specific inflammatory processes possibly due to autoimmune related conditions. Steroid responsive disease with presentation of inflammatory tissue over the cavernous sinus and clinical painful ophthalmoplegia is characteristic. However, the typical image may invite other possible explanations, such as sarcoidosis or lymphoma, which need to be excluded.

SLE may have neuropsychiatric manifestations, typically delirium, seizure and psychosis. Previous studies have suggested cavernous sinus syndrome in SLE may be due to cranial nerve ischaemia, venous sinus thrombosis or arterial occlusion due to vasculitis[4,7]. Previous studies have suggested complement level may be a good parameter of such a possibility[8]. In such cases, MRI may show non-opacification of the ophthalmic vein or even the cavernous sinus. In our case, MRI showed no evidence of venous sinus thrombosis or infarction. Hence, those diagnoses were excluded.

A lupus erythematosus patient presenting with THS is extremely rare with only about 3 known case reports [4,9,10]. These cases were all already known, with lupus erythematous changes under disease modifying anti-rheumatic drugs, and all have clear dermatological manifestations. Intracranial hypertension was reported in 1 case but not the others. Two were female with an average age of 46.3.

Unlike the previous cases, our case is one of newly diagnosed SLE and painful ophthalmoplegia as his first sign. The patient had no definite rashes or skin lesions but did show haemolytic anaemia and was relatively young in comparison with earlier cases. Despite the above differences, all cases responded well to immunosuppressant therapy with no recurrence of disease.

In conclusion, our report may guide neurologists and ophthalmologists in the evaluation of painful ophthalmoplegia. We should not overlook the possibility of secondary causes. Our report illustrates a case with concurrent SLE, AIHA and THS. Further study could focus on the underlying autoimmune dysregulation of the 3 once thought independent diseases, and whether they have a confluent pathogenesis.

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