Tolosa-Hunt Syndrome with Unusual Clinical Courses

—Two Case Reports—

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Abstract

Two cases of Tolosa-Hunt syndrome with unusual clinical courses are described. The clinical onset of the first patient was typical, but was unresponsive to steroid hormone treatment. The symptoms resolved spontaneously after 1 year. Computed tomography (CT) and magnetic resonance (MR) imaging revealed enlargement of the affected cavernous sinus, which did not change after the symptoms resolved. The clinical presentation in the second patient included marked pupillary dilatation, a sign which is absent in the classical criteria. CT showed no abnormal findings, but MR imaging revealed a mass located in the medial side of the cavernous sinus extending to the lateral wall, which might have caused the pupillary dilatation. After steroid therapy the symptoms disappeared and MR imaging showed remarkable reduction of the mass in the cavernous sinus. Tolosa-Hunt syndrome usually responds promptly to steroid therapy and rarely manifests marked pupillary dilatation. Such variation in presentation adds to the difficulties in diagnosis and treatment of this disease of unknown etiology.

Key words: Tolosa-Hunt syndrome, computed tomography, magnetic resonance imaging, steroid hormone, internal ophthalmoplegia

Introduction

Tolosa-Hunt syndrome is a disease of unknown etiology characterized by six criteria: 1) a steady, gnawing, retro-orbital pain; 2) defects in the third, fourth, or sixth cranial nerves, or first branch of the fifth cranial nerve, with less common involvement of the optic nerve or sympathetic fibers around the cavernous carotid artery; 3) symptoms lasting days to weeks; 4) occasional spontaneous remission; 5) recurrent attacks; and 6) prompt response to steroid therapy.⁹⁾ Modern neuroimaging methods have also shown abnormal findings in the region of the cavernous sinus.^{3,5,8,10,11,13,14,16,17,19)} Tolosa-Hunt syndrome remains a diagnosis of exclusion from certain other conditions, including intracavernous aneurysm of the internal carotid artery, cavernous sinus thrombosis, invasive tumors from the paranasal sinus and sella turcica, neoplasms arising from structures within the cavernous sinus and overlying meninges,

and nonspecific inflammatory involvement of cranial nerves.^{3,6,11)}

Recurrent painful ophthalmoplegia may also be associated with Tolosa-Hunt syndrome. Tolosa¹⁸⁾ described a male patient with left-sided retro-orbital pain and ophthalmoplegia who died soon after an operation to explore the sella turcica. Necropsy found granulomatous tissue surrounding the left intracavernous carotid artery. Hunt *et al.*⁹⁾ also described six patients with remittent unilateral retro-orbital pain, extraocular palsies, and occasional supraorbital numbness or blindness that rapidly improved with corticosteroid therapy.

We describe two patients with Tolosa-Hunt syndrome whose clinical presentation was not completely typical and with non-uniform radiological findings.

Case Reports

Case 1: A 36-year-old male presented with a 3-day history of retro-orbital discomfort, diplopia, and

Fig. 1 Case 1. Pre- (left) and post-contrast CT scans (right) on admission, showing enlargement of the right cavernous sinus (right, arrow).

Fig. 3 Case 2. Pre- (left) and post-contrast CT scans (right) on admission, showing no abnormal findings.

Fig. 2 Case 1. T₂-weighted MR image (A) and T₁-weighted MR image with Gd-DTPA (B) on admission, showing enlargement of the right cavernous sinus (B, arrow). T₂-weighted MR image (C) and T₁-weighted MR image with Gd-DTPA (D) 1 year later, showing no reduction in the size of the enlarged right cavernous sinus (D, arrow).

Fig. 4 Case 2. T₂-weighted MR image (A) and T₁-weighted MR image with Gd-DTPA (B) on admission, showing a low-intensity mass in the left cavernous sinus (A, arrow) not enhanced by contrast medium (B, arrow). T₂-weighted MR image (C) and T₁-weighted MR image with Gd-DTPA (D) 10 days later, showing remarkable reduction in the size of mass in the cavernous sinus (arrow).

drooping of his right eyelid in November, 1992. Physical examination revealed restriction of ocular movements in all directions in the right eye, with normal pupillary reactions. His vision and fundi were normal on both sides. There was no objective sensory deficit on his face. His blood cell count, erythrocyte sedimentation rate, and other blood examinations were all within normal limits. Postcontrast computed tomography (CT) and magnetic resonance (MR) imaging revealed enlargement of the right cavernous sinus (Figs. 1 and 2A, B). Bilateral carotid angiography demonstrated no abnormalities.

Steroid therapy (oral prednisolone 60 mg daily) was started and continued for 1 month. The retro-orbital discomfort and ptosis resolved, but restriction of ocular movement persisted. His eye movement became normal completely 1 year later although MR imaging showed the enlarged right cavernous sinus was not reduced in size (Fig. 2C, D).

Case 2: A 52-year-old male was referred to our clinic in June, 1993 with headache on the left side. Physical examination, including brain CT, was normal. One day later he developed double vision, followed by

drooping of his left eyelid. On admission, he had complete third cranial nerve palsy on the left. Marked pupillary dilatation was observed and the light reflex was absent in the left eye, but his vision and fundi were normal on both sides. His hematological and blood chemistry parameters were within normal limits. Repeat CT of the brain found no abnormalities (Fig. 3), but MR imaging revealed an abnormal intensity area in the left cavernous sinus. T₂-weighted imaging revealed a low-intensity area within the abnormality (Fig. 4A). MR imaging with gadolinium-diethylenetriaminepenta-acetic acid (Gd-DTPA) also showed a non-enhanced lesion (Fig. 4B). Angiography showed no abnormal findings. High-dose steroid therapy with intravenous hydrocortisone (1000 mg) was given for 3 consecutive days. His headache subsided, and over the next 7 days his ocular movements became normal. However, his pupillary function remained impaired until 4 weeks after steroid therapy was started. Repeat MR imaging showed that the size of the mass had diminished remarkably (Fig. 4C, D).

Discussion

Tolosa-Hunt syndrome responds promptly to steroid therapy and usually starts to resolve within 48 hours.⁷⁾ A spontaneous cure also may occur within 8 weeks.¹⁾ Our first patient did not respond to steroid therapy and spontaneous cure only occurred after 1 year. Steroid therapy was discontinued after 1 month, although Hunt⁷⁾ recommended that treatment should be discontinued 2 weeks after the disappearance of pain, as there is nothing to be gained by long-term steroid therapy. This case was atypical in the ineffectiveness of steroid therapy and the long delay before spontaneous cure developed.

Pupillary involvement occurred in about 25% of 300 cases of Tolosa-Hunt syndrome.¹⁾ The parasympathetic pupilloconstrictor fibers of the third cranial nerve and the sympathetic pupillodilator fibers in the pericarotid plexus may be involved.⁷⁾ However, depending on illumination levels, anisocoria may or may not be apparent and the loss of both sympathetic and parasympathetic fibers may be overlooked.⁸⁾ Therefore, remarkable pupillary dilatation in Tolosa-Hunt syndrome seems to be rare. Our second patient had marked pupillary dilatation in addition to extraocular paralysis. Granulomatous lesion in Tolosa-Hunt syndrome is usually located in the lateral wall of the cavernous sinus.⁴⁾ MR imaging demonstrated a large mass located in the medial side of the cavernous sinus extending to the lateral wall (Fig. 4A, B), which might have caused pupillary

dilatation by compression of the third cranial nerve from the medial side in the cavernous sinus.

Present neuroimaging techniques can demonstrate abnormal findings in the cavernous sinus of Tolosa-Hunt syndrome patients.^{3,5,8,13,15-17,19)} High resolution CT has shown soft tissue abnormalities in the cavernous sinus,^{11,14)} including asymmetric enlargement of the cavernous sinus, abnormal nodular enhancement of the prepontine cistern, and inflammatory soft tissue in the orbital apices. MR imaging of cavernous sinus abnormalities shows lesions isointense with muscle on short repetition time (TR)/echo time (TE) images, and isointense with fat on long TR/TE images. Enlargement of the affected cavernous sinus with extension of the pathological process into the orbital apex, which occurs in many cases, is suggestive of Tolosa-Hunt syndrome.¹⁹⁾ However, a few patients have normal MR imaging findings.¹⁹⁾

Definite diagnosis of Tolosa-Hunt syndrome remains difficult despite recent neuroimaging techniques because of the non-uniform changes observed. CT and MR imaging of the first patient showed enlargement of the cavernous sinus, while CT was normal and MR imaging showed some abnormal findings in the second patient. Additionally, CT and MR imaging showed contrast enhancement in the first but not the second patient. Similar variations have been reported in other patients.^{3,19)}

The variety of radiological observations in Tolosa-Hunt syndrome may reflect granulomatous inflammatory changes, preventing definite diagnosis and evaluation of the prognosis only from radiological images. Clinical recovery does not always coincide with the improvement of radiological images. After clinical recovery, CT and MR imaging of our first patient showed no reduction in the size of the enlarged cavernous sinus, but the lesion of the second patient diminished in size dramatically.

Surgical exploration to treat steroid-resistant Tolosa-Hunt syndrome has been reported,^{2,13)} but long-term observation is recommended after steroid therapy, if the possibility of aneurysm is excluded, because spontaneous cure can eventually be expected.

Another possibility is that Tolosa-Hunt syndrome is caused by immunological lupus erythematosus cells or even the presence of systemic lupus erythematosus.¹²⁾ If this hypothesis of immunological phlebothrombosis or periphlebitis is true, other immunosuppressants should be evaluated for treatment of steroid-resistant Tolosa-Hunt syndrome.

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