P1: KWW/KKL P2: KWW/HCN QC: KWW/FLX T1: KWW
GRBT050-126 Olesen- 2057G GRBT050-Olesen-v6.cls August 17, 2005 2:54

Chapter 126

Pain of Cranial Nerve and Cervical Nerve Origin Other Than Primary Neuralgias

Nikolai Bogduk

C2 OR C3 NERVE COMPRESSION

International Headache Society (IHS) code and diagnosis: 13.12 Constant pain caused by compression, irritation, or distortion of cranial nerves or upper cervical roots by structural lesions
WHO code and diagnosis: G44.848
Short description: Headaches caused by a lesion that compresses or otherwise compromises the C2 or C3 spinal nerves or their roots. The majority of reported cases, however, have involved the C2 nerve.
Other terms: C2 neuralgia

ANATOMY AND PATHOLOGY

The C3 spinal nerve occupies a typical intervertebral foramen and is vulnerable to any of the causes of foraminal stenosis: disc herniation, spondylosis, zygapophysial osteoarthrosis, etc. However, such disorders are relatively uncommon at the C2 to C3 level.

The C2 spinal nerve is relatively immune to entrapment or compression because, unlike the typical spinal nerves, it does not run in an intervertebral foramen. Consequently, it is not subject to the hazards of intervertebral disc herniation or spondylosis. Nor is it vulnerable to compression during extension injuries of the neck because the height of the articular pillars of C1 and C2 protects it from compression by the posterior arch of the atlas (6). The C2 nerve runs behind the lateral atlantoaxial joint, resting on its capsule (7,8) (Fig. 126-1). Inflammatory or other disorders of the joint may result in the nerve becoming incorporated in the fibrotic changes of chronic inflammation (40,64).

Otherwise, the C2 spinal nerve and its roots are surrounded by a sleeve of dura mater and a plexus of epiradicular veins, lesions of which can compromise the nerve. These include meningioma (51) and neurinoma (40), but most reported cases have involved vascular abnormalities ranging from single or densely interwoven dilated veins surrounding the C2 spinal nerve and its roots (39) to U-shaped arterial loops or angiomas compressing the C2 dorsal root ganglion (31,39,40). Nerves affected by vascular abnormalities exhibit a variety of features indicative of neuropathy, such as myelin breakdown, chronic hemorrhage, axon degeneration and regeneration, and increased endoneurial and pericapsular connective tissue (39). It is not clear, however, whether the vascular abnormality causes these neuropathic changes or is only coincident with them.

PATHOPHYSIOLOGY

The pathophysiology of C2 neuralgia is unknown, but the neuralgic quality of pain strongly implies a neurogenic basis. Ectopic, nociceptive impulses could be generated by ischemia or mechanical compression of the dorsal root ganglion.

CLINICAL FEATURES

IHS diagnostic criteria for compression of cervical nerves (Revised International Classification of Headache Disorders [ICHD II]) (30)

A. Constant and/or jabbing pain in the territory supplied by a cervical nerve, fulfilling criteria C and D.
B. Evidence of compression, irritation, or distortion of the appropriate nerve.
C. Pain and compression, irritation, or distortion occur simultaneously and correspond in location.
D. Pain is relieved by removal of the cause of compression, irritation, or distortion.

C2 neuralgia is a distinctive condition characterized by intermittent, lancinating pain in the occipital region

P1: KWW/KKL P2: KWW/HCN QC: KWW/FLX T1: KWW
GRBT050-126 Olesen- 2057G GRBT050-Olesen-v6.cls August 17, 2005 2:54

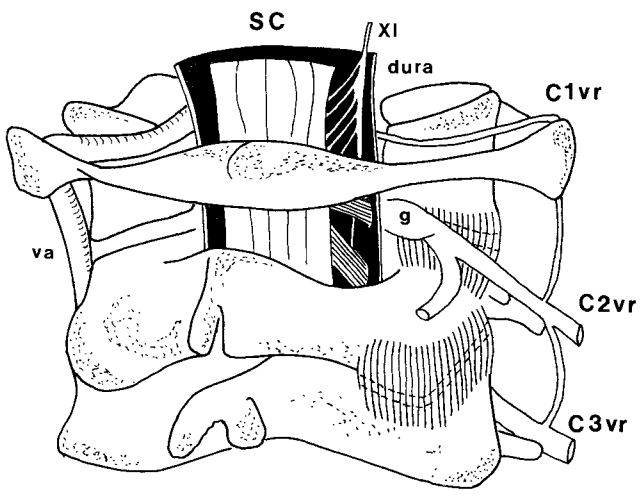

FIGURE 126-1. A posterior view of the right atlantoaxial region, showing the relationship of the C2 ganglion (*g*) and ventral ramus (*vr*) to the posterior aspect of the lateral atlantoaxial joint. The dural sac has been opened posteriorly to show the upper end of the spinal cord (*SC*), the C2 and C3 nerve roots, and the roots of the accessory nerve (*XI*). The vertebral artery (*va*) is shown on the left.

associated with lacrimation and ciliary injection. The pain typically occurs in association with a background of dull occipital pain and dull, referred pain in the temporal, frontal, and orbital regions. Most often, this latter pain is focused on the frontoorbital region but encompasses all three regions when severe. The distinguishing feature of this condition is a cutting or tearing sensation in the occipital region, which is the hallmark of its neurogenic basis.

The frequency of attacks varies from four to five per day to two to seven per week, alternating with pain-free intervals of days, weeks, or months (39,40). Approximately 75% of patients suffer the associated features of ipsilateral conjunctival and ciliary injection and lacrimation (39,40). Blurred vision, rhinorrhea, and dizziness are less common accompaniments. Neurologic examination is normal. In particular, hypoaesthesia in the territory of the trigeminal or cervical nerves is not present.

C2 neuralgia is distinguished from occipital neuralgia and referred pain from the neck by its neurogenic quality, its periodicity, and its association with lacrimation and ciliary injection. The latter association has attracted the appellation of clusterlike headache (51).

The cardinal diagnostic feature is complete relief of pain following local anaesthetic blockade of the suspected nerve root, typically the C2 spinal nerve, but occasionally the C3 nerve. These blocks are performed under radiologic control and employ discrete amounts (0.6 to 0.8 mL) of long-acting local anaesthetic to block the target nerve selectively (40).

Plain radiographs, computed tomography (CT), myelo-CT, or myelography reveal no suggestion of these lesions. No provocative test reveals arterial lesions (39), but in most patients with venous lesions, challenge with 0.8 mg nitroglycerin provokes an attack of pain, and conversely, inhalation of 100% O_2 at 10 L/min for 5 minutes relieves the pain (39).

MANAGEMENT

There is no evidence that C2 neuralgia responds to pharmacotherapy (39). Surgery appears to be the only definitive means of treatment. Nerves entrapped by scarring may be liberated (64); meningiomas may be excised (51). With respect to vascular lesions, resection of the vascular abnormality alone does not reliably relieve the pain; resection or thermocoagulation of the nerve appears to be necessary to guarantee relief of pain (39). However, data on long-term outcomes after thermocoagulation have not been published.

ACUTE HERPES ZOSTER

IHS code and diagnosis: 13.15.1 Head or facial pain attributed to acute herpes zoster
WHO code and diagnosis: G44.881
Short description: pain in the head or face associated with acute herpes zoster infection

EPIDEMIOLOGY

Herpes zoster affects between one and three people per 1000 population per year (33,42,43,68). The disease can affect any age group but is more frequent in the elderly (42,66,68) and in patients who are immunocompromised (44,66).

ANATOMY AND PATHOLOGY

Herpes zoster is a disease of dorsal root ganglia characterized by a vesicular eruption in the affected dermatome. It is a reactivation of a latent infection by the varicella virus (58,66). The thoracic nerve roots are most commonly affected (66), but about 12% of presentations involve the cervical spinal nerves, and 13% involve the trigeminal nerve (68). The ophthalmic division is affected in 80% of trigeminal presentations. The pathology of the disease involves inflammation, hemorrhage, and necrosis of the affected ganglion and dorsal horn, with intranuclear inclusion bodies in satellite cells and ganglion cells (58). Pathologic changes may extend from the dorsal root ganglion into the spinal cord or into the peripheral nerve (98).

P1: KWW/KKL P2: KWW/HCN QC: KWW/FLX T1: KWW
GRBT050-126 Olesen- 2057G GRBT050-Olesen-v6.cls August 17, 2005 2:54

PATHOPHYSIOLOGY

The mechanism of pain is unknown but possibly involves ectopic discharges from the affected dorsal root ganglion cells (66).

CLINICAL FEATURES

IHS diagnostic criteria for herpes zoster (ICHD-II) (30)

A. Head or facial pain in the distribution of a nerve or nerve division and fulfilling criteria C and D.
B. Herpetic eruption in the territory of the same nerve.
C. Pain precedes herpetic eruption by <7 days.
D. Pain resolves within 3 months.

The onset of acute herpes zoster is usually heralded by pain that precedes the vesicular eruption by a few days. When the trigeminal or C2 ganglion is affected, the pain occurs in the forehead or occipital region; however, no practical method has been found to establish the diagnosis when pain is the only feature. The condition declares itself once the vesicular eruption occurs. In rare instances the geniculate ganglion can be affected, presenting with otalgia or facial pain before the eruption of vesicles in the external auditory meatus and palate (34).

The initial rash of zoster may mimic that of herpes simplex, and the two conditions can be confused (78,81). If required, the diagnosis can be established by polymerase chain reaction of fluid taken from the vesicles (78,81).

PROGNOSIS

The usual course of herpes zoster infection is that the vesicles dry out within about 1 week and heal within about 1 month (58,66). When the nasociliary nerve is affected, uveitis, keratitis, and iridocyclitis are complications that may threaten vision as well as cause ocular pain.

The cardinal complication is postherpetic neuralgia. Approximately 16% of patients continue to have pain at 6 months, and 5 to 10% still have pain at 12 months (42,43, 68,81).

MANAGEMENT

The mainstay of treatment has become the administration of oral antiviral agents, such as acyclovir, valacyclovir, or famciclovir. All three drugs reduce acute pain, speed rash healing, shorten the period of viral shedding, and shorten the duration of pain, compared with placebo (22,38,43, 44,103). Guidelines recommend that these drugs be used in patients of any age presenting with ophthalmic involvement within the first 72 hours after onset of rash, and in any patients with active zoster affecting the neck, limbs, and perineum (41,45). A newer agent, brivudine, has proved superior to acyclovir in reducing the period of new blister formation and shortening the period of acute pain (67).

Antiviral therapy also decreases the subsequent incidence of postherpetic neuralgia by about 80% (22,38,43, 44,103). Nevertheless, despite adequate therapy, 20% of patients continue to suffer pain (44).

Simple analgesics are not of proven benefit for the relief of pain (58,66). Tramadol, however, was superior to placebo in a controlled study (9), and tricyclic antidepressants can relieve residual pain when added to a regimen of antiviral agent (42). Furthermore, amitriptyline reduces the incidence of postherpetic neuralgia (10). Finally, systemic steroids have been used for acute herpes zoster, particularly ophthalmic herpes, but they have no demonstrable effect on reducing pain, although they do seem to help in improving quality of life (22,44,100,102).

Sympathetic nerve blocks are advocated by some, but the literature is devoid of sufficiently powerful controlled trials and remains divided (2,41,42,58,66,105). For patients with severe pain, one study has shown that epidural infusion of bupivacaine and methylprednisolone over 7 days is more effective than intravenous acyclovir combined with prednisolone (63). Epidural therapy also reduces the incidence of postherpetic neuralgia.

POSTHERPETIC NEURALGIA

IHS code and diagnosis: 13.15.2 Postherpetic neuralgia
WHO code and diagnosis: G44.847
Short description: Postherpetic neuralgia is a neuralgic pain that persists in the affected dermatome long after the vesicular eruption of acute herpes zoster has healed.

EPIDEMIOLOGY

About 16% of patients continue to have pain at 6 months after the onset of herpes zoster, and between 5 and 10% still have pain at 12 months (42,43,81). Risk factors for postherpetic neuralgia are severe or prolonged prodromal pain, moderate to severe acute pain, severe rash, and advanced age (11,43,44). More than 60% of patients older than 60 years develop pain, and up to 50% or more suffer pain lasting more than 1 year (66,96).

ANATOMY AND PATHOLOGY

The pathology of postherpetic neuralgia involves atrophy of the dorsal horn and cell loss, axon loss, and demyelination with fibrosis in the dorsal root ganglion (98). These changes appear to be specific for patients with pain, whereas demyelination and axon loss in the affected

P1: KWW/KKL P2: KWW/HCN QC: KWW/FLX T1: KWW
GRBT050-126 Olesen- 2057G GRBT050-Olesen-v6.cls August 17, 2005 2:54

peripheral nerve occur in patients both with pain and without pain (98).

PATHOPHYSIOLOGY

The pathophysiology of postherpetic pain is unknown but may involve central deafferentation rather than mechanisms in the peripheral nerves or sensory ganglia (66).

CLINICAL FEATURES

IHS diagnostic criteria for chronic postherpetic neuralgia (ICHD-II) (30)

A. Head or facial pain in the distribution of nerve or nerve division and fulfilling criteria C and D.
B. Herpetic eruption in the territory of the same nerve.
C. Pain precedes herpetic eruption by <7 days.
D. Pain persists after 3 months.

The pain is archetypical of neuralgia, characterized by constant burning and aching with superimposed jabs of shooting or lancinating pain. The skin of the affected dermatome is hypoaesthetic but may involve zones of hyperaesthesia from which attacks of pain may be triggered by light touch or brushing (96). Midthoracic dermatomes and the first-division trigeminal nerve are most commonly affected (96).

MANAGEMENT

Amitriptyline and related tricyclic antidepressants (nortriptyline, desipramine) have been the most widely used and most thoroughly studied agents for the treatment of postherpetic neuralgia. The odds ratio for these drugs having a beneficial effect is 0.15 (92), and the number needed to treat is between two and four (44). The recommended regimen (for amitriptyline) is to start with 10 mg at bedtime and progress to 25 mg to 150 mg as needed (5). However, only between 47% and 67% of patients respond (5,47,74).

Gabapentin has emerged as an effective agent (43,44). It reduces pain by 33% (70,74) and provides complete relief of pain in 16% of patients (74). For relief of pain the NNT was 3.2 (74). The recommended regimen is 300 mg three times a day, increasing to 1200 mg three times a day if required (79).

Topical capsaicin provides improvement in pain in between 15% and 30% of patients (5), and the odds ratio for relief of pain is 0.29 (92). Topical lignocaine is also effective, although the effect is only temporary (21,72,73,75).

Aspirin in diethyl ether has been shown to be effective, particularly in ophthalmic postherpetic neuralgia (13), but some authorities report disappointment with this therapy (42). Problems with risk of inhalation, fire hazard, and disposal limit its utility (42). Aspirin in chloroform is an alternative (46,97).

For pain resistant to tricyclics and gabapentin, authorities recommend opioids, such as oxycodone, morphine, or methadone (5,42,44,62,94). Morphine is more effective than tricyclics and placebo but is associated with a greater incidence of side effects such as constipation, nausea, dizziness, drowsiness, and dry mouth (69).

Intravenous lignocaine and intravenous morphine are both more effective than placebo for relieving pain (76) and might be used in an attempt to interrupt persistent pain unrelieved by other measures. Ophthalmic postherpetic neuralgia is relieved temporarily by somatic blocks but not by sympathetic blocks (96). Intrathecal methylprednisolone has been shown to be effective (50), but the risk of arachnoiditis tempers widespread enthusiasm for this intervention.

The evidence for topical nonsteroidal anti-inflammatory drugs (NSAIDs) is inconclusive (42), and oral NSAIDs afford little benefit (42). The selective serotonin reuptake inhibitors (e.g., zimelidine) have little effect on postherpetic neuralgia (41,95,99). Acupuncture is distinctly unsuccessful for postherpetic neuralgia (56).

Other options have not been vindicated by controlled trials but may be required for patients whose pain is resistant to established measures. Adding fluphenazine may improve the response in some patients not responsive to amitriptyline alone (58,66,88,96). Transcutaneous electrical nerve stimulation is palliative in some patients but response cannot be predicted (58,66,96). Other pharmaceutical options include amantadine, adenosine, baclofen, and haloperidol (42,60).

Various surgical interventions have been advocated for trigeminal postherpetic neuralgia, including trigeminal rhizotomy, avulsion, alcohol injection or cryocoagulation of the supraorbital nerve, alcohol injection of the trigeminal ganglion, and trigeminal tractotomy, but none of these procedures has been found to work consistently or to achieve prolonged relief of pain (58,66). Thalamic stimulation is claimed to offer excellent pain relief in properly selected patients (58), and approximately 70% of patients with ophthalmic neuralgia are said to benefit long term from nucleus caudalis DREZ lesions (3) or stereotactic nucleotomy (80).

PAINFUL OPHTHALMOPLEGIA

IHS code and diagnosis: 13.16 Tolosa-Hunt syndrome
WHO Code and diagnosis: G44.850
Short description: episodic orbital pain associated with paralysis of one or more of the third, fourth, and/or sixth cranial nerves, which usually resolves spontaneously but tends to relapse and remit
Other terms: *Painful ophthalmoplegia* is a generic term that systematically embraces conditions that have

P1: KWW/KKL P2: KWW/HCN QC: KWW/FLX T1: KWW
GRBT050-126 Olesen- 2057G GRBT050-Olesen-v6.cls August 17, 2005 2:54

previously been referred to as *superior orbital fissure syndrome*, *orbital apex syndrome*, *cavernous sinus syndrome*, *parasellar syndrome*, *Collier syndrome,* and *Tolosa-Hunt syndrome*.

ANATOMY AND PATHOLOGY

The anatomic basis for *painful ophthalmoplegia* lies in the density of relationships in the cavernous sinus between the internal carotid artery, the trigeminal nerve, the third, fourth, and sixth cranial nerves, and the parasympathetic and sympathetic nerves of the eye. *Painful ophthalmoplegia* arises when a pain-producing lesion also involves one or more of these nerves. Such lesions may be vascular, neurologic, space-occupying, inflammatory, or infiltrative (Table 126-1). Different clinical manifestations arise depending on whether the causative lesion affects the sinus extensively or the lesion is focal and located anteriorly or posteriorly in the sinus.

TABLE 126-1 The Differential Diagnosis of Painful Ophthalmoplegia

Cause	*Diagnostic Test*
Vascular	
Internal carotid aneurysm	Angiography
Carotico-cavernous fistula	Ocular features
Cavernous sinus thrombosis	
Temporal arteritis	ESR, biopsy
Neurologic	
Diabetic neuropathy	Blood glucose
Ophthalmoplegic migraine	
Neoplastic	
Nasopharyngeal tumors	CT, MRI
Tumors of skull base	
Parasellar meningioma	
Metastases	
Pituitary tumours	
Chondroma	
Chordoma	
Neurinoma	
Leiomyosarcoma	
Retrobulbar tumors	CT, angiography
Infectious	
Actinomycosis	Biopsy, serology
Actinomycetemcomitans	
Aspergillosis	
Tuberculosis	
Infiltrative	
Systemic lupus erythematosus	Serology
Lymphoma	Biopsy
Sarcoid	Serology, biopsy
Syphilis	Serology
Miscellaneous	
Pseudotumor of the orbit	CT, angiography
Sphenoid sinus mucocele	CT
Epidermoid tumor	CT

CT, computed tomography; ESR, elevated sedimentation rate; MRI, magnetic resonance imaging.

PATHOPHYSIOLOGY

Orbital pain or headache arises presumably as a result of inflammation or distension of the meningeal walls of the cavernous sinus or as a result of irritation of the frontal branch of the trigeminal nerve. Ophthalmoplegia arises as a result of compression or ischemia of the third, fourth, or sixth cranial nerves.

CLINICAL FEATURES

IHS diagnostic criteria for Tolosa-Hunt syndrome (ICHD-II) (30):

A. One or more episodes of unilateral orbital pain persisting for weeks if untreated.
B. Paresis of one or more of the third, fourth, and/or sixth cranial nerves and/or demonstration of granuloma by magnetic resonance imaging (MRI) or biopsy.
C. Paresis coincides with the onset of pain or follows it within 2 weeks.
D. Pain and paresis resolve within 72 hours when treated adequately with corticosteroids.
E. Other causes have been excluded by appropriate investigations.

The third nerve is involved in about 90% of presentations; in 40%, the fourth or sixth nerves are also involved or affected alone (35,59). The incidence of demonstrable lesions in the cavernous sinus increases with the number of cranial nerves involved (57). The third nerve involvement manifests most obviously by paralysis or paresis of the ocular muscles it supplies. Parasympathoplegia is not overt but may be evident as a sluggish pupillary light reflex (1,35,59). Involvement of the ocular sympathetic fibers is evident in the form of ptosis and poor mydriasis (1,35,59). Involvement of the frontal nerve manifests by depression of the corneal reflex and periorbital hypoaesthesia (1,59,83). About 10% of patients may have involvement of the optic nerve in the form of diminished visual acuity, but papilledema or venous congestion of the optic disc is not a feature (35,37,59). Optic nerve involvement suggests anterior extension of the causative lesion from the cavernous sinus. Posterior extension may involve the second division of the trigeminal nerve (82).

Clinical examination alone is insufficient to elucidate the causative lesion of painful ophthalmoplegia. Biochemical and serologic investigations could confirm or exclude diabetic neuropathy, immunologic disorders, and infection; carotid angiography is required to confirm or exclude

P1: KWW/KKL P2: KWW/HCN QC: KWW/FLX T1: KWW
GRBT050-126 Olesen- 2057G GRBT050-Olesen-v6.cls August 17, 2005 2:54

internal carotid aneurysm; and CT or MRI is required to identify space-occupying and infiltrative lesions (Table 126-1). No firm guidelines are available to distinguish painful ophthalmoplegia from ophthalmoplegic migraine. Indeed, the distinction has been questioned, because some patients diagnosed as suffering ophthalmoplegic migraine have been found on investigation to have structural lesions (15).

Painful ophthalmoplegia is distinguishable from *pseudotumor of the orbit* because the latter typically involves chemosis, proptosis, and inflammatory symptoms, and typically it spares the fifth nerve (1,59,82). It has been suggested, however, that painful ophthalmoplegia and pseudotumor of the orbit may only be anatomic variants of the same basic condition (71,93).

Temporal arteritis is distinguished by a raised erythrocyte sedimentation rate and typically affects elderly patients with an average age of 70 (83), whereas patients with painful ophthalmoplegia have an average age of 41 (1,59,83). Also, temporal arteritis rarely affects the sixth nerve (83), and temporal artery biopsy should confirm the diagnosis in the majority.

Certain variants of painful ophthalmoplegia have attracted specific appellations but constitute no more than examples of lesions in particular locations. Thus, *Gradenigo syndrome* is a variant involving a sixth nerve palsy caused by lesions at the apex of the petrous temporal bone. *Raeder paratrigeminal neuralgia* is a not a distinct entity; the term has been applied to painful ophthalmoplegia involving sympathoplegia of the eye ascribed inconsistently to various lesions of the internal carotid artery or its relations in the cavernous sinus. For lack of pathologic specificity and consistency the term is no longer credited (30).

Historically, *Tolosa-Hunt syndrome* has been regarded as a distinctive variant of painful ophthalmoplegia ostensibly caused by granulomatous infiltration of the cavernous sinus (35,37). The criteria for its diagnosis were failure to identify a structural cause, a response to steroids, and a relapsing course. Whereas these criteria were attractive when the syndrome was first described, they are now either untenable or have been refuted.

Previous reports of granulomatous tissue in this condition can be questioned on the grounds that epithelioid cells, which are the sine qua non of granulomata, had not been properly recorded in Tolosa-Hunt syndrome; rather, what had been described was either ambiguous or not more than chronic inflammation (12). Angiographic and phlebographic abnormalities thought to be consistent with arteritis or occlusion of the cavernous sinus are exceptions rather than the rule in apparent Tolosa-Hunt syndrome and are not specific for this condition (26–28,35,59,83,87).

Although dramatic, the response of Tolosa-Hunt syndrome to systemic steroids is not specific. A response to steroids has been reported in cases of painful ophthalmoplegia caused by tumors (84,89), lymphoma (19,84,89), aneurysm (19,49,84,89), nasopharyngeal carcinoma (84), pituitary adenoma (49), parasellar epidermoid tumor (48), metastases (84), and actinomycosis (15).

CT scanning may reveal enhancing lesions in the cavernous sinus or orbital apex (12,23,24,52,90), but more often there is no abnormality characteristic of Tolosa-Hunt syndrome (23–26,65,77,86). Thickening of the lateral wall or infiltration of the cavernous sinus has been found by using MRI (14,24,52,106), which is consistent with previous notions of a granulomatous cause of Tolosa-Hunt syndrome, but MRI does not disclose the nature of this tissue.

One study, however, of a patient with Tolosa-Hunt syndrome using CT-guided needle biopsy of the cavernous sinus has raised a challenging observation (77). CT revealed an enhancing lesion at the orbital apex and anterior cavernous sinus. Biopsy of the lesion revealed inflammatory tissue and frequent epithelioid cells, the latter satisfying the criterion for granuloma. Further study of the specimen revealed hyphae, however, which were shown to be those of aspergillus. In a similar case, open biopsy revealed a purulent infection of the cavernous sinus caused by *Actinobacillus* (91). These cases suggest that what may have been regarded as idiopathic granulomata in previously recorded cases of Tolosa-Hunt syndrome could have been unrecognized fungal infections.

On the other hand, some evidence suggests that Tolosa-Hunt syndrome may be but one manifestation of a wider spectrum of disorders involving multiple cranial nerves. Some instances of Tolosa-Hunt syndrome also involve the seventh cranial nerve (26,86), and an entity has been described that involves not only the cranial nerves of the cavernous sinus but also the first, seventh, eighth, ninth, 10th, or 12th cranial nerves (32,36,85). The anatomic separation of these nerves denies a single focal cause such as those known for painful ophthalmoplegia and suggests a systemic or idiosyncratic basis. Thus, what has been regarded as Tolosa-Hunt syndrome may only be a subset of a more general disorder of cranial nerves and not necessarily a condition that uniquely affects the cavernous sinus.

OPHTHALMOPLEGIC MIGRAINE

IHS code and diagnosis: 13.17 Ophthalmoplegic migraine
WHO code and diagnosis: G43.80
Short description: Recurrent attacks of headache with migrainous characteristics associated with paresis of one or more ocular cranial nerves (commonly the third nerve) in the absence of any demonstrable intracranial lesion other than MRI changes within the affected nerve

EPIDEMIOLOGY

Ophthalmoplegic migraine is a rare disorder. Surveys have identified the condition in 8 of 5000 patients with migraine

P1: KWW/KKL P2: KWW/HCN QC: KWW/FLX T1: KWW
GRBT050-126 Olesen- 2057G GRBT050-Olesen-v6.cls August 17, 2005 2:54

(20), with an annual incidence of 0.7 per million population (29). Otherwise, it has been reported only in case studies (16,55,104).

ANATOMY AND PATHOLOGY

The only known pathology is enhancement of the oculomotor nerve on MRI with gadolinium (61,101). Accordingly, the condition has been interpreted as a recurrent demyelinating neuropathy rather than a variant of migraine (54).

PATHOPHYSIOLOGY

The pathophysiology is unknown.

CLINICAL FEATURES

IHS diagnostic criteria for ophthalmoplegic migraine (ICHD-II) (30):

A. At least two attacks fulfilling criterion B
B. Migrainelike headache accompanied or followed within 4 days of its onset by paresis of one or more of the third, fourth, and/or sixth cranial nerves
C. Parasellar, orbital fissure, and posterior fossa lesions ruled out by appropriate investigations

The diagnosis is essentially one of exclusion. The resemblance to painful ophthalmoplegia requires that parasellar lesions and aneurysms affecting the oculomotor nerves be excluded. Similarly, demyelinating neuropathy should be excluded. With those provisions, the entity of ophthalmoplegic migraine may disappear eventually from the lexicon of headache.

MANAGEMENT

The headaches are treated as for migraine.

NECK–TONGUE SYNDROME

IHS code and diagnosis: 13.9 Neck–tongue syndrome
WHO code and diagnosis: G44.851
Short description: the sudden onset of pain in the occiput or upper neck associated with abnormal sensation in the same side of the tongue

ANATOMY AND PATHOLOGY

The C2 spinal nerve lies behind the lateral atlantoaxial joint, which is innervated by the C2 ventral ramus (7). During rotation of the atlas, its ipsilateral, inferior articular process subluxates backwards. If the range of movement is excessive the capsule of the joint is strained and the C2 nerve may be impacted by the edge of the inferior articular process and stretched around it (8).

Neck–tongue syndrome usually occurs in otherwise normal individuals (53), but it has been reported in patients with rheumatoid arthritis or with congenital joint laxity (4). Hypomobility in the contralateral, lateral atlantoaxial joint may predispose to the condition (4).

PATHOPHYSIOLOGY

If the lateral atlantoaxial joint temporarily subluxates, stretching of its capsule produces joint pain that is perceived in the occipital region (8). Numbness of the tongue arises because of impingement, or stretching, of the C2 ventral ramus against the edge of the subluxated articular process (8) (Fig. 126-2) and is produced by compression of proprioceptive afferents from the tongue, which pass from the ansa hypoglossi into the C2 ventral ramus (53).

Operative findings have confirmed that the syndrome involves compression of the C2 spinal nerves by the lateral atlantoaxial joint (17).

CLINICAL FEATURES

IHS diagnostic criteria for neck–tongue syndrome (ICHD-II) (30):

A. Pain lasting seconds or minutes, with or without simultaneous dysesthesia, in the area of distribution of

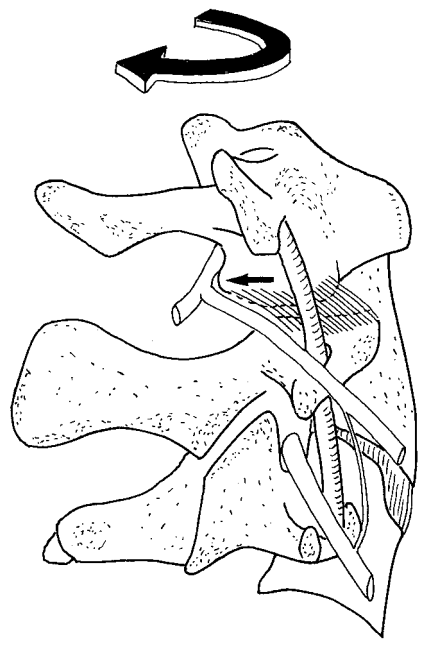

FIGURE 126-2. A lateral view of a right atlantoaxial joint in which the atlas has rotated to the right. Its inferior articular process impacts and stretches the C2 spinal nerve and ventral ramus (*arrow*).

P1: KWW/KKL P2: KWW/HCN QC: KWW/FLX T1: KWW
GRBT050-126 Olesen- 2057G GRBT050-Olesen-v6.cls August 17, 2005 2:54

the lingual nerve and second cervical root and fulfilling criteria B and C.

B. Pain has acute onset.

C. Pain is commonly precipitated by sudden turning of the head.

Management

Reportedly, effective therapies include immobilization by a soft collar (18), atlantoaxial fusion (4), and resection of the C2 spinal nerves (17).

REFERENCES

1. Aaron-Rosa D, Doyan D, Salamon G, et al. Tolosa-Hunt syndrome. *Ann Ophthalmol* 1978;10:1161–1168.
2. Ali NM. Does sympathetic ganglionic block prevent postherpetic neuralgia [Review]? *Reg Anesth* 1995;20:227–233.
3. Bernard EJ, Nashold BS, Caputi F, et al. Nucleus caudalis DREZ lesions for facial pain. *Br J Neurosurg* 1987;1:81–91.
4. Bertoft ES, Westerberg CE. Further observations on the neck-tongue syndrome. *Cephalalgia* 1985;5[Suppl 3]:312–313.
5. Beydoun A. Postherpetic neuralgia: role of gabapentin and other treatment modalities. *Epilepsia* 1999;40:S51–S56.
6. Bogduk N. The anatomy of occipital neuralgia. *Clin Exp Neurol* 1980;17:167–184.
7. Bogduk N. Local anaesthetic blocks of the second cervical ganglion: a technique with application in occipital headache. *Cephalalgia* 1981;1:41–50.
8. Bogduk N. An anatomical basis for neck tongue syndrome. *J Neurol Neurosurg Psychiatry* 1981;44:202–208.
9. Boureau F, Legallicier P, Kabit-Ahmadi M. Tramadol in post-herpetic neuralgia: a randomized, double-blind, placebo-controlled trial. *Pain* 2003;104:323–331.
10. Bowsher D. The effects of pre-emptive treatment of postherpetic neuralgia with amitriptyline: a randomized, double-blind, placebo-controlled trial. *J Pain Symptom Manage* 1997;13:327–331.
11. Bruxelle J. Prospective epidemiologic study of painful and neurologic sequelae induced by herpes zoster in patients treated early with oral acyclovir. *Neurology* 1995;45[Suppl 8]:S79.
12. Campbell RJ, Ikazaki H. Painful ophthalmoplegia (Tolosa-Hunt variant): autopsy findings in a patient with necrotizing intracavernous carotid vasculitis and inflammatory disease of the orbit. *Mayo Clinic Proc* 1987;62:520–526.
13. De Benedittis G, Besana F, Lorenzetti A. A new topical treatment for acute herpetic neuralgia and post-herpetic neuralgia: the aspirin/diethyl ether mixture. An open-label study plus a double-blind controlled clinical trial. *Pain* 1992;48:383–390.
14. Desai SP, Carter J, Jinkins JR. Contrast-enhanced MR imaging of Tolosa-Hunt Syndrome: a case report. *AJNR* 1991;12:182–183.
15. Dornan TL, Espir MLE, Gale EAM, et al. Remittent painful ophthalmoplegia: the Tolosa-Hunt syndrome? *J Neurol Neurosurg Psychiatry* 1979;42:270–275.
16. Durkan GP, Troost BT, Slamovits TL, et al. Recurrent painless ocular motor palsy in children: a variant of ophthalmoplegic migraine. *Headache* 1981;21:58.
17. Elisevich K, Stratford J, Bray G, et al. Neck tongue syndrome: operative management. *J Neurol Neurosurg Psychiatry* 1984;47:407–409.
18. Fortin CJ, Biller J. Neck tongue syndrome. *Headache* 1985;25:255–258.
19. Fowler TJ, Earl CJ, McAllister VL, et al. Tolosa-Hunt syndrome: the dangers of an eponym. *Br J Ophthalmol* 1975;59:149–154.
20. Friedman AP, Harter DH, Merritt HH. Ophthalmoplegic migraine. *Arch Neurol* 1962;7:320.
21. Galer BS, Rowbotham MC, Perander J, et al. Topical lidocaine patch relieves postherpetic neuralgia more effectively than a vehicle topical patch: results of an en enriched enrollment study. *Pain* 1999;80:533–538.
22. Gnann JW, Whitley RJ. Herpes zoster. *N Engl J Med* 2002;347:340–346.
23. Goadsby PJ, Lance JW. Clinicopathological correlation in a case of painful ophthalmoplegia: Tolosa-Hunt syndrome. *J Neurol Neurosurg Psychiatry* 1989;52:1290–1293.
24. Goto Y, Hosokawa S, Goto I, et al. Abnormality in the cavernous sinus in three patients with Tolosa-Hunt syndrome: MRI and CT findings. *J Neurol Neurosurg Psychiatry* 1990;55:231–234.
25. Hannerz J. Pain characteristics of painful ophthalmoplegia (the Tolosa-Hunt syndrome). *Cephalalgia* 1985;5:103–106.
26. Hannerz J. Recurrent Tolosa-Hunt syndrome. *Cephalalgia* 1992;12:45–51.
27. Hannerz J, Ericson K, Bergstrand G. Orbital phlebography in patients with Tolosa-Hunt's syndrome in comparison with normal subjects. *Acta Radiol (Diagn)* 1984;25:457–463.
28. Hannerz J, Ericson K, Bergstrand G. Orbital phlebography in patients with cluster headache. *Cephalalgia* 1987;7:207–211.
29. Hansen SL, Borelli-Moller L, Strange P. Ophthalmoplegic migraine: diagnostic criteria, incidence of hospitalisation and possible etiology. *Acta Neurol Scand* 1990;81:54–60.
30. Headache Classification Subcommittee of the International Headache Society. The international classification of headache disorders, 2nd edition. *Cephalalgia* 2004;24[Suppl 1]:1–160.
31. Hildebrandt J, Jansen J. Vascular compression of the C2 and C3 roots—yet another cause of chronic intermittent hemicrania? *Cephalalgia* 1984;4:167–170.
32. Hokkanen E, Haltia T, Myllyla VV. Recurrent multiple cranial neuropathies. *Eur Neurol* 1978;17:32–37.
33. Hope-Simpson RE. The nature of herpes zoster: a long-term study and a new hypothesis. *Proc Roy Soc Med* 1965;58:9–20.
34. Hunt JR. On herpetic inflammations of the geniculate ganglion. A new syndrome and its complications. *J Nerv Ment Dis* 1907;34:73–96.
35. Hunt WE. Tolosa-Hunt syndrome: one cause of painful ophthalmoplegia. *J Neurosurg* 1976;44:544–549.
36. Hunt WE, Brightman RP. The Tolosa-Hunt syndrome: a problem in differential diagnosis. *Acta Neurochir* 1988;42:248–252.
37. Hunt WE, Meagher JN, Lefever HE, et al. Painful ophthalmoplegia: its relation to indolent inflammation of the cavernous sinus. *Neurology* 1961;11:56–62.
38. Jackson JL, Gibbons R, Meyer G, et al. The effect of treating herpes zoster with oral acyclovir in preventing postherpetic neuralgia: a meta-analysis. *Arch Int Med* 1997;157:909–912.
39. Jansen J, Bardosi A, Hildebrandt J, et al. Cervicogenic, hemicranial attacks associated with vascular irritation or compression of the cervical nerve root C2. Clinical manifestations and morphological findings. *Pain* 1989;39:203–212.
40. Jansen J, Markakis E, Rama B, et al. Hemicranial attacks or permanent hemicrania—a sequel of upper cervical root compression. *Cephalalgia* 1989;9:123–130.
41. Johnson RW. Aspects of postherpetic neuralgia: can we zap Z-ap? *Pain Reviews* 1996;3:117–135.
42. Johnson RW. Herpes zoster and postherpetic neuralgia. Optimal treatment. *Drugs Aging* 1997;10:81–94.
43. Johnson RW. Herpes zoster—predicting and minimizing the impact of post-herpetic neuralgia. *J Antimicrob Chemother* 2001;47:Topic T1, 1—8.
44. Johnson RW, Dworkin RH. Treatment of herpes zoster and postherpetic neuralgia. *BMJ* 2003;326:748–750.
45. Johnson RW, Mandal BK. Guidelines for the management of shingles. Report of a working group of the British society for the study of Infection. *J Infect* 1995;30:193–200.
46. King RB. Concerning the management of pain associated with herpes zoster and postherpetic neuralgia. *Pain* 1988;33:73–78.
47. Kingery WS. A critical review of controlled clinical trials for peripheral neuropathic pain and complex regional pain syndromes. *Pain* 1997;73:123–139.
48. Kline LB, Galbraith JG. Parasellar epidermoid tumour presenting as painful ophthalmoplegia. *J Neurosurg* 1981;54:113–117.
49. Koppel BS. Steroid responsive painful ophthalmoplegia is not always Tolosa-Hunt. *Neurology* 1987;37:544.
50. Kotani N, Kushikata T, Hashimoto H, et al. Intrathecal methylprednisolone for intractable postherpetic neuralgia. *N Engl J Med* 2000;343:1514–1519.

P1: KWW/KKL P2: KWW/HCN QC: KWW/FLX T1: KWW
GRBT050-126 Olesen- 2057G GRBT050-Olesen-v6.cls August 17, 2005 2:54

51. Kuritzky A. Cluster headache-like pain caused by an upper cervical meningioma. *Cephalalgia* 1984;4:185–186.
52. Kwan ESK, Wolpert SM, Hedges TR, et al. Tolosa-Hunt syndrome revisited: not necessarily a diagnosis of exclusion. *AJNR* 1987;8:1067–1072.
53. Lance JW, Anthony M. Neck tongue syndrome on sudden turning of the head. *J Neurol Neurosurg Psychiatry* 1980;43:97–101.
54. Lance JW, Zagami AS. Ophthalmoplegic migraine: a recurrent demyelinating neuropathy? *Cephalalgia* 2001;21:84–89.
55. Leone M, Grazzi L, Moschiano F, et al. Internal ophthalmoplegia associated migraine attacks. *Cephalalgia* 1994;14:461–462.
56. Lewith GT, Field J, Machin D. Acupuncture compared with placebo in post-herpetic pain. *Pain* 1983;17:361–368.
57. Lin CC, Tsai JJ. Relationship between the number of involved cranial nerves and the percentage of lesions located in the cavernous sinus. *Eur Neurol* 2003;49:98–102.
58. Loeser JD. Herpes zoster and postherpetic neuralgia. *Pain* 1986;25: 149–164.
59. Matthew NT, Chandy J. Painful ophthalmoplegia. *J Neurol Sci* 1970; 11:243–256.
60. McQuay H, Carroll D, Jadad AR, et al. Anticonvulsant drugs for the management of pain: a systematic review. *Br Med J* 1995;311:1047–1052.
61. Ostergaard JR, Moller HU, Christensen T. Recurrent ophthalmoplegia in childhood: diagnostic and aetiologic considerations. *Cephalalgia* 1996;16:27–29.
62. Pappagallo M, Campbell JN. Chronic opioid therapy as alternative treatment for post-herpetic neuralgia. *Ann Neurol* 1994;35:54–56.
63. Pasqualucci A, Pasqualucci V, Galla F, et al. Prevention of postherpetic neuralgia: acyclovir and prednisolone versus epidural local anesthetic and methylprednisolone. *Acta Anaesthesiol Scand* 2000;44:910–918.
64. Poletti CE, Sweet WH. Entrapment of the C2 root and ganglion by the atlanto-epistrophic ligament: clinical syndrome and surgical anatomy. *Neurosurgery* 1990;27:288–291.
65. Polsky M, Janicki PC, Gunderson CH. Tolosa-Hunt syndrome with sellar erosion. *Ann Neurol* 1979;6:129–131.
66. Portenoy RK, Duma C, Foley KM. Acute herpetic and postherpetic neuralgia: clinical review and current management. *Ann Neurol* 1986;20:651–664.
67. Rabasseda X. Brivudine: a herpes virostatic with rapid antiviral activity and once-daily dosing. *Drugs Today (Barcelona)* 2003;39:359–371.
68. Ragazzino MW, Melton IJ, Kurland LT, et al. Population-based study of herpes zoster and its sequelae. *Medicine* 1982;61:310–316.
69. Raja SN, Haythornthwaite JA, Pappagallo M, et al. Opioids versus antidepressants in postherpetic neuralgia. A randomized, placebo-controlled trial. *Neurology* 2002;59:1015–1021.
70. Rice AS, Maton S. Gabapentin in postherpetic neuralgia: a randomised, double-blind, placebo controlled study. *Pain* 2001;94:215–224.
71. Rosenbaum DH, David MJ, Song IS. The syndrome of painful ophthalmoplegia: a case with intraorbital mass and hypervascularity. *Arch Neurol* 1979;36:41–43.
72. Rowbotham MC, Fields HL. Topical lignocaine reduces pain in postherpetic neuralgia. *Pain* 1989;39:297–301.
73. Rowbotham MC, Davies PS, Verkempinck C, et al. Lidocaine patch: double-blind controlled study of a new treatment method for postherpetic neuralgia. *Pain* 1996;65:39–44.
74. Rowbotham M, Harden N, Stacey B, et al. Gabapentin for the treatment of postherpetic neuralgia. A randomized controlled trial. *JAMA* 1998;280:1837–1842.
75. Rowbotham MC, Miller KV, Davies P. Topical lidocaine for postherpetic neuralgia pain: results of a double-blind, vehicle controlled trial. *Neurology* 1992;42:390.
76. Rowbotham MC, Reisner-Keller LA, Fields HL. Both intravenous lidocaine and morphine reduce the pain of postherpetic neuralgia. *Neurology* 1991;41:1024–1028.
77. Rowed DW, Kassel EE, Lewis AJ. Transorbital intracavernous needle biopsy in painful ophthalmoplegia. *J Neurosurg* 1985;62:776–780.
78. Rubben A, Baron JM, Grussendorf-Conen EI. Routine detection of herpes simplex virus and varicella zoster virus by polymerase chain reaction reveals that initial herpes zoster is frequently misdiagnosed as herpes as herpes simplex. *Br J Dermatol* 1997;137:259–261.
79. Scheinfeld N. The role of gabapentin in treating diseases with cutaneous manifestations and pain. *Int J Dermatol* 2003;42:491–495.
80. Schvarcz JR. Craniofacial postherpetic neuralgia managed by stereotactic spinal trigeminal nucleotomy. *Acta Neurchir Suppl* 1989;46:62–64.
81. Scott FT, Leedham ME, Barrett-Muir WY, et al. A study of shingles and the development of postherpetic neuralgia in East London. *J Med Virol* 2003;70:S24–S30.
82. Smith JL, Taxdal DSR. Painful ophthalmoplegia: the Tolosa-Hunt syndrome. *Am J Ophthalmol* 1966;61:1466–1472.
83. Sondheimer FK, Knapp J. Angiographic findings in the Tolosa-Hunt Syndrome: painful ophthalmoplegia. *Radiology* 1973;106:105–112.
84. Spector RH, Fiandaca MS. The "sinister" Tolosa-Hunt syndrome. *Neurology* 1986;36:198–203.
85. Steele JC, Vasuvar A. Recurrent multiple cranial nerve palsies: a distinctive syndrome of cranial polyneuropathy. *J Neurol Neurosurg Psychiatry* 1970;33:828–832.
86. Swerdlow B. Tolosa-Hunt syndrome: a case with associated facial nerve palsy. *Ann Neurol* 1980;8:542–543.
87. Takeoka T, Gotoh F, Fukuchi V, et al. Tolosa-Hunt syndrome: arteriographic evidence of improvement in carotid narrowing. *Arch Neurol* 1978;35:219–223.
88. Taub A. Relief of postherpetic neuralgia with psychotropic drugs. *J Neurosurg* 1973;39:235–239.
89. Thomas DJB, Charlesworth MC, Afshar F, et al. Computerised axial tomography and magnetic resonance scanning in the Tolosa-Hunt syndrome. *Br J Ophthalmol* 1988;72:299–302.
90. Thomas JE, Yoss RE. The parasellar syndrome: problems in determining etiology. *Mayo Clin Proc* 1970;45:617–623.
91. Tobias S, Lee JH, Tomford JW. Rare actinobacilis infection of the cavernous sinus causing painful ophthalmoplegia: case report. *Neurosurgery* 2002;51:807–809.
92. Volmink J, Lancaster T, Gray S, et al. Treatments for postherpetic neuralgia—a systematic review of randomized controlled trials. *Family Practice* 1996;13:84–91.
93. Wasmeier C, Pfadenhauer K, Roster A. Idiopathic inflammatory pseudotumor of the orbit and Tolosa-Hunt syndrome—are they the same disease? *J Neurol* 2002;249:1237–1241.
94. Watson CP, Babul N. Efficacy of oxycodone in neuropathic pain: a randomised trial in postherpetic neuralgia. *Neurology* 1998;50: 1837–1841.
95. Watson CPN, Evans RJ. A comparative trial of amitriptyline and zimelidine in post-herpetic neuralgia. *Pain* 1985;28:387–394.
96. Watson CPN, Evans RJ, Watt VR, et al. Post-herpetic neuralgia: 208 cases. *Pain* 1988;35:289–297.
97. Watson CPN, Watt VR, Chipman M, et al. The prognosis of postherpetic neuralgia. *Pain* 1991;46:195–199.
98. Watson CPN, Deck JH, Morshead C, et al. Post-herpetic neuralgia: further post-mortem studies of cases with and without pain. *Pain* 1991;44:105–117.
99. Watson CPN, Chipman M, Reed K, et al. Maprotiline is postherpetic neuralgia: a randomized double-blind, crossover trial. *Pain* 1992;48: 29–36.
100. Whitley RJ, Weiss W, Guann J, et al, and the NIAID Collaborative Antiviral Study Group. The efficacy of steroids and acyclovir therapy of herpes zoster in the elderly. *Antiviral Res* 1995;26:A303.
101. Wong V, Wong WC. Enhancement of oculomotor nerve—a diagnostic criterion for ophthalmoplegic migraine. *Pediatr Neurol* 1997;17: 70–73.
102. Wood MJ, Johnson RW, McKendrick MW, et al. A randomized trial of acyclovir for 7 days of 21 days with and without prednisolone for treatment of acute herpes zoster. *N Engl J Med* 1994;330:896–900.
103. Wood MJ, Kay R, Dworkin RH, et al. Oral acyclovir therapy accelerates pain resolution n patients with herpes zoster: a meta-analysis of placebo-controlled trials. *Clin Infect Dis* 1996;22:341–147.
104. Woody RC, Blaw ME. Ophthalmoplegic migraine in infancy. *Clin Pediatr* 1986;25:82–84.
105. Wu CI, Marsh A, Dworkin RH. The role of sympathetic nerve blocks in herpes zoster and postherpetic neuralgia. *Pain* 2000;87:121–129.
106. Yousem DM, Atlas SW, Grossman RI, et al. MR Imaging of Tolosa-Hunt syndrome. *AJNR* 1989;10:1181–1184.