Review Article

Tolosa–Hunt Syndrome: A Review of Diagnostic Criteria and Unresolved Issues

Paromita Dutta, Kamlesh Anand

Guru Nanak Eye Centre, Department of Ophthalmology, Maulana Azad Medical College, New Delhi, India

Abstract

Purpose: To review the diagnostic criteria for Tolosa–Hunt syndrome (THS) and utility of recent modifications.

Methods: We searched PubMed for keywords Tolosa Hunt and magnetic resonance imaging. We compared the three editions of International Classification of Headache Disorders and isolated case reports and case series with the assessment of cavernous internal carotid artery (ICA) caliber to find the prevalence of vascular anomalies. We also evaluated cases of THS with the involvement of extracavernous structures and the possible role of idiopathic hypertrophic pachymeningitis (HP). Cases diagnosed falsely as THS were also reviewed for the presence of atypical features and relevance of criterion D. We assessed nonconforming cases (those with normal neuroimaging benign THS) and idiopathic inflammatory orbital pseudotumor (IIPO).

Results: Vascular abnormalities were found in 36.36% of THS cases. Benign THS may also show changes in ICA caliber. Evidence suggestive of idiopathic HP could be found in 57% of cases with the involvement of extracavernous structures, such as facial nerve and pituitary gland. Both THS and IIPO are steroid-responsive pathologies with similar clinical and radiological features. False-positive diagnosis of THS results from early labeling, based solely on clinical features and symptom resolution after steroid therapy.

Conclusions: Benign THS may be a result of limitation of resolution of available neuroimaging technique or early testing. Early and late vascular changes can be seen in both THS and its benign variant; some of them are not innocuous. THS may be considered a type of focal idiopathic HP. IIPO may represent an anterior variant of THS. In the absence of histopathological diagnosis, steroid-induced resolution of symptoms should be confirmed radiologically and followed-up.

Keywords: Cavernous sinus, Internal carotid artery, Pachymeningitis, Tolosa Hunt

Address for correspondence: Paromita Dutta, Room No. 111, OPD Block, Guru Nanak Eye Centre, Maulana Azad Medical College, New Delhi, India.
E-mail: mitad_4@yahoo.com
Submitted: 27-Sep-2020; **Revised:** 14-Dec-2020; **Accepted:** 21-Dec-2020; **Published:** 05-Jul-2021

Introduction

Tolosa–Hunt syndrome (THS) is one of the most well-recognized eponyms in the field of medicine, unfortunately often misused, due to nonadherence to the diagnostic criteria. This condition, characterized by recurrent painful ophthalmoplegia (PO) caused by granulomatous inflammation of the cavernous sinus (CS) region, was described by Tolosa in 1954.[1] In 1961, Hunt *et al*.[2] described six more similar cases and proposed the following additional criteria:

1. Retrobulbar pain that may precede ophthalmoplegia by several days or may not appear until later
2. Neurological involvement may include third, fourth, and sixth cranial nerves (CNs), as well as the first (and occasionally the second) division of the trigeminal nerve The optic nerve and the oculosympathetic fibers may occasionally be involved
3. The symptoms last for weeks or month
4. Spontaneous remission may occur, sometimes with residual neurological deficit

Access this article online

Quick Response Code:

Website: www.jcurrophthalmol.org

DOI: 10.4103/joco.joco_134_20

How cite this article: Dutta P, Anand K. Tolosa–Hunt syndrome: A review of diagnostic criteria and unresolved issues. J Curr Ophthalmol 2021;33:104-11.

5. Attacks recur at intervals of months or years
6. Exhaustive studies, including angiography and surgical exploration, have produced no evidence of involvement of structures outside the CS.

In 1966, Smith and Taxdal introduced the eponym THS for the triad of unilateral orbital pain, accompanying CN palsies, and a dramatic response of the symptoms to systemic corticosteroid treatment.[3] This remarkable response to steroids is still used as a surrogate marker for confirming the diagnosis and is the most common cause for misdiagnosis.

THS was recognized as a distinct clinical entity by the International Headache Society classification criteria published in 1988.[4] The diagnostic criteria were modified by expert consensus, subsequently, in 2004 and 2018.[5,6] These three editions of International Classification of Headache Disorders (ICHD) diagnostic criteria for THS reflect the reliance on improved imaging techniques and emphasize on pathological confirmation of an inflammatory etiology [Table 1].

This study was conducted to evaluate the changes in diagnostic criteria and explore the lacunae in the existing classification. We also reviewed cases with false-positive (FP) diagnosis and assessed the utility of continued use of the eponym, THS.

Methods

We searched PubMed for the terms "Tolosa Hunt" and "Magnetic Resonance Imaging" or "MRI". Articles published till date (September 25, 2020) were considered. Case reports and single cases from larger case series were studied in detail. Cases were assessed whether they qualified on the basis of ICHD-3 beta or ICHD-2 criteria for THS. Exclusion criteria included: (1) lack of precise diagnostic information, (2) non-English papers without English translation, and (3) single cases that were part of larger series from which individual patient information could not be ascertained. The isolated reports were further evaluated for the presence of vascular abnormalities, atypical features, and evidence of hypertrophic pachymeningitis (HP). Cases wrongly diagnosed and managed as THS were also evaluated. The extracted papers were evaluated by P.D. (neuro-ophthalmologist with 12 years of experience) and K.A. (strabismologist with 40 years of experience).

Results

Our search revealed 244 articles, out of which 153 were considered. There were 30 case series (out of which 8 were prospective), two meta-analyses, one clinical trial, and 77 case reports. Changes in diagnostic criteria for THS and limitations of the same are discussed.

Role of magnetic resonance imaging

The role of magnetic resonance imaging (MRI) in the diagnosis of THS has undergone a paradigm shift. While MRI received no mention in ICHD-1, it was an optional investigation in ICHD-2, and currently, it is an essential diagnostic investigation as an alternative to biopsy for confirmation of inflammatory etiology. MRI has been found to be the most valuable imaging technique to distinguish THS from other THS-like entities and permits a precise assessment, management, and therapeutic planning of the underlying pathological conditions.[7]

The superiority of MRI over computed tomography (CT) scan in detecting soft tissue lesions in the area of the CS was demonstrated by de Arcaya *et al*.[8] MRI features suggestive of CS involvement in THS include enlargement and dural margin convexity, with or without abnormal tissue, which is isointense with gray matter on T1-weighted images and isointense to slightly hypointense on T2-weighted sequences. The abnormal tissue enhances markedly with contrast. There may be focal narrowing of the cavernous portion of the internal carotid artery (ICA).[7,9] The lesion may extend into the ipsilateral orbital apex (OA), sphenoid sinus, or middle cranial fossa (MCF). The limitation of relying on MRI alone for diagnosis is that it detects any abnormal tissue and not only granulomatous inflammation. The lesion may enhance with contrast, depending upon the presence of leaky vasculature. Thus, FP may be seen in neoplasms (meningioma, lymphoma), inflammatory lesions (sarcoidosis), and infections. Förderreuthe and Straube cautioned that positive MRI or CT findings compatible with inflammatory tissue neither exclude nor confirm THS and remain suspect until a malignant tumor or inflammation other than THS is excluded.[10] With great foresight, they recommended clinical and radiological follow-up examinations for at least 2 years, even in patients with negative findings on MRI at onset.

MRI changes before and after systemic corticosteroid therapy are used to be an essential diagnostic criterion to confirm a diagnosis of THS and to differentiate it from other CS lesions that simulate THS both clinically and radiologically.[11,12] However, radiological resolution lags behind clinical response and findings may not resolve up to several months.[11,13] In the absence of a histopathological confirmation of diagnosis, follow-up imaging is all the more essential to detect partial or no response to steroids, progression of lesion, and determining when to stop steroids.[13]

Atypical features on MRI in cases of PO that should raise suspicion of an alternative diagnosis include lesions extending into the sellar fossa, MCF or the infratemporal fossa, lesions located posteriorly to the prepontine cistern, or invading the paranasal sinuses, brain parenchyma, skull and/or causing bone erosion, and evidence of superior orbital vein (SOV) enhancement and dilatation.[14]

Benign Tolosa–Hunt syndrome

In 1990, Yousem *et al*. reported that a small percentage of patients with clinically apparent THS may have normal imaging.[9] La Mantia *et al*. termed this variant "benign" THS.[11] In a retrospective review of published THS cases between 1998 and 2002, they found that 48% of cases meeting the ICHD-2

Table 1: The International Classification of Headache Disorders

	ICHD-1 (1988)	ICHD-2 (2004)	ICHD-3 (2018)
Category of classification	Cranial neuralgias, nerve trunk pain, deafferentation pain (12.1.5)	Cranial neuralgias, central and primary facial pain, and other headaches (13.16)	Painful lesions of the CNs and other facial pain (13.8)
Description	Episodic orbital pain associated with paralysis of one or more of the third, fourth, or sixth CN which resolves spontaneously but may relapse and remit	Episodic orbital pain associated with paralysis of one or more of the third, fourth, and/or sixth CNs which usually resolve spontaneously but tend to relapse and remit	Unilateral orbital pain associated with paresis of one or more of the third, fourth, and/or sixth CNs caused by a granulomatous inflammation in the cavernous sinus, superior orbital fissure, or orbit
Diagnostic criteria			
A	Episode or episodes of unilateral orbital pain for an average of 8 weeks if untreated	One or more episodes of unilateral orbital pain persisting for weeks if untreated	Unilateral headache fulfilling criterion C
B	Association with paralysis of one or more of the third, fourth, and sixth CNs which may coincide with the onset of the pain or follow it by a period of up to 2 weeks	Paresis of one or more of the third, fourth, and/or sixth CNs and/or demonstration of granuloma by MRI or biopsy	Both of the following: (1) Granulomatous inflammation of the cavernous sinus, superior orbital fissure or orbit, demonstrated by MRI or biopsy. (2) Paresis of one or more of the ipsilateral III, IV, and/or VI CN
C	Pain is relieved within 72 h after initiation of corticosteroid therapy	Paresis coincides with the onset of pain or follows it within 2 weeks	Evidence of causation demonstrated by both of the following: (1) Headache preceded paresis of the III, IV, and/or VI nerves by 2 weeks, or developed with it. (2). Headache is localized around the ipsilateral brow and eye
D	Exclusion of other causative lesions by neuroimaging and (not compulsory) carotid angiography	Pain and paresis resolve within 72 h when treated adequately with corticosteroids	Not better accounted for by another ICHD-3 diagnosis
E		Other causes have been excluded by appropriate investigations. (Other causes of painful ophthalmoplegia include tumors, vasculitis, basal meningitis, sarcoid, diabetes mellitus, and ophthalmoplegic "migraine.")	
Comments	Some reported cases of THS had additional involvement of the trigeminal nerve (commonly the first division) or optic, facial, or acoustic nerves. Sympathetic innervation of the pupil is occasionally affected. The syndrome has been caused by granulomatous material in some biopsied cases but the etiology is unknown. The sites affected are the cavernous sinus, superior orbital fissure, or orbit. Demonstration of obstruction of the superior ophthalmic vein, poor filling of the cavernous sinus, and collateral venous flow can be demonstrated by orbital phlebography in >50% of cases. Gradenigo syndrome and Raeder's paratrigeminal neuralgia are not specific diagnoses, but syndromes indicating a particular location of intracranial pathology	Some reported cases of THS had additional involvement of the trigeminal nerve (commonly the first division) or optic, facial, or acoustic nerves. Sympathetic innervation of the pupil is occasionally affected. The syndrome has been caused by granulomatous material in the cavernous sinus, superior orbital fissure, or orbit in some biopsied cases. Careful follow-up is required to exclude other possible causes of painful ophthalmoplegia	Some reported cases of THS had additional involvement of the 5th nerve (commonly the first division) or optic, 7th, or 8th nerves. Sympathetic innervation of the pupil is occasionally affected. Careful follow-up is required to exclude other causes of painful ophthalmoplegia such as tumors, vasculitis, basal meningitis, sarcoid or diabetes mellitus. Pain and paresis of THS resolve when it is treated adequately with corticosteroids

CN: Cranial nerves, MRI: Magnetic resonance imaging, THS: Tolosa-Hunt Syndrome, ICHD: International Classification of Headache Disorders

diagnostic criteria for THS had normal neuroimaging. This was reiterated in other retrospective studies, the prevalence ranging from 18.18% to 57%.[15-17] In all these reports, patients were diagnosed on the basis of ICHD-2 criteria as it allowed inclusion of such cases (proof of granulomatous inflammation was nonmandatory) and steroid response was considered a diagnostic criterion. However, these cases would not be labeled THS by ICHD-3 criteria unless a biopsy shows evidence of granulomatous inflammation. In such cases, it is also essential to rule out other causes of PO such as diabetic ischemic ocular motor nerve palsy and adult-onset recurrent painful ophthalmoplegic neuropathy. The sensitivity and specificity of the current ICHD-3 beta diagnostic criteria have been questioned.[15,17,18]

Limitation of available imaging technique may be one of the contributory factors for apparently normal neuroimaging.[9] Lesions less than 1 mm in size may not be detected by a

3-T MRI with a best spatial resolution (with contrast) of 1.0–2.0 mm.[16] In such cases, dynamic, contrast-enhanced high-resolution MRI with fat suppression may aid in the detection of lesions otherwise missed by conventional MRI.[15,17] Advanced MRI protocols such as constructive interference steady state, selective partial inversion recovery, and three-dimensional fast-imaging employing steady-state acquisition may help in demonstrating the causative lesion.[19-21]

Timing of MRI may also play a role in the detection of lesions. Radiologically, visible lesions may take some time to develop, and therefore, a normal MRI should not preclude a diagnosis of THS.[17,22] Mikhail *et al*. highlighted this radiological lag in two apparently benign THS cases.[22] They suggested repeat MRI after a few days or weeks, in case of persistence of headache, nerve palsy, or evidence of progressive involvement of other CN in the CS region. Kóbor *et al*. reported THS in a pediatric patient, where initial MRI and magnetic resonance angiography (MRA) at 4 weeks after presentation were normal. An enhancing lesion in the CS of the affected side was detected only after 5 months.[23]

Inflammatory THS (those with evidence of granulomatous inflammation on MRI or biopsy) and benign THS have been found to have similar clinical presentation and response to steroids, though the former may be younger, have associated optic nerve dysfunction, and have a longer disease duration.[16]

Mullen *et al*. highlighted a very relevant point that false-negative diagnoses of THS (due to normal neuroimaging or contraindication to MRI) were not harmful to the patients, as their symptoms remitted with the use of steroids. However, it may not be prudent to label such presentations as benign, without repeat imaging or follow-up, especially in the presence of associated systemic features.[24]

To include cases that do not fulfill all current ICHD-3 criteria, Zhang *et al*.[15] suggested grading and ranking of diagnostic criteria into definite, probable, and possible THS, depending upon three levels of clinical features.

- Essential characteristics: PO and recurrence of attacks
- Primary characteristics: Granulomatous inflammation (demonstrated by MRI or pathology) and good response to corticosteroid therapy
- Secondary characteristics: Localization and/or extent of the inflammatory lesion and the temporal relation between onset of pain and ophthalmoplegia.

Vascular imaging

Stenosis of the ICA was an integral component of the original case described by Tolosa in 1954.[1] Vascular imaging in the form of cerebral angiography was considered in ICHD-1 but has not been included in ICHD-2 and ICHD-3. Vascular imaging in the form of digital subtraction angiography, CT angiography (CTA), and MRA have an important role to play in the diagnosis of vascular conditions, such as carotid cavernous fistula, cavernous and parasellar aneurysm, giant cell arteritis, and hemangioma, which may mimic THS clinically and radiologically.

The carotid angiographic abnormalities in THS have been described as irregular narrowing, flattening, and displacement of the cavernous portion of the ICA, sometimes suggesting a mass lesion of the sinus, as well as arterial stationary wave phenomenon and constriction of the internal carotid siphon.[7] These angiographic findings have been reported as reversible following systemic corticosteroid therapy.[11] In addition, venous abnormalities such as obstruction of the third portion of the ipsilateral SOV and altered flow within the ipsilateral CS have also been found on orbital phlebography. These changes, however, were not specific for THS, and the investigation became less relevant with the advent of MRI.[7]

Other pathologies such as neoplasms, infections, granulomatous lesions of the CS, and juxtasellar areas, which may infiltrate or compress the CS, may secondarily constrict the cavernous portion of ICA. However, there are distinguishing features which may help differentiate THS-associated ICA narrowing from other conditions.

Pituitary adenomas may encase the ICA but generally do not narrow the artery.[25] Meningiomas encasing the cavernous ICA often narrow the lumen of the vessel but do not show reversal after steroid therapy and may have characteristic features, such as broad dural base and dural tail.[11] Lymphomas generally cause enlargement of the CS without compressing the ICA and may also show evidence of extension through skull base foramina.[25] Normalization of the ICA caliber after steroids indicates an inflammatory component in the causative lesion. Sarcoidosis of the CS does not have distinguishing features, and diagnosis depends on additional signs such as adjacent dural thickening, pachymeningeal or leptomeningeal enhancement, thickened CN, and evidence of pituitary or orbital involvement. Evidence of pulmonary and/or other systemic involvement aids in cinching the diagnosis.[25] Granulomatosis with polyangiitis-related CS lesions show markedly low-signal intensity on T2-weighted imaging due to internal fibrous tissue and variable enhancement. Involvement of the paranasal sinuses and orbit is typically present in association.[25] ICA stenosis or occlusion can be seen in fungal infections of the CS and carry a high risk of mycotic aneurysm, subarachnoid bleeding, and cerebral infarction.[26,27] On imaging, the CS is typically abnormally enlarged with intense nonhomogeneous enhancement, often with extension of the lesion to the OA and superior orbital fissure (SOF). There may be associated paranasal sinus disease along with bone destruction. These invasive fungal invasions (mainly *Aspergillus* and *Mucor*) may or may not show steroid sensitivity clinically, but the radiological signs generally do not resolve. CS *Actinomyces* infection in the CS, too, may show ICA narrowing with poor steroid sensitivity.[28]

In our literature review, we identified 121 cases of THS (adult and pediatric), where the ICA caliber had been assessed either by MRI, MRA, CTA, or cerebral angiography. Abnormality of the vasculature was found in 44 cases (36.36%), the most common anomaly being narrowing of cavernous

ICA (39/43) [Supplementary Tables 1 and 2]. The more ominous abnormalities included ICA aneurysm and dissection.[29-32] Out of 54 cases of benign THS [Supplementary Tables 2 and 3], four showed vascular anomalies,[33-36] two of which were late-onset dural arteriovenous (AV) fistulas.

While the cases with ICA narrowing showed poststeroid resolution or significant reduction, cases that developed ICA aneurysms and dural AV fistulas required coil embolization.

Narrowing of the cavernous ICA has been described in 44% of pediatric cases with THS.[37] Although this finding is not specific for THS, angiography in THS has a definitive role in aiding the diagnosis[38] and can act as an indirect confirmation of diagnosis on the basis of steroid-induced reversal in cases with ICA narrowing. Slattery *et al*. diagnosed a case of THS in a patient thought to be suffering from Gradenigo syndrome, on the basis of MRA finding of ICA stenosis and subsequent reversal after steroid administration.[39] Associated ICA stenosis has been used as a criterion for radiological diagnosis of THS in large series.[16] Vascular imaging is also essential for the detection of the rarer, but more severe complications. In addition, angiographic findings may offer valuable diagnostic information in some cases with benign THS.[37]

Steroids

While cases of THS may show spontaneous resolution, it is an established fact that the pain element is exquisitely responsive to steroids.[40] However, there is no evidence that corticosteroids hasten the recovery of CN palsy or have an effect on the extent of recovery.[41] Hunt *et al*. were the first to report steroid sensitivity as a feature of this syndrome, which later was to become one of the most recognized elements.[2] This particular feature was even considered one of the essential diagnostic criteria in ICHD-1 and ICHD-2. However, while the former defined it as pain resolution with 72 h of initiation of steroid, the latter required both pain and paresis to resolve within 72 h of adequate dose of steroid administration. The utility of this modification was questioned, since it was ascertained that CN paresis takes longer to resolve.[13,15] Moreover, the optimal dose or duration of treatment has not been defined. A widely accepted treatment regimen is high-dose steroids (>0.5–1 mg/kg) tapered slowly over 3–4 months or longer in some cases.[16,41] Nonetheless, there is no consensus about the efficacy of high-dose steroids over low dose, in inducing resolution and avoiding recurrences.[13,16] In addition, there are no guidelines for the management of THS in children.[37,42]

In ICHD-3, response to steroids was removed altogether, as response to treatment should not be the basis of diagnosis. Instances of FP diagnosis, some of which had adverse outcomes, have discouraged empirical treatment with steroids. Steroid responsiveness may be seen in conditions such as sarcoidosis, infections, lymphomas, and other neoplasms. Further, steroids may mask the true histopathological features and therefore should not be given before biopsy.[43]

However, changes in diagnostic criteria have not completely translated into practice and glucocorticoid administration continues to be a useful diagnostic clue.[14] Zhang *et al*. questioned the logic behind complete removal of steroid response as a criterion, since treatment response to corticosteroids is still a very characteristic feature of THS, and resolution after steroid treatment is required to confirm a diagnosis of THS.[15] Absence or inadequate clinical and radiological response to steroids indicates noninflammatory pathology such as meningioma, infection, or lymphoma.[7,18]

Careful clinical and imaging follow-up is required in patients with PO, after glucocorticoid treatment. Alert should be raised if symptoms recur during steroid treatment or after steroid withdrawal.[14] It is essential to distinguish between recurrence of THS and progression of PO of any other etiology.[14,43] In retrospect, cases which were misdiagnosed as THS on the basis of steroid response, or MRI and clinical presentation, had the following additional features either at presentation or at follow-up.

1. Presence of additional systemic features[26,44-51]
2. Other neurological deficits[52-54]
3. Evidence of immune suppression or previous malignancy[55-63]
4. Atypical features on MRI including nonenhancement on contrast[45,51,53,63-65]
5. Involvement of mandibular or maxillary division of trigeminal (THS is primarily an inflammation of anterior CS)[28,44]
6. Failure of resolution clinically/on MRI[26,28,46,53,66]
7. Severe vision loss.[26]

Idiopathic hypertrophic pachymeningitis and involvement of extracavernous structures

The CS is a pair of dura lined venous spaces on either side of the sphenoid bone. The dura of the roof is continuous with the diaphragma sellae medially, while posteriorly, it is continuous with the tentorium cerebelli at its attachment at the posterior clinoid process. The lateral wall is formed by the visceral layer of dura mater. HP is a chronic progressive diffuse inflammatory fibrosis of the dura mater with or without associated inflammatory changes seen on histopathology.[67] HP may be idiopathic, or associated with trauma, infections, tumors, autoimmune/inflammatory diseases (including IgG4-related disease), and spontaneous intracranial hypotension. Radiologically, HP appears as enhancement of the dura that is evident both on CT and MRI. Contrast-enhanced MRI is the preferred imaging modality.[68] Biopsy is essential for diagnosis. Steroids and immunosuppressants are required for management. HP can affect any part of the intracranial or spinal dura, manifesting as headache, neck rigidity, altered CSF composition (high protein content with or without pleocytosis, predominantly lymphocytic), and focal neurological deficits.[69]

Autopsy finding in the case reported by Tolosa was described as granulomatous tissue of the CS that encircled cavernous portion of the ICA and invaded the adjacent CN.[1] In 1962, Lakke described

a case of Superior Orbital Fissure syndrome caused by local pachymeningitis.[70] He commented on its similarity of clinical and histopathological findings to the case described by Tolosa. It was suggested that since the SOF and CS are immediately adjacent, inflammation occurring in one can spread to the other. THS has been considered a type of focal HP.[71] Granulomatous inflammation in the dural layers of the CS compress the ICA and nerve trunks in the lateral wall of the CS. Dense fibrous entrapment and ischemic damage by hypertrophic tissue cause CN deficits. HP can involve other CNs such as VII and VIII. Miwa *et al*. were one of the earliest to remark on the possibility of a relationship between pachymeningitis and involvement of additional nerves such as CNs VII and VIII in THS.[71] Idiopathic HP has not been considered in any of the versions of ICHD. Involvement of CNs VII and/or VIII cannot be explained on inflammatory tissue in the CS alone. Such cases are bound to have a more diffuse pathology, and careful attention to dural enhancement on MRI and biopsy may confirm the presence of HP.

We reviewed cases of THS and idiopathic HP (biopsy proven and/or radiologically suggestive, i.e., thickening and/or extension of dural enhancement beyond CS) from published literature, where detailed reports along with MRI images were available. Out of 26 such cases, 15 had additional signs such as bilateral PO, CN VII, VIII, or X involvement and pituitary involvement manifesting as hypopituitarism and diabetes insipidus [Supplementary Table 4]. Evidence of pituitary dysfunction in association with CS inflammation has been ascribed to spreading of inflammation from one site to another and termed parasellar chronic inflammatory disease.[72]

However, evidence of HP could not be found in all cases of facial palsy associated with THS.[73] Other reports have documented perineural enhancement in the MCF in addition to CS findings.[74,75] Nevertheless, it is imperative to look for a diffuse/multifocal pathology in all cases with the involvement of extracavernous structures.

Location of inflammation

ICHD-3 limits the location of inflammation to CS, SOF, and orbit (generally interpreted as OA) but does not specify if idiopathic inflammatory pseudotumor of the orbit (IIPO) should be considered a type of THS. Both IIPO and THS result from chronic granulomatous inflammatory processes of unknown origin. IIPO appears isointense with gray matter on Tl-weighted MRI, isointense, or slightly hypointense on T2 scans and enhance with gladolinium, similar to THS.[8,9,76] Both conditions have similar clinical presentation and are generally responsive to steroids.[16] IIPO can have associated myositis, dacryoadenitis, peristyle, or perineuritis. Anatomical contiguity of the CS, SOF, and OA lends support to the theory that THS and IIPO are manifestations of the same inflammatory process in different locations. Thus, anterior inflammations present as IIPO while posterior lesions are seen as THS.[40] There have been instances where IIPO transitioned into THS.[76]

In addition, intracranial extension of the inflammatory tissue beyond the CS has also been documented, some with associated facial palsy.[8,13,14,17,77-79] There are no guidelines for these atypical cases.

Location of pain

Though the essential criterion of PO has remained constant, the description of pain has been changed from orbital pain to unilateral localized headache (around ipsilateral brow and eye), in ICDH-3. The utility of this modification has been questioned as it neither adds to the specificity of diagnosis nor is accurate localization possible in all cases.[17] The most common presenting symptom is retroorbital or/and periorbital pain, while the headache may be hemicranial, frontal, temporal, generalized, or even diffuse [Supplementary Tables 1-3]. The cause of pain is trigeminal neuropathy, and it may manifest as any type of headache, depending upon the dural branches affected. The temporal relation to ophthalmoplegia may vary, possibly depending on which CN is affected first.

Ignoring the importance of criterion D

The list of differential diagnoses for PO is a very long one, with some of the conditions being extremely rare[80] and new ones being reported. All versions of ICHD require the exclusion of other conditions. Thus, short of confirmation by biopsy, THS still remains a diagnosis of exclusion. The onus is now on an extremely detailed evaluation to rule out all other possible causes. It may be relevant to weigh the benefits of a biopsy-aided confirmation of diagnosis versus the risks of a technically challenging invasive procedure. Otherwise, the question remains: How long and how intensively should we keep testing, and not initiate treatment? However, most often, any further diagnostic investigations are prematurely halted once symptoms resolve with steroids, resulting in delayed diagnoses of mimicking pathologies.[44] A close follow-up after steroids with repeat neuroimaging should help early detection of FP cases and hence could be an acceptable alternative.

Discussion

THS is not a diagnosis, but a cluster of symptoms, which may result from a number of pathological conditions. While the eponym aids easy recall of the elements of the syndrome, the fact is that THS is not common and constitutes only 2.9%–3.4% of all the cases of PO.[7] In their assessment of 149 patients presenting with PO, Anagnostou *et al*. ascertained that diabetic microvascular nerve palsy was the most common etiology.[81]

Lubomski *et al*. recommended retiring the term THS and instead using a simple description "PO resolving with corticosteroids" which inherently implies uncertainty and a need for careful review.[47] They favored biopsy in all cases, where a lesion is visible on imaging, unless contraindicated, to avoid delayed/misdiagnosis. Lueck proposed using the terminology "presumed granulomatous inflammation" to emphasize the need for re-evaluation of the diagnosis from time to time.[82]

After a detailed literature review, we propose reverting back to the old terminology of cavernous sinus syndrome (CSS),

qualifying it with the terms painful, presumed inflammatory, steroid responsive, recurrent, etc. CSS can be caused by a number of conditions including vascular, traumatic, neoplastic, infectious, and miscellaneous inflammatory disorders. Large case series on CSS have included THS, defining it as involvement of two or more of the third, fourth, fifth (V1, V2), or sixth CN or involvement of only one of them in combination with a neuroimaging confirmed lesion in the CS.[83-85]

There appears to be no apparent treatment benefit in adhering to the old eponym THS. This label in its true sense implies idiopathic inflammation, but is unfortunately used rather loosely in the context of PO, and is invariably associated with trial of steroids. Premature labeling of a case as THS may be harmful to the patient and may even ensue in medico-legal issues, especially without supporting histopathological diagnosis and radiological confirmation of resolution of lesion after steroids. Use of the CSS nomenclature instead would avoid any presumptive bias with regard to diagnosis and permit modification of the diagnosis as per the course of the disease and investigations. In addition, it would allow inclusion of cases with normal MRI, with evidence of HP or extension of inflammation beyond the CS region, i.e., cases that do not fit current ICHD-3 criteria.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1. Tolosa E. Periarteritic lesions of the carotid siphon with the clinical features of a carotid infraclinoidal aneurysm. J Neurol Neurosurg Psychiatry 1954;17:300-2.
2. Hunt WE, Meagher JN, Lefever HE, Zeman W. Painful opthalmoplegia. Its relation to indolent inflammation of the carvernous sinus. Neurology 1961;11:56-62.
3. Smith JL, Taxdal DS. Painful ophthalmoplegia. The Tolosa-Hunt syndrome. Am J Ophthalmol 1966;61:1466-72.
4. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Headache Classification Committee of the International Headache Society. Cephalalgia 1988;8 Suppl 7:1-96.
5. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 2nd edition. Cephalalgia 2004;24 Suppl 1:9-160.
6. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia 2018;38:1-211.
7. Cakirer S. MRI findings in the patients with the presumptive clinical diagnosis of Tolosa-Hunt syndrome. Eur Radiol 2003;13:17-28.
8. de Arcaya AA, Cerezal L, Canga A, Polo JM, Berciano J, Pascual J. Neuroimaging diagnosis of Tolosa-Hunt syndrome: MRI contribution. Headache 1999;39:321-5.
9. Yousem DM, Atlas SW, Grossman RI, Sergott RC, Savino PJ, Bosley TM. MR imaging of Tolosa-Hunt syndrome. Am J Roentgenol 1990;154:167-70.
10. Förderreuther S, Straube A. The criteria of the International Headache Society for Tolosa-Hunt syndrome need to be revised. J Neurol 1999;246:371-7.
11. Cakirer S. MRI findings in Tolosa-Hunt syndrome before and after systemic corticosteroid therapy. Eur J Radiol 2003;45:83-90.
12. La Mantia L, Curone M, Rapoport AM, Bussone G; International Headache Society. Tolosa-Hunt syndrome: Critical literature review based on IHS 2004 criteria. Cephalalgia 2006;26:772-81.
13. Colnaghi S, Versino M, Marchioni E, Pichiecchio A, Bastianello S, Cosi V, *et al*. ICHD-II diagnostic criteria for Tolosa-Hunt syndrome in idiopathic inflammatory syndromes of the orbit and/or the cavernous sinus. Cephalalgia 2008;28:577-84.
14. Hung CH, Chang KH, Chen YL, Wu YM, Lai CL, Chang HS, *et al*. Clinical and radiological findings suggesting disorders other than tolosa-hunt syndrome among ophthalmoplegic patients: A retrospective analysis. Headache 2015;55:252-64.
15. Zhang X, Zhou Z, Steiner TJ, Zhang W, Liu R, Dong Z, *et al*. Validation of ICHD-3 beta diagnostic criteria for 13.7 Tolosa-Hunt syndrome: Analysis of 77 cases of painful ophthalmoplegia. Cephalalgia 2014;34:624-32.
16. Hung CH, Chang KH, Wu YM, Chen YL, Lyu RK, Chang HS, *et al*. A comparison of benign and inflammatory manifestations of Tolosa-Hunt syndrome. Cephalalgia 2013;33:842-52.
17. Hao R, He Y, Zhang H, Zhang W, Li X, Ke Y. The evaluation of ICHD-3 beta diagnostic criteria for Tolosa-Hunt syndrome: A study of 22 cases of Tolosa-Hunt syndrome. Neurol Sci 2015;36:899-905.
18. Mullen E, Green M, Hersh E, Iloreta AM, Bederson J, Shrivastava R. Tolosa-Hunt Syndrome: Appraising the ICHD-3 beta diagnostic criteria. Cephalalgia 2018;38:1696-700.
19. Wani NA, Jehangir M, Lone PA. Tolosa-Hunt syndrome demonstrated by constructive interference steady state magnetic resonance imaging. J Ophthalmic Vis Res 2017;12:106-9.
20. Colnaghi S, Pichiecchio A, Bastianello S, Versino M. SPIR MRI usefulness for steroid treatment management in Tolosa-Hunt syndrome. Neurol Sci 2006;27:137-9.
21. Okawa S, Hanazono A, Sugawara M, Takahashi S, Otani T, Hanyu N, *et al*. Contrast-enhanced 3D FIESTA imaging in Tolosa-Hunt syndrome. Headache 2012;52:822-4.
22. Mikhail M, Basilious A, Jabehdar Maralani P, Sundaram AN. Tolosa-Hunt syndrome: Case series on the timed use of diagnostic magnetic resonance imaging. Can J Ophthalmol 2020;55:e135-9.
23. Kóbor J, Vörös E, Deák A. Magnetic resonance imaging in Tolosa-Hunt syndrome. Eur J Pediatr 2004;163:753-4.
24. Abdelghany M, Orozco D, Fink W, Begley C. Probable Tolosa-Hunt syndrome with a normal MRI. Cephalalgia 2015;35:449-52.
25. Munawar K, Nayak G, Fatterpekar GM, Sen C, Zagzag D, Zan E, *et al*. Cavernous sinus lesions. Clin Imaging 2020;68:71-89.
26. Marcet MM, Yang W, Albert DM, Salamat MS, Appen RE. Aspergillus infection of the orbital apex masquerading as Tolosa-Hunt syndrome. Arch Ophthalmol 2007;125:563-6.
27. Endo H, Beppu T, Arai H, Ogasawara K, Suzuki T, Suzuki M, *et al*. A case report of aspergillus granuloma in the cavernous sinus. No Shinkei Geka 2001;29:325-9.
28. Tobias S, Lee JH, Tomford JW. Rare *Actinobacillus* infection of the cavernous sinus causing painful ophthalmoplegia: Case report. Neurosurgery 2002;51:807-9.
29. Takasuna H, Sasaki R, Shiraishi M, Doi M, Wakui D, Ito H, *et al*. Steroid-resistant Tolosa-Hunt syndrome with a de novo intracavernous aneurysm: A case report. Surg Neurol Int 2016;7:S779-84.
30. Zhou Z, Zhou G, Lu T, Xu G, Liu X. Tolosa-Hunt syndrome with reversible dissection aneurysm. Neurol Sci 2010;31:777-9.
31. Tsutsumi S, Shimizu Y, Akiyama O, Nonaka Y, Abe Y, Yasumoto Y, *et al*. [Simultaneous presentation of Tolosa-Hunt syndrome and oculomotor nerve palsy due to the nonruptured internal carotid-posterior communicating artery aneurysm: A case report. No Shinkei Geka 2009;37:393-7.
32. Kambe A, Tanaka Y, Numata H, Kawakami S, Kurosaki M, Ohtake M, *et al*. A case of Tolosa-Hunt syndrome affecting both the cavernous sinuses and the hypophysis, and associated with C3 and C4 aneurysms. Surg Neurol 2006;65:304-7.
33. Itokawa K, Fukui M, Yamamoto T, Tamura N, Ishihara S, Araki N. Dural arteriovenous fistula as a possible cause of Tolosa-Hunt syndrome: A case report. J Neurol 2010;257:846-7.
34. Sugano H, Iizuka Y, Arai H, Sato K. Progression of Tolosa-Hunt syndrome to a cavernous dural arteriovenous fistula: A case report. Headache 2003;43:122-6.
35. Ozawa T, Minakawa T, Saito A, Yoneoka Y, Yoshimura J, Arai H. MRA demonstration of "periarteritis" in Tolosa-Hunt syndrome. Acta Neurochir (Wien) 2001;143:309-12.
36. Wu CY, Wang PY, Shen WC. Angiographic findings in Tolosa-Hunt

syndrome: A case report. Zhonghua Yi Xue Za Zhi (Taipei) 1995;55:405-7.
37. Pérez CA, Evangelista M. Evaluation and management of Tolosa-Hunt syndrome in children: A clinical update. Pediatr Neurol 2016;62:18-26.
38. Akpinar ÇK, Özbenli T, Doğru H, Incesu L. Tolosa-Hunt syndrome – Cranial neuroimaging findings. Noro Psikiyatr Ars 2017;54:251-4.
39. Slattery E, White AJ, Gauthier M, Linscott L, Hirose K. Tolosa-Hunt syndrome masquerading as Gradenigo syndrome in a teenager. Int J Pediatr Otorhinolaryngol 2013;77:1219-21.
40. Kline LB, Hoyt WF. The Tolosa-Hunt syndrome. J Neurol Neurosurg Psychiatry 2001;71:577-82.
41. Gladstone JP. An approach to the patient with painful ophthalmoplegia, with a focus on Tolosa-Hunt syndrome. Curr Pain Headache Rep 2007;11:317-25.
42. Pienczk-Reclawowicz K, Pilarska E, Lemka M, Konieczna S. Paediatric Tolosa-Hunt syndrome: The need for treatment guidelines and renewed criteria. Dev Med Child Neurol 2010;52:873-4.
43. Leiba H, Jaggi GP, Boltshauser E, Landau K. Prediction of the clinical outcome of cavernous sinus lesions in children. Neuropediatrics 2013;44:191-8.
44. Mullen E, Rutland JW, Green MW, Bederson J, Shrivastava R. Reappraising the Tolosa-Hunt syndrome diagnostic criteria: A case series. Headache 2020;60:259-64.
45. Douleh DG, Morone PJ, Johnson JE, Paueksakon P, Wellons JC 3rd. Actinomycosis mimicking Tolosa-Hunt syndrome in a 6-year-old boy: Case report. Pediatr Neurosurg 2016;51:214-7.
46. Ohta S, Nishizawa S, Namba H, Sugimura H. Bilateral cavernous sinus actinomycosis resulting in painful ophthalmoplegia. Case report. J Neurosurg 2002;96:600-2.
47. Lubomski M, Dalgliesh J, Lee K, Damodaran O, McKew G, Reddel S. *Actinomyces* cavernous sinus infection: A case and systematic literature review. Pract Neurol 2018;18:373-7.
48. Brandy-García A, Suárez-Cuervo C, Caminal-Montero L. Tolosa-Hunt syndrome as an initial presentation of sarcoidosis. Reumatol Clin 2021;17:178-9.
49. Calistri V, Mostardini C, Pantano P, Pierallini A, Colonnese C, Caramia F. Tolosa-Hunt syndrome in a patient with systemic lupus erythematosus. Eur Radiol 2002;12:341-4.
50. Yu AW, Finkelsztein EJ, Cheng NT. A case of Tolosa-Hunt syndrome with discoid lupus erythematosus. Neurohospitalist 2020;10:48-50.
51. Sánchez Pina C, Pascual-Castroviejo I, Martínez Fernández V, Martínez Jiménez AL, Carrasco Sanz A. Burkitt's lymphoma presenting as Tolosa-Hunt syndrome. Pediatr Neurol 1993;9:157-8.
52. Sakamoto N, Aoyagi Y, Ozaki Y, Kanayama M, Kimula Y, Akabane H. Hodgkin's disease associated with Tolosa-Hunt syndrome. Rinsho Ketsueki 1990;31:172-6.
53. Ruff MW, Carabenciov ID, Johnson DR, Pollock BE, Parisi JE, Klaas JP. A cavernous sinus lesion clinically responsive to steroids. J Clin Neurosci 2018;53:239-40.
54. Oomura M, Uchida Y, Sakurai K, Toyoda T, Okita K, Matsukawa N. Miller Fisher syndrome mimicking Tolosa-Hunt syndrome. Intern Med 2018;57:2735-8.
55. Peddi P, Gallagher KM, Chandrasekharan C, Wang Q, Gonzalez-Toledo E, Nair BS, *et al*. Tolosa-hunt syndrome in double-hit lymphoma. Case Rep Oncol Med. 2015;2015:249891
56. Ghosn J, Brazille P, Zeller V, Stankoff B, Katlama C, Bricaire F. Tolosa-Hunt syndrome revealing Burkitt lymphoma in an HIV-seropositive patient. Presse Med 2003;32:1319-22.
57. Baig I, Webb A, Crowell EL, Supsupin EP, Adesina OO. Burkitt lymphoma masquerading as Tolosa-Hunt syndrome in an HIV-seropositive patient. Eur J Ophthalmol 2020;30:NP41-NP46.
58. Raheja A, Sowder A, Palmer C, Rodriguez FJ, Couldwell WT. Epstein-Barr virus-associated smooth muscle tumor of the cavernous sinus: A delayed complication of allogenic peripheral blood stem cell transplantation: Case report. J Neurosurg 2017;126:1479-83.
59. Shazly TA, Mitchell EB, Bonhomme GR, Schuman JS. Lymphoma of the orbit masquerading as Tolosa-Hunt syndrome. BMC Ophthalmol 2015;15:51.
60. Sedwick LA, Kaufman DI, Fratkin J. Really painful double vision. Surv Ophthalmol 2000;45:155-9.
61. Esmaeli B, Ginsberg L, Goepfert H, Deavers M. Squamous cell carcinoma with perineural invasion presenting as a Tolosa-Hunt-like syndrome: A potential pitfall in diagnosis. Ophthalmic Plast Reconstr Surg 2000;16:450-2.
62. Nieto Enriquez J, Medel Jiménez R, Huguet Redecilla P. Undiagnosed squamous cell carcinoma of the forehead presenting as a Tolosa-Hunt syndrome. Orbit 2009;28:290-2.
63. Pagliani L, Campi L, Cavallini GM. Orbital actinomycosis associated with painful ophthalmoplegia. Actinomycosis of the orbit. Ophthalmologica 2006;220:201-5.
64. Prete B, Sowka J. Painful ophthalmoplegia as an initial presentation of sarcoidosis. Clin Exp Optom 2017;100:291-3.
65. Demirkaya M, Sevinir B, Ozdemir O, Nazlioğlu HO, Okan M. Lymphoma of the cavernous sinus mimicking Tolosa-Hunt syndrome in a child. Pediatr Neurol 2010;42:351-4.
66. Mandrioli J, Frank G, Sola P, Leone ME, Guaraldi G, Guaraldi P, *et al*. Tolosa-Hunt syndrome due to actinomycosis of the cavernous sinus: The infectious hypothesis revisited. Headache 2004;44:806-11.
67. Kupersmith MJ, Martin V, Heller G, Shah A, Mitnick HJ. Idiopathic hypertrophic pachymeningitis. Neurology 2004;62:686-94.
68. Muthukumar N, Senthilbabu S, Usharani K. Idiopathic hypertrophic cranial pachymeningitis masquerading as Tolosa-Hunt syndrome. J Clin Neurosci 2005;12:589-92.
69. Dutta P. Tolosa-Hunt syndrome as a manifestation of hypertrophic pachymeningitis. Eur J Rheumatol 2021;8:51-2. [doi: 10.5152/eurjrheum. 2020.20114].
70. Lakke JP. Superior orbital fissure syndrome. Report of a case caused by local pachymeningitis. Arch Neurol 1962;7:289-300.
71. Miwa H, Koshimura I, Mizuno Y. Recurrent cranial neuropathy as a clinical presentation of idiopathic inflammation of the dura mater: A possible relationship to Tolosa-Hunt syndrome and cranial pachymeningitis. J Neurol Sci 1998;154:101-5.
72. Hama S, Arita K, Kurisu K, Sumida M, Kurihara K. Parasellar chronic inflammatory disease presenting Tolosa-Hunt syndrome, hypopituitarism and diabetes insipidus: A case report. Endocr J 1996;43:503-10.
73. Tsirigotaki M, Ntoulios G, Lioumpas M, Voutoufianakis S, Vorgia P. Tolosa-Hunt syndrome: Clinical manifestations in children. Pediatr Neurol 2019;99:60-3.
74. Lasam G, Kapur S. A Rare Case of Tolosa-Hunt-Like Syndrome in a Poorly Controlled Diabetes Mellitus. Case Rep Med. 2016;2016:9763621. doi: 10.1155/2016/9763621.
75. Kang H, Park KJ, Son S, Choi DS, Ryoo JW, Kwon OY, *et al*. MRI in Tolosa-Hunt syndrome associated with facial nerve palsy. Headache 2006;46:336-9.
76. Wasmeier C, Pfadenhauer K, Rösler A. Idiopathic inflammatory pseudotumor of the orbit and Tolosa-Hunt syndrome – Are they the same disease? J Neurol 2002;249:1237-41.
77. Iaconetta G, Stella L, Esposito M, Cappabianca P. Tolosa-Hunt syndrome extending in the cerebello-pontine angle. Cephalalgia 2005;25:746-50.
78. Cerisola A, González G, Scavone C. Tolosa-Hunt syndrome preceded by facial palsy in a child. Pediatr Neurol 2011;44:61-4.
79. Navi BB, Safdieh JE. Recurrent, alternating Tolosa-Hunt syndrome. Neurologist 2010;16:54-5.
80. Höhne C, Schuh E, Kümpfel T, Straube A. Cryopyrin-associated periodic fever syndrome manifesting as Tolosa-Hunt syndrome. Cephalalgia 2016;36:1392-6.
81. Anagnostou E, Kouzi I, Kararizou E. Painful ophthalmoplegia: The role of imaging and steroid response in the acute and subacute setting. J Neurol Sci 2013;331:145-9.
82. Lueck CJ. Time to retire the Tolosa-Hunt syndrome? Pract Neurol 2018;18:350-1.
83. Keane JR. Cavernous sinus syndrome. Analysis of 151 cases. Arch Neurol 1996;53:967-71.
84. Bhatkar S, Goyal MK, Takkar A, Mukherjee KK, Singh P, Singh R, *et al*. Cavernous sinus syndrome: A prospective study of 73 cases at a tertiary care centre in Northern India. Clin Neurol Neurosurg 2017;155:63-9.
85. Fernández S, Godino O, Martínez-Yélamos S, Mesa E, Arruga J, Ramón JM, *et al*. Cavernous sinus syndrome: A series of 126 patients. Medicine (Baltimore) 2007;86:278-81.

Supplementary Table 1: Tolosa-Hunt syndrome (fulfilling International Classification of Headache 3 criteria) case reports with cavernous internal carotid artery caliber assessment

Author (year)	Age/sex	Vascular imaging	Response to steroid	Pain localization
Dholoo *et al*. (2020)[1]	47/female	CTA - normal, CTV - normal	Complete resolution without steroids	No pain
Rodriguez-Homs *et al*. (2019)[2]	17/female	MRA - normal, MRV - normal	Clinical improvement, radiological - not mentioned	Hemicranial headache, heaviness above the eye
Jarholm *et al*. (2018)[3]	23/female	CTA - normal, CTV - normal	Complete resolution	Retrobulbar pain
Ravindran *et al*. (2018)[4]	26/female	Cerebral angiography - hypervascularity in CS + meningohypophyseal trunk aneurysm	Complete, resolution of vascular changes, clinical improvement	Hemicranial headache, retrobulbar discomfort
Zečević Penić *et al*. (2017)[5]	47/male	MRA - normal	Complete clinical, significant radiological resolution	Frontal headache, periorbital pain
Murtaza *et al*. (2017)[6]	33/male	MRA - A1 segment hypoplastic, no critical stenosis or aneurysm	Complete clinical resolution, radiological - not mentioned	Retro-orbital pain
Świątkowska-Stodulska *et al*. (2017)[7]	80/female	MRI - mild segmental thickening of ICA	Spontaneous complete resolution (without steroids in <6-8 weeks)	Retro-orbital pain + headache
Chakraborty *et al*. (2017)[8]	22/male	MRI - narrowing of ICA	Near complete clinical resolution, radiological - not mentioned	Frontotemporal headache
Pérez and Evangelista (2016)[9]	15/female	Angiography - ICA stenosis	Complete clinical and significant radiological resolution	Periorbital + Retro-orbital
Takasuna *et al*. (2016)[10]	53/female	MRA - initially normal, ICA aneurysm in C4 part of ICA 1 month later	Bilateral sequential PO, steroid resistant, clinical signs improved after surgical drainage, MTX, and antibiotics. Radiological signs decreased, ICA aneurysm persisting	Retro-orbital
Lasam and Kapur (2016)[11]	50/female	Angiography - severe narrowing, encasement, and displacement of cavernous ICA	Complete clinical and radiological resolution	Retro-orbital + headache
Kastirr *et al*. (2016)[12]	47/male	CTA - normal	Complete clinical resolution. Radiological changes persisting on steroids and MTX	Periorbital
Taylor *et al*. (2014)[13]	58/female	CTA - stenosis of cavernous ICA	Complete clinical and radiological resolution	Periorbital + headache
Singh *et al*. (2014)[14]	25/male	MRI - no abnormality of vasculature	Clinical improvement, radiology not mentioned	Retro-orbital
Zurawski and Akhondi (2013)[15]	54/female	MRA - normal	Complete clinical and radiological resolution	Retro-orbital
Kakisaka *et al*. (2013)[16]	11/male	MRA - narrowing of ICA	Complete clinical and radiological resolution	Periorbital + hemicranial
Slattery *et al*. (2013)[17]	17/female	MRA - stenosis of cavernous and distal petrous ICA on affected side	Complete clinical and radiological resolution	Hemicranial headache + facial pain
Beckham *et al*. (2013)[18]	20/male	MRA - normal	Complete clinical and radiological resolution	Retro-orbital
Cerisola *et al*. (2011)[19]	11/male	MRA, cerebral arteriogram - normal Follow-up MRA (at 2 years) - ICA reduced caliber	Complete clinical and radiological resolution except ICA narrowing. Steroid dependence	Periorbital
Benzohra *et al*. (2011)[20]	4/female	MRI - ICA narrowing	Complete radiological resolution, few sequelae of ischemic lesions	Not available
Cornish *et al*. (2011)[21]	10/male	MRA - normal	Complete resolution without steroids	No pain
Kang *et al*. (2011)[22]	7/male	MRA - ICA stenosis	Complete radiological resolution with steroids. Ophthalmoplegia persisting. Bacterial meningitis after 2 weeks, treated with antibiotics. No neurological sequelae	Retro-orbital + frontal
Pienczk-Reclawowicz *et al*. (2010)[23]	14/female	MRA - narrowing of ICA	Complete clinical and radiological resolution	Retro-orbital + frontal
Navi and Safdieh (2010)[24]	24/female	MRA - normal CTA - normal	Complete resolution after steroids, AZT, and MTX	Facial pain
Zhou *et al*. (2010)[25]	49/female	DSA - ICA stenosis and dissection	Complete resolution clinically and radiologically	Retro-orbital

Contd...

Supplementary Table 1: Contd...

Guedes *et al*. (2010)[26]	23/female	MRI - ICA luminal narrowing	Complete clinical and radiological resolution	Occipital headache radiating holocranially
Zanus *et al*. (2009)[27]	8/female	MRI - decreased caliber of ICA of affected side	Complete clinical and radiological resolution	Supraorbital
Tsutsumi *et al*. (2009)[28]	45/female	Cerebral angiography - saccular aneurysm of PCA at branching site	Partially resolved with steroids and coil embolization	Facial pain
Lachanas *et al*. (2008)[29]	40/male	Cerebral angiography - normal	Complete clinical and radiological resolution	Periorbital
Gladstone (2007)[30]	34/male	MRA - narrowing of ICA	Complete clinical and radiological resolution	Periorbital + frontal headache
Kambe *et al*. (2006)[31]	58/female	Cerebral angiography- Focal narrowing of bilateral ICA, aneurysms of bilateral ICA in the left C3 and right C4, absence of blood flow in the right ophthalmic artery	Clinical resolution after steroids. ICA stenosis resolved, but left C3 aneurysm persisting treated by coiling	Retro-orbital + temporal headache
Muthukumar *et al*. (2005)[32]	60/female	MRA - normal	Almost complete clinical resolution. Radiological follow-up not available	Headache (nonspecific)
Foubert-Samier *et al*. (2005)[33]	41/male	Cerebral angiography - normal, orbital venography - normal	Steroid-dependent, complete clinical and partial resolution radiologically after focal radiotherapy	Orbital pain
Iaconetta *et al*. (2005)[34]	65/female	MRI - lesion encasing ICA	Complete clinical and radiological resolution	Periorbital
Yeung *et al*. (2004)[35]	9/male	MRI - compression of ICA and but patent	Complete clinical resolution. Radiological finding reduced	Eye pain + frontal headache
Kóbor *et al*. (2004)[36]	12/female	MRA - normal	Steroid-resistant, complete clinical and radiological resolution	Periorbital
Khan *et al*. (2004)[37]	33/female	MRI - partial obliteration with intimal thickening of the ICA	Complete clinical resolution, radiological - not mentioned	Retro-orbital + temporal headache
Koul and Jain (2003)[38]	Child	MRI - narrowed ICA	Complete clinical and resolution of radiological findings	Headache (nonspecific)
Akçam *et al*. (2003)[39]	22/male	MRA - absence of left ICA and A1 segment of ACA	Complete resolution clinically, radiological signs persisting (query salivary gland tissue)	Retro-orbital + hemicranial headache
del Toro *et al*. (2001)[40]	10/male	MRA and cerebral angiography - ICA stenosis	Complete clinical and radiological resolution without steroids	Retro-orbital
Mormont *et al*. (2000)[41]	32/female	Cerebral angiography - normal, orbital venography - decreased perfusion of CS	Steroid dependent. Complete clinical and radiological resolution after radiotherapy	Temporo-orbital pain
Sumida *et al*. (2000)[42]	48/female	Angiography - stenosis of left ICA	Clinical resolution, regrowth of tentorial lesion on MRI after 1 year, decreased with steroid	Orbital pain
Gonzales GR (1998)[43]	65/female	Cerebral angiography - normal	Partial clinical and complete radiological resolution	Frontal headache + paresthesia
Odabaşi *et al*. (1997)[44]	23/male	Cerebral angiography - decreased caliber of petrous and cavernous ICA	Complete clinical and radiological resolution	PO
Hama *et al*. (1996)[45]	60/male	Cerebral angiography - irregular narrowing of ICA with obstruction in the cavernous portion	Complete resolution of ophthalmoplegia, decrease in the size of the hypophysis and infundibulum, persisting hypopituitarism and DI	PO
Nezu *et al*. (1995)[46]	12/female	MRA - narrowing of carotid siphon	Radiological findings persisting, optic atrophy	Retro-orbital
Zournas *et al*. (1995)[47]	54/male	Digital arteriogram - normal	Complete clinical and radiological resolution	Retro-orbital + frontal pain
Drevelengas *et al*. (1993)[48]	49/male	Angiography - narrowed ICA	Complete clinical and significant radiological resolution	Retro-orbital + bifrontal headache
Thomas *et al*. (1988)[49]	50/male	Arteriography - normal-	Complete clinical and radiological resolution, steroid dependent	Hemicranial

CTA: Computerized tomographic angiography, MRA: Magnetic resonance angiography, CS: Cavernous sinus, ICA: Internal carotid artery (cavernous), PO: Painful ophthalmoplegia, MTX: Methotrexate, AZT: Azathioprine, DSA: Digital subtraction angiography, PCA: Posterior communicating artery, CTV: Computerized tomographic venography, MRV: Magnetic resonance venography, MRI: Magnetic resonance imaging, DI: Diabetes insipidus

Supplementary Table 2: Tolosa Hunt Syndrome (fulfilling International Classification of Headache Disorders 3/2 criteria) case series with cavernous internal carotid artery caliber assessment

Author (year)	Number of cases	Vascular imaging	Response to steroids	Pain localization
Tsirigotaki *et al*. (2019)[50]	2 (pediatric)	MRI - no evidence of ICA narrowing		Periorbital + temporal pain Periorbital
Akpinar *et al*. (2017)[51]	7	All CTA normal		Not available
Hung *et al*. (2013)[52]	49 (28 benign)	MRA/DSA - 1 had evidence of ICA narrowing		Not available
Schuknecht *et al*. (2009)[53]	15	MRI - 7 had evidence of ICA narrowing	Complete resolution	Periorbital in all
Jain *et al*. (2008)[54]	7	MRI - 1 had evidence of ICA narrowing	Complete resolution	Retro-orbital in all
Monzillo *et al*. (2005)[55]	6 (5 benign)	Angiography - no evidence of vascular malformations (query image suggestive of narrowed ICA caliber on MRI)		Periocular in all
Haque *et al*. (2004)[56]	5	Dynamic MRI - normal flow voids in ICA		Retro-orbital Retro-orbital Periorbital + facial pain Periorbital + trigeminal neuralgia Periorbital + headache
Cakirer (2003)[57]	5	MRI - 2 had mild narrowing of ICA	Complete or partial resolution at 8 weeks	Orbital + periorbital pain in all
Wasmeier *et al*. (2002)[58]	2	Cerebral angiography, MRI - both had narrowing of ICA	Complete resolution	Periorbital + temporal headache, dysesthesia in V1 region Periorbital
Tessitore and Tessitore (2000)[59]	2	MRA - 1 had compressed in ICA		Fronto-temporal headache Fronto-orbital headache
Miwa *et al*. (1998)[60]	10 (9 benign THS)	MRA/cerebral angiography - normal in all		Periorbital in all
Takahashi *et al*. (1996)[61]	2	Cerebral angiography - 1 had stenosis of ICA	Significant radiological improvement at 7 weeks	Retro-orbital Headache
Imai *et al*. (1995)[62]	2	Carotid angiography - No evidence of ICA narrowing		Retro-orbital Hemicranial headache

MRI: Magnetic resonance imaging, CTA: Computerized tomographic angiography, ICA: Internal carotid artery (cavernous), MRA: Magnetic resonance angiography, DSA: Digital subtraction angiography, THS: Tolosa Hunt Syndrome

Supplementary Table 3: Enign Tolosa Hunt Syndrome (fulfilling International Classification of Headache Disorders 2 criteria) case reports with cavernous internal carotid artery caliber assessment

Author (year)	Age/sex	Vascular imaging	Response to steroid	Pain localization
Li *et al*. (2020)[63]	63/male	MRA - normal	Complete resolution	Retro-orbital
İlgen Uslu and Özkan (2015)[64]	45/female	MRA - normal	Complete resolution	Retro-orbital + periorbital
Abdelghany *et al*. (2015)[65]	60/female	MRA - normal	Query extent of clinical resolution	Retro-orbital + periorbital + headache
Tsuda *et al*. (2012)[66]	67/female	MRA - normal	Complete resolution	Periorbital
Itokawa *et al*. (2010)[67]	71/female	Cerebral angiography - dural AV fistula in CS (barrow Class D)	Partial clinical resolution with steroids, complete after transvenous cavernous coiling	Orbital + facial
Paci *et al*. (2010)[68]	76/female	MRA - normal	Complete resolution	Retro-orbital
O‘ Connor and Hutchinson (2009)[69]	39/female	MRA - normal	Steroid resistant, complete resolution after infliximab	Orbital + frontal pain + numbness
Mendez *et al*. (2009)[70]	19/female	MRA - normal	Complete resolution	Periorbital
Sugano *et al*. (2003)[71]	58/female	MRA - abnormal signal around ICA Follow up cerebral angiography at 4 months Class D CCF (Barrow’s classification)	Partial clinical resolution with steroids, complete resolution after transvenous cavernous coiling	Painful ophthalmoplegia

Contd...

Supplementary Table 3: Contd...

Ozawa *et al*. (2001)[72]	47/female	MRA - narrowing of ICA, clinoid, and ophthalmic artery. Incidental right MCA aneurysms-clipped	Complete resolution	Periorbital
Foerderreuther *et al*. (1997)[73]	31/male	MRA - no evidence of ICA narrowing	Complete clinical resolution, recurrence of headache	Bioccipital, bifrontal, retro-orbital
Wu *et al*. (1995)[74]	71/male	Angiography - irregularity in carotid siphon	Complete clinical resolution radiological not known	Hemicranial

AV: Arterio-venous, CS: Cavernous sinus, ICA: Internal carotid artery (cavernous), CCF: Carotid cavernous fistula, MRA: Magnetic resonance angiography, MCA: Middle cerebral artery

Supplementary Table 4: Tolosa Hunt Syndrome case reports with associated idiopathic hypertrophic pachymeningitis

Author (year)	Age/sex	MRI	Biopsy	HP	Additional deficits
Yu (2020)[75]	34/male	Enhancement of CS, pituitary and its stalk, mild pressure effect on chiasma		Radiologically suggestive of HP	Hypopituitarism, DI
Madhavan *et al*. (2020)[76]	19/female	Abnormal enhancement involving the left cavernous sinus, Meckel's cave, V2, V3, SOF, and temporal dura	Chronic lymphoplasmacytic inflammatory changes	Biopsy proven HP	Sequential B/L facial palsy
Cação *et al*. (2019)[77]	52/female	Dural thickening of CS		Radiologically suggestive of HP	
Zečević Penić *et al*. (2017)[5]	47/male	Enhancing lesion in CS, extending to trigeminal cave and OA, dural enhancement in CS and along clivus dura		Radiologically suggestive of HP	
Świątkowska-Stodulska *et al*. (2017)[7]	80/female	Infiltrate involving B/L CS, SOF, and sella turcica. Mild segmental thickening of right ICA		Radiologically suggestive of HP	B/L THS
Takasuna *et al*. (2016)[10]	53/female	MRI - enlarged bilateral CS, hypertrophied dura around sella	Granulomatous inflammation	Biopsy proven HP	Bilateral THS with HP, anterior hypopituitarism
Sánchez Vallejo *et al*. (2014)[78]	36/male	Enhancing soft tissue in CS extending to SOF and OA. Hyperenhanced thickened temporal dura, tentorium and orbital apex of affected side		Radiologically suggestive HP	
Kodera *et al*. (2013)[79]	59/male	Enhancing lesion in CS	Thickened dura with inflammatory infiltrate	Biopsy proven HP	B/L THS (sequential)
Slattery *et al*. (2013)[17]	17/female	Enhancement of CS, Meckel's cave and petrous apex of affected side		Radiologically suggestive of HP	
Beraldin *et al*. (2013)[80]	60/male	Enhancing mass in CS-suspected tumor	Nonspecific granulomatous inflammation	Biopsy proven HP	
Sugie *et al*. (2011)[81]	54/male	Diffuse enhancement of bilateral CS with surrounding cranial base dural thickening		Radiologically suggestive HP in poorly controlled DM	B/L sequential THS
Wu *et al*. (2011)[82]	59/female	Bilateral CS and sellar enhancement with extension to right SOF		Radiologically suggestive HP	
Kita *et al*. (2007)[83]	50/female	Mass in CS with thickened sellar dura and swollen pituitary	Thickened dura with inflammatory infiltration	Biopsy-proven HP	DI
Kambe *et al*. (2006)[31]	58/female	Enhancement of pituitary (enlarged) and bilateral CS R>L	Granulomatous inflammation	Biopsy-proven HP	B/L sequential THS
McKinney *et al*. (2006)[84]	50/male	Prominence of CS of affected side, leptomeningeal CN enhancement (II, V1-V3, and X), orbital and infraorbital masses, diffuse dural enhancement	Inflammatory myofibroblastic tumor	Biopsy proven HP	CN X
Muthukumar *et al*. (2005)[32]	60/female	Enhancement of t temporal dura of the base with extension to CS of affected side	Fibrocollagenous tissue with inflammatory infiltrate	Biopsy proven HP	

Contd...

Supplementary Table 4: Contd...

del Toro *et al*. (2001)[40]	10/male	Enlarged CS with enhancement (with inferior extension of dural enhancement)		Radiologically suggestive of HP	
Mormont *et al*. (2000)[41]	32/female	Enhancing mass lesion in CS extending to foramen ovale, Gasserian ganglion, tentorial notch and OA		Radiologically suggestive of HP	
Sumida *et al*. (2000)[42]	48/female	Enhanced mass extending from left CS to sellar floor dura, contralateral CS, and cerebellar tentorium	Thickened dura with abundant collagen fibers with hyalinization	Biopsy proven HP	
Bosch *et al*. (2000)[85]	62/male	Extra-parenchymatous infiltrating lesion in MCF	HP	Biopsy proven HP	CN VII, VIII
Tessitore and Tessitore (2000)[59]	54/female	No evidence of enhancing tissue in CS, only compression of cavernous ICA		Radiologically suggestive of HP	CN VII
Hatano *et al*. (1999)[86]	56/male	Linear enhancement of CS dura		Radiologically suggestive HP	
	69/female	Nodular enhancement of CS and sella	Nonspecific inflammation with lymphocytes, plasma cells and histiocytes	Biopsy proven HP	Sequential B/L THS
Takahashi *et al*. (1996)[61]	46/female	Enhancement of B/L enlarged CS, pituitary, along cerebral convexity		Radiologically suggestive HP	
Hama *et al*. (1996)[45]	54/female	Nonhomogeneous enhancement of CS extending to intrasellar region along edge of cerebellar tentorium		Radiologically suggestive HP	Hypopituitarism
Drevelengas *et al*. (1993)[48]	60/male	Enlargement and enhancement of CS, and hypophysis, thickening of infundibulum, obstruction of ICA. Absent normal high intensity in posterior pituitary lobe	Chronic inflammation in the hypophysis, mucosa of the sphenoid sinus, and dura mater	Biopsy proven HP	Hypopituitarism and DI
Okubo K, *et al*.,1992[87]	49/male	Enhancing mass in sphenoid sinus and CS, causing ICA stenosis CT-demineralisation of sellar floor and left anterior clinoid process		Radiologically suggestive of HP	
	37/male	Enhanced left cavernous sinus and adjacent thickened duramater in the middle cranial fossa		Radiologically suggestive HP	CN VII and VIII (vestibular)

CS: Cavernous sinus, HP: Hypertrophic pachymeningitis, SOF: Superior orbital fissure, OA: Orbital apex, ICA: Internal carotid artery (cavernous), THS: Tolosa Hunt Syndrome, MRI: Magnetic resonance imaging, DI: Diabetes insipidus, CN: Cranial nerves, B/L: Bilateral, MCF: Middle cranial fossa

References

1. Dholoo F, Shabana A, Paschali M, Mandal AK, Missouris CG. Gone in the blink of an eye – A Tolosa-Hunt syndrome variant. J Clin Neurosci 2020;72:458-60.
2. Rodriguez-Homs LG, Goerlitz-Jessen M, Das SU. A 17-Year-Old Girl With Unilateral Headache and Double Vision. J Investig Med High Impact Case Rep. 2019 Jan-Dec;7:2324709619838309. doi: 10.1177/2324709619838309.
3. Jarholm JA, Faiz KW, Nysted T, Zarnovicky S, Kristoffersen ES. Orbital pain, ophthalmoplegia, and oligoclonal bands in the cerebrospinal fluid: A case report of Tolosa-Hunt syndrome. Headache 2018;58:758-60.
4. Ravindran K, Schmalz P, Torun N, Ronthal M, Chang YM, Thomas AJ. Angiographic findings in the Tolosa-Hunt syndrome and resolution after corticosteroid treatment. Neuroophthalmology 2018;42:159-63.
5. Zečević Penić S, Lisak M, Gregurić T, Hećimović H, Bašić Kes V. Tolosa-Hunt syndrome – Case report. Acta Clin Croat 2017;56:331-7.
6. Murtaza G, Konowitz N, Lu H, Faqah A, Kuruvilla A. An Interesting Case of Tolosa-Hunt Syndrome in a Young Male. J Investig Med High Impact Case Rep 201;5:2324709616689478. doi: 10.1177/2324709616689478.
7. Świątkowska-Stodulska R, Stodulski D, Babińska A, Piskunowicz M, Sworczak K. Bilateral Tolosa-Hunt syndrome mimicking pituitary adenoma. Endocrine 2017;58:582-6.
8. Chakraborty PP, Patra S, Barman H, Biswas SN. Cranial neuropathies in uncontrolled diabetes: May not always be due to diabetic microangiopathy. BMJ Case Rep 2017;2017:bcr2017220054.
9. Pérez CA, Evangelista M. Evaluation and management of Tolosa-Hunt syndrome in children: A clinical update. Pediatr Neurol 2016;62:18-26.
10. Takasuna H, Sasaki R, Shiraishi M, Doi M, Wakui D, Ito H, *et al*. Steroid-resistant Tolosa-Hunt syndrome with a *de novo* intracavernous aneurysm: A case report. Surg Neurol Int 2016;7:S779-84.
11. Lasam G, Kapur S. A Rare Case of Tolosa-Hunt-Like Syndrome in a Poorly Controlled Diabetes Mellitus. Case Rep Med. 2016;2016:9763621. doi:

10.1155/2016/9763621.
12. Kastirr I, Kamusella P, Andresen R. Bilateral painful ophthalmoplegia: A case of assumed Tolosa-Hunt syndrome. J Clin Diagn Res 2016;10:TD16-7.
13. Taylor EJ, Anders UM, Martel JR, Martel JB. Tolosa-Hunt syndrome masquerading as a carotid artery dissection. Clin Ophthalmol 2014;8:707-10.
14. Singh MK, Marshall B, Hawley J. Painful ophthalmoplegia: A case of Tolosa-Hunt syndrome. Mil Med 2014;179:e1409-10.
15. Zurawski J, Akhondi H. Tolosa-Hunt syndrome – A rare cause of headache and ophthalmoplegia. Lancet 2013;382:912.
16. Kakisaka Y, Kobayashi T, Uematsu M, Numata Y, Hirose M, Hino-Fukuyo N, *et al*. Utility of thallium-201 scintigraphy in Tolosa-Hunt syndrome. Tohoku J Exp Med 2013;229:83-6.
17. Slattery E, White AJ, Gauthier M, Linscott L, Hirose K. Tolosa-Hunt syndrome masquerading as Gradenigo syndrome in a teenager. Int J Pediatr Otorhinolaryngol 2013;77:1219-21.
18. Beckham S, Kim H, Truong A. Painful ophthalmoplegia of the right eye in a 20-year-old man. J Emerg Med 2013;44:e231-4.
19. Cerisola A, González G, Scavone C. Tolosa-Hunt syndrome preceded by facial palsy in a child. Pediatr Neurol 2011;44:61-4.
20. Benzohra DE, Damry N, Delpierre I, Huybrechts S, Monier A, Christophe C. Tolosa-Hunt syndrome in children. JBR-BTR 2011;94:290-2.
21. Cornish KS, Cornish DS, Vella M. An unusual case of pediatric painless ophthalmoplegia. Semin Ophthalmol 2011;26:47-9.
22. Kang CH, Huang YC, Lui CC, Chang YC, Hung PL. Unusual clinical course in pediatric Tolosa-Hunt syndrome. Pediatr Neurol 2011;44:471-4.
23. Pienczk-Reclawowicz K, Pilarska E, Lemka M, Konieczna S. Paediatric Tolosa-Hunt syndrome: The need for treatment guidelines and renewed criteria. Dev Med Child Neurol 2010;52:873-4.
24. Navi BB, Safdieh JE. Recurrent, alternating Tolosa-Hunt syndrome. Neurologist 2010;16:54-5.
25. Zhou Z, Zhou G, Lu T, Xu G, Liu X. Tolosa-Hunt syndrome with reversible dissection aneurysm. Neurol Sci 2010;31:777-9.
26. Guedes BV, da Rocha AJ, Zuppani HB, da Silva CJ, Sanvito WL. A case review of the MRI features in alternating Tolosa-Hunt syndrome. Cephalalgia 2010;30:1133-6.
27. Zanus C, Furlan C, Costa P, Cosentini D, Carrozzi M. The Tolosa-Hunt syndrome in children: A case report. Cephalalgia 2009;29:1232-7.
28. Tsutsumi S, Shimizu Y, Akiyama O, Nonaka Y, Abe Y, Yasumoto Y, *et al*. Simultaneous presentation of Tolosa-Hunt syndrome and oculomotor nerve palsy due to the nonruptured internal carotid-posterior communicating artery aneurysm: A case report. No Shinkei Geka 2009;37:393-7.
29. Lachanas VA, Karatzias GT, Tsitiridis I, Panaras I, Sandris VG. Tolosa-Hunt syndrome misdiagnosed as sinusitis complication. J Laryngol Otol 2008;122:97-9.
30. Gladstone JP. An approach to the patient with painful ophthalmoplegia, with a focus on Tolosa-Hunt syndrome. Curr Pain Headache Rep 2007;11:317-25.
31. Kambe A, Tanaka Y, Numata H, Kawakami S, Kurosaki M, Ohtake M, *et al*. A case of Tolosa-Hunt syndrome affecting both the cavernous sinuses and the hypophysis, and associated with C3 and C4 aneurysms. Surg Neurol 2006;65:304-7.
32. Muthukumar N, Senthilbabu S, Usharani K. Idiopathic hypertrophic cranial pachymeningitis masquerading as Tolosa-Hunt syndrome. J Clin Neurosci 2005;12:589-92.
33. Foubert-Samier A, Sibon I, Maire JP, Tison F. Long-term cure of Tolosa-Hunt syndrome after low-dose focal radiotherapy. Headache 2005;45:389-91.
34. Iaconetta G, Stella L, Esposito M, Cappabianca P. Tolosa-Hunt syndrome extending in the cerebello-pontine angle. Cephalalgia 2005;25:746-50.
35. Yeung MC, Kwong KL, Wong YC, Wong SN. Paediatric Tolosa-Hunt syndrome. J Paediatr Child Health 2004;40:410-3.
36. Kóbor J, Vörös E, Deák A. Magnetic resonance imaging in Tolosa-Hunt syndrome. Eur J Pediatr 2004;163:753-4.
37. Khan MA, Hashmi SM, Prinsley PR, Premachandra DJ. Reidel's thyroiditis and Tolosa-Hunt syndrome, a rare association. J Laryngol Otol 2004;118:159-61.
38. Koul R, Jain R. Tolosa-Hunt syndrome: MRI before and after treatment. Neurol India 2003;51:137.
39. Akçam T, Kocaoğlu M, Gerek M, Birkent H, Ozkaptan Y, Tayfun C. Tolosa-Hunt syndrome with heterotopic salivary gland tissue and absence of internal carotid artery. Auris Nasus Larynx 2003;30:325-9.
40. del Toro M, Macaya A, Vazquez E, Roig M. Painful ophthalmoplegia with reversible carotid stenosis in a child. Pediatr Neurol 2001;24:317-9.
41. Mormont E, Laloux P, Vauthier J, Ossemann M. Radiotherapy in a case of Tolosa-Hunt syndrome. Cephalalgia 2000;20:931-3.
42. Sumida M, Taguchi H, Eguchi K, Kuroki K. A case of idiopathic cranial hypertrophic pachymeningitis presenting Tolosa-Hunt syndrome. No To Shinkei 2000;52:523-7.
43. Gonzales GR. Pain in Tolosa-Hunt syndrome. J Pain Symptom Manage 1998;16:199-204.
44. Odabaşi Z, Gökçil Z, Atilla S, Pabuşçu Y, Vural O, Yardim M. The value of MRI in a case of Tolosa-Hunt syndrome. Clin Neurol Neurosurg 1997;99:151-4.
45. Hama S, Arita K, Kurisu K, Sumida M, Kurihara K. Parasellar chronic inflammatory disease presenting Tolosa-Hunt syndrome, hypopituitarism and diabetes insipidus: A case report. Endocr J 1996;43:503-10.
46. Nezu A, Kimura S, Osaka H. Tolosa-Hunt syndrome with pseudotumor cerebri. Report of an unusual case. Brain Dev 1995;17:216-8.
47. Zournas C, Trakadas S, Kapaki E, Doris S, Gatzonis S, Gouliamos A, *et al*. Gadopentetate dimeglumine-enhanced MR in the diagnosis of the Tolosa-Hunt syndrome. Am J Neuroradiol 1995;16:942-4.
48. Drevelengas A, Kalaitzoglou I, Tsolaki M. Tolosa-Hunt syndrome with sellar erosion: Case report. Neuroradiology 1993;35:451-3.
49. Thomas DJ, Charlesworth MC, Afshar F, Galton DJ. Computerised axial tomography and magnetic resonance scanning in the Tolosa-Hunt syndrome. Br J Ophthalmol 1988;72:299-302.
50. Tsirigotaki M, Ntoulios G, Lioumpas M, Voutoufianakis S, Vorgia P. Tolosa-Hunt syndrome: Clinical manifestations in children. Pediatr Neurol 2019;99:60-3.
51. Akpinar ÇK, Özbenli T, Doğru H, Incesu L. Tolosa-Hunt syndrome – Cranial neuroimaging findings. Noro Psikiyatr Ars 2017;54:251-4.
52. Hung CH, Chang KH, Wu YM, Chen YL, Lyu RK, Chang HS, *et al*. A comparison of benign and inflammatory manifestations of Tolosa-Hunt syndrome. Cephalalgia 2013;33:842-52.
53. Schuknecht B, Sturm V, Huisman TA, Landau K. Tolosa-Hunt syndrome: MR imaging features in 15 patients with 20 episodes of painful ophthalmoplegia. Eur J Radiol 2009;69:445-53.
54. Jain R, Sawhney S, Koul RL, Chand P. Tolosa-Hunt syndrome: MRI appearances. J Med Imaging Radiat Oncol 2008;52:447-51.
55. Monzillo PH, Saab VM, Protti GG, Costa AR, Sanvito WL. Síndrome de Tolosa-Hunt: Análise de seis casos. Arq Neuropsiquiatr 2005;63:648-51.
56. Haque TL, Miki Y, Kashii S, Yamamoto A, Kanagaki M, Takahashi T, *et al*. Dynamic MR imaging in Tolosa-Hunt syndrome. Eur J Radiol 2004;51:209-17.
57. Cakirer S. MRI findings in Tolosa-Hunt syndrome before and after systemic corticosteroid therapy. Eur J Radiol 2003;45:83-90.
58. Wasmeier C, Pfadenhauer K, Rösler A. Idiopathic inflammatory pseudotumor of the orbit and Tolosa-Hunt syndrome – Are they the same disease? J Neurol 2002;249:1237-41.
59. Tessitore E, Tessitore A. Tolosa-Hunt syndrome preceded by facial palsy. Headache 2000;40:393-6.
60. Miwa H, Koshimura I, Mizuno Y. Recurrent cranial neuropathy as a clinical presentation of idiopathic inflammation of the dura mater: A possible relationship to Tolosa-Hunt syndrome and cranial pachymeningitis. J Neurol Sci 1998;154:101-5.
61. Takahashi Y, Abe T, Kojima K, Ochiai S, Miyagi J, Shigemori M. Tolosa-Hunt syndrome with atypical intrasellar and juxtasellar lesions – Two case reports. Kurume Med J 1996;43:165-70.

62. Imai F, Kiya N, Ogura Y, Nomura M, Gireesh K, Sano H, *et al*. Tolosa-Hunt syndrome with unusual clinical courses – Two case reports. Neurol Med Chir (Tokyo) 1995;35:28-31.
63. Li L, Wang Z, Lu MO. Tolosa-Hunt syndrome with general myasthenia gravis involvement. J Integr Neurosci 2020;19:355-7.
64. İlgen Uslu F, Özkan M. Painful ophthalmoplegia: A case report and literature review. Agri 2015;27:219-23.
65. Abdelghany M, Orozco D, Fink W, Begley C. Probable Tolosa-Hunt syndrome with a normal MRI. Cephalalgia 2015;35:449-52.
66. Tsuda H, Hisada M, Tanaka K, Miura Y, Kishida S. Isolated trochlear nerve palsy in Tolosa-Hunt syndrome. Intern Med 2012;51:1591-3.
67. Itokawa K, Fukui M, Yamamoto T, Tamura N, Ishihara S, Araki N. Dural arteriovenous fistula as a possible cause of Tolosa-Hunt syndrome: A case report. J Neurol 2010;257:846-7.
68. Paci M, Wein TH, Bekhor S. An unusual case of retro-orbital pain with diplopia. Can J Neurol Sci 2010;37:888-9.
69. O' Connor G, Hutchinson M. Tolosa-Hunt syndrome responsive to infliximab therapy. J Neurol 2009;256:660-1.
70. Mendez JA, Arias CR, Sanchez D, Pesci LM, Lopez BS, Lopez R, *et al*. Painful ophthalmoplegia of the left eye in a 19-year-old female, with an emphasis in Tolosa-Hunt syndrome: A case report. Cases J 2009;2:8271.
71. Sugano H, Iizuka Y, Arai H, Sato K. Progression of Tolosa-Hunt syndrome to a cavernous dural arteriovenous fistula: A case report. Headache 2003;43:122-6.
72. Ozawa T, Minakawa T, Saito A, Yoneoka Y, Yoshimura J, Arai H. MRA demonstration of "periarteritis" in Tolosa-Hunt syndrome. Acta Neurochir (Wien) 2001;143:309-12.
73. Foerderreuther S, von Maydell R, Straube A. A CPH-like picture in two patients with an orbitocavernous sinus syndrome. Cephalalgia 1997;17:608-11.
74. Wu CY, Wang PY, Shen WC. Angiographic findings in Tolosa-Hunt syndrome: A case report. Zhonghua Yi Xue Za Zhi (Taipei) 1995;55:405-7.
75. Yu R. Tolosa-Hunt syndrome with pituitary involvement. Endocr Pract 2020 Mar 11. doi: 10.4158/EP-2020-0049. Epub ahead of print. PMID: 32160047.
76. Madhavan AA, DeLone DR, Verdoorn JT. Bilateral facial nerve involvement in a patient with Tolosa-Hunt syndrome. Neuroradiol J 2020;33:424-7.
77. Cação G, Calejo M, Alves JE, Medeiros PB, Vila-Cha N, Mendonça T, *et al*. Clinical features of hypertrophic pachymeningitis in a center survey. Neurol Sci 2019;40:543-51.
78. Sánchez Vallejo R, Lopez-Rueda A, Olarte AM, San Roman L. MRI findings in Tolosa-Hunt syndrome (THS). BMJ Case Rep 2014;2014:bcr2014206629.
79. Kodera T, Takeuchi H, Arishima H, Tsunetoshi K, Kitai R, Arai Y, *et al*. Microsurgical findings of Tolosa-Hunt syndrome. World Neurosurg 2013;79:594.e1-4.
80. Beraldin BS, Felippu A, Martinelli F, Patricio HC. Tolosa-Hunt syndrome mimicking cavernous sinus tumor. Braz J Otorhinolaryngol 2013;79:256.
81. Sugie K, Morikawa M, Taoka T, Hirano M, Ueno S. Serial neuroimaging in tolosa-hunt syndrome with acute bilateral complete ophthalmoplegia. J Neuroimaging 2011;21:79-82.
82. Wu YC, Hsieh TC, Kao CH, Liu YL, Yen KY, Sun SS. A rare case of Tolosa-Hunt syndrome imaged with FDG PET/CT and MRI. Clin Nucl Med 2011;36:574-5.
83. Kita D, Tachibana O, Nagai Y, Sano H, Yamashita J. Granulomatous pachymeningitis around the sella turcica (Tolosa-Hunt syndrome) involving the hypophysis – Case report. Neurol Med Chir (Tokyo) 2007;47:85-8.
84. McKinney AM, Short J, Lucato L, SantaCruz K, McKinney Z, Kim Y. Inflammatory myofibroblastic tumor of the orbit with associated enhancement of the meninges and multiple cranial nerves. AJNR Am J Neuroradiol 2006;27:2217-20.
85. Bosch J, Ortega-Aznar A, Tintoré M, Río J, Ferreira R, Rubio E, *et al*. Paquimeningitis hipertrófica. Revisión histórica a propósito de dos casos y relación patogénica con el síndrome Tolosa-Hunt y el pseudotumor orbitario. Rev Neurol 2000;31:946-51.
86. Hatano N, Behari S, Nagatani T, Kimura M, Ooka K, Saito K, *et al*. Idiopathic hypertrophic cranial pachymeningitis: Clinicoradiological spectrum and therapeutic options. Neurosurgery 1999;45:1336-42.
87. Okubo K, Tokuda T, Nakamura A, Hashimoto T, Koh CS, Yanagisawa N. A case of Tolosa-Hunt syndrome accompanied by facial and vestibular nerve damage. No To Shinkei 1992;44:655-9.