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

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

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKLRRPMedknow_reprints@wolterskluwer.com

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.

© 2021 Journal of Current Ophthalmology | Published by Wolters Kluwer - Medknow
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. 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. The diagnostic criteria were modified by expert consensus, subsequently, in 2004 and 2018. 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.

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. 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). 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 (sarcoïdosis), 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. 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. However, radiological resolution lags behind clinical response and findings may not resolve up to several months. 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.

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 preptine cistern, or invading the paranasal sinuses, brain parenchyma, skull and/or causing bone erosion, and evidence of superior orbital vein (SOV) enhancement and dilatation.

**Benign Tolosa–Hunt syndrome**

In 1990, Yousem et al. reported that a small percentage of patients with clinically apparent THS may have normal imaging. La Mantia et al. termed this variant “benign” THS. In a retrospective review of published THS cases between 1998 and 2002, they found that 48% of cases meeting the ICHD-2
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. In such cases, dynamic, contrast-enhanced high-resolution MRI with fat suppression may aid in the detection of lesions otherwise missed by conventional MRI. 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.

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. Mikhail et al. highlighted this radiological lag in two apparently benign THS cases. 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. Köbor 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.

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.

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.

To include cases that do not fulfill all current ICHD-3 criteria, Zhang et al. 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. 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. These angiographic findings have been reported as reversible following systemic corticosteroid therapy. 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.

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 en-case the ICA but generally do not narrow the artery. 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. Lymphomas generally cause enlargement of the CS without compressing the ICA and may also show evidence of extension through skull base foramina. 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. 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. 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. 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 Actinomycetes infection in the CS, too, may show ICA narrowing with poor steroid sensitivity.

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.26,32 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 diagnosis38 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 the 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.15,15 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.41 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 features26,44,51
2. Other neurological deficits52–54
3. Evidence of immune suppression or previous malignancy55–63
4. Atypical features on MRI including nonenhancement on contrast45,51,53,63–65
5. Involvement of mandibular or maxillary division of trigeminal (THS is primarily an inflammation of anterior CS)29,44
6. Failure of resolution clinically/on MRI26,28,46,53,66
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. 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. 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. 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. 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. 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.

However, evidence of HP could not be found in all cases of facial palsy associated with THS. Other reports have documented perineural enhancement in the MCF in addition to CS findings. Nevertheless, it is imperative to look for a diffuse-multifocal pathology in all cases with the involvement of extravascular 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 TI-weighted MRI, isointense, or slightly hypointense on T2 scans and enhance with gadolinium, similar to THS. Both conditions have similar clinical presentation and are generally responsive to steroids. 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. There have been instances where IIPO transitioned into THS.

In addition, intracranial extension of the inflammatory tissue beyond the CS has also been documented, some with associated facial palsy. 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 ICHD-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. 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 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. 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. In their assessment of 149 patients presenting with PO, Anagnostou et al. ascertained that diabetic microvascular nerve palsy was the most common etiology. 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. 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.

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. 3-8

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 infraclinoidial aneurysm. J Neurol Neurosurg Psychiatry 1954;17:300-2.
2. Hunt WE, Meagher JN, Lefever HE, Zeman W. Painful ophthalmoplegia. Its relation to indolent inflammation of the carvenous 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. Caikner 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, Cereal L, Canga A, Polo JM, Berciano J, Pascual J. MR imaging of Tolosa-Hunt syndrome. Am J Roentgenol 1990;154:167-70.
9. Fördrederuther S, Straube A. The criteria of the International Headache Society for Tolosa-Hunt syndrome need to be revised. J Neurol 1999;246:371-7.
10. Caikner S. MRI findings in Tolosa-Hunt syndrome before and after systemic corticosteroid therapy. Eur J Radiol 2003;45:83-90.
11. La Mantia L, Cuccure M, Rapoport AM, Busseone G. International Headache Society. Tolosa-Hunt syndrome: Critical literature review based on IHS 2004 criteria. Cephalalgia 2006;26:772-81.
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 Neurosurg 2016;62:18-26.
38. Akpinar ÇK, Özbenli T, Doğru H, Incesu L. Tolosa-Hunt syndrome – Cranial neuroimaging findings. Noro Psikiyat Ars 2017;54:251-4.
39. Slaterrry E, White AJ, Gauthier M, Linscott L, Hirose K. Tolosa-Hunt syndrome masquerading as Gradengo 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. Pienczecklawowiczk K, Pilarska E, Lemka M, Konieczna S. Paediatric Tolosa-Hunt syndrome: The need for treatment guidelines and renewed criteria. Dev Med Child Neurolo 2010;52:873-4.
43. Leiba H, Jaggi GP, Boltschauer E, Landau K. Prediction of the clinical outcome of cavernous sinus lesions in children. Neuropediatrics 2013;44:191-8.
44. Muller 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, Paukekson P, Wellons JC 3rd. Actinomyces 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 Neurol Neurosurg Psychiatry 2002;69:600-2.
47. Lubomski M, Dalgliesh J, Lee K, Damodaran O, McKew G, Reddel S. Tolosa-Hunt syndrome: The need for treatment guidelines and renewed criteria. Dev Med Child Neurol 2010;52:873-4.
48. Mitchell EB, Bonhomme GR, Schuman JS. Lymphoma of the cavernous sinus: A delayed complication of allogenic peripheral blood stem cell transplantation. Case report. J Neurosurg 2017;126:1479-83.
49. Shazly TA, Mitchell EB, Bonhomme GR, Schuman JS. Lymphoma of the orbit masquerading as Tolosa-Hunt syndrome. BMC Ophthalmol 2015;15:51.
50. Sedwick LA, Kaufman DI, Fratkin J. Really painful double vision. Surv Ophthalmol 2008;45:155-9.
51. Sánchez Pina C, Pascual-Castroviejo I, Martínez Fernández V. Actinomyces meningitis or cavernous sinus actinomycosis resulting in painful ophthalmoplegia. Case report. Actinomycosis mimicking Tolosa-Hunt syndrome. Pediatr Neurol 1993;9:157-8.
52. Martínez Jiménez AL, Carrasco Sanz A. Burkitt's lymphoma presenting as Tolosa-Hunt syndrome. Rinsho Ketsueki 1990;31:172-6.
53. Ruff MW, Carabencio 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 as a manifestation of hypertrophic pachymeningitis. J Neurol Sci 1998;154:105-15.
57. Hamza S, Arita K, Kuriu S, 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.
58. Tsirigotaki M, Ntoulios G, Lioumpas M, Voutoufanakis S, Vorgia P. Tolosa-Hunt syndrome: Clinical manifestations in children. Pediatr Neurol 2019;60:60-9.
59. Lam S, Capur 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.
60. 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.
61. Wasmiecr M, Pfludenhauer K, Rösler A. Idiopathic inflammatory pseudotumor of the orbit and Tolosa-Hunt syndrome – Are they the same disease? J Neurol Neurosurg Psychiatry 2002;72:249-57.
62. Jaconet G, Steila L, Esposito M, Cappabianca P, Tolosa-Hunt syndrome extending in the cerebellum-pontine angle. Cephalalgia 2005;25:746-50.
63. Capur S, Boltschauer E, Landau K. Painful ophthalmoplegia mimicking Tolosa-Hunt syndrome – Cranial pachymeningitis masquerading as Tolosa-Hunt syndrome. J Neurol Neurosci 2013;44:1237-41.
64. Casal S, Gómez G, Scavone C. Tolosa-Hunt syndrome preceded by facial palsy in a child. Pediatr Neurol 2011;44:61-4.
65. Ruhl CE. Time to retire the Tolosa-Hunt syndrome? Pract Neurol 2018;18:350-1.
66. Keane JR. Cavernous sinus syndrome. Analysis of 151 cases. Arch Neurol 1996;53:967-71.
67. Bhaktar 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.
68. 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;86:278-91.
### 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 |
|---------------|---------|------------------|---------------------|-------------------|
| Dhooloo et al. (2020) | 47/female | CTA - normal, CTV - normal | Complete resolution without steroids | No pain |
| Rodriguez-Homs et al. (2019) | 17/female | MRA - normal, MRV - normal | Clinical improvement, radiological - not mentioned | Hemicranial headache, heaviness above the eye |
| Jarholm et al. (2018) | 23/female | CTA - normal, CTV - normal | Complete resolution | Retrobulbar pain |
| Ravindran et al. (2018) | 26/female | Cerebral angiography - hypervascularity in CS + meningohypophyseal trunk aneurysm | Complete, resolution of vascular changes, clinical improvement | Hemicranial headache, retrobulbar discomfort |
| Zečević Pienić et al. (2017) | 47/male | MRA - normal | Complete clinical, significant radiological resolution | Frontal headache, periorbital pain |
| Murtaza et al. (2017) | 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) | 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) | 22/male | MRI - narrowing of ICA | Near complete clinical resolution, radiological - not mentioned | Frontotemporal headache |
| Pérez and Evangelista (2016) | 15/female | Angiography - ICA stenosis | Complete clinical and significant radiological resolution | Periorbital + Retro-orbital |
| Takasuna et al. (2016) | 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) | 50/female | Angiography - severe narrowing, encasement, and displacement of cavernous ICA | Complete clinical and radiological resolution | Retro-orbital + headache |
| Kastirr et al. (2016) | 47/male | CTA - normal | Complete clinical resolution. Radiological changes persisting on steroids and MTX | Periorbital |
| Taylor et al. (2014) | 58/female | CTA - stenosis of cavernous ICA | Complete clinical and radiological resolution | Periorbital + headache |
| Singh et al. (2014) | 25/male | MRI - no abnormality of vasculature | Clinical improvement, radiology not mentioned | Retro-orbital |
| Zurawski and Akhondi (2013) | 54/female | MRA - normal | Complete clinical and radiological resolution | Periorbital |
| Kakisaka et al. (2013) | 11/male | MRA - narrowing of ICA | Complete clinical and radiological resolution | Periorbital + hemicranial |
| Slattery et al. (2013) | 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) | 20/male | MRA - normal | Complete clinical and radiological resolution | Retro-orbital |
| Cerisola et al. (2011) | 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) | 4/female | MRI - ICA narrowing | Complete radiological resolution, few sequelae of ischemic lesions | Not available |
| Cornish et al. (2011) | 10/male | MRA - normal | Complete resolution without steroids | No pain |
| Kang et al. (2011) | 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) | 14/female | MRA - narrowing of ICA | Complete clinical and radiological resolution | Retro-orbital + frontal |
| Navi and Safdieh (2010) | 24/female | MRA - normal CTA - normal | Complete resolution after steroids, AZT, and MTX | Facial pain |
| Zhou et al. (2010) | 49/female | DSA - ICA stenosis and dissection | Complete resolution clinically and radiologically | Retro-orbital |

*Contd...*
| Reference                                    | Age  | Sex  | Diagnosis                                                                 | Clinical Resolution                                      | Radiological Resolution                                      | Headache Type                                      |
|----------------------------------------------|------|------|---------------------------------------------------------------------------|----------------------------------------------------------|-------------------------------------------------------------|-------------------------------------------------|
| Guedes et al. (2010)                         | 23   | female | MRI - ICA luminal narrowing                                              | Complete clinical and radiological resolution            | Occipital headache radiating holocranially                  |                                                 |
| Zanus et al. (2009)                          | 8    | female | MRI - decreased caliber of ICA of affected side                          | Complete clinical and radiological resolution            | Supraorbital                                                |                                                 |
| Tsutsumi et al. (2009)                       | 45   | female | Cerebral angiography - saccular aneurysm of PCA at branching site         | Partially resolved with steroids and coil embolization   | Facial pain                                                  |                                                 |
| Lachanas et al. (2008)                       | 40   | female | Cerebral angiography - normal                                            | Complete clinical and radiological resolution            | Periorbital                                                  |                                                 |
| Gladstone (2007)                             | 34   | male  | MRA - narrowing of ICA                                                  | Complete clinical and radiological resolution            | Periorbital + frontal headache                               |                                                 |
| Kambe et al. (2006)                          | 58   | female | Cerebral angiography- Focal narrowing of bilateral ICA,                  | Clinical resolution after steroids.                     | Retro-orbital + temporal headache                           |                                                 |
| Muthukumar et al. (2005)                     | 60   | female | MRI - lesion encasing ICA                                                | Almost complete clinical resolution.                    | Headache (nonspecific)                                      |                                                 |
| Foubert-Samier et al. (2005)                 | 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)                      | 65   | female | MRI - compression of ICA and but patent                                   | Complete clinical resolution.                           | Periorbital                                                  |                                                 |
| Yeung et al. (2004)                          | 9    | male  | MRI - compression of ICA and but patent                                   | Complete clinical resolution.                           | Eye pain + frontal headache                                 |                                                 |
| Kóbor et al. (2004)                          | 12   | female | MRA - normal                                                              | Steroid-resistant, complete clinical and radiological resolution | Periorbital                                                 |                                                 |
| Khan et al. (2004)                           | 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)                         | Child|                            | MRI - narrowed ICA                                                        | Complete clinical and resolution of radiological findings | Headache (nonspecific)                                      |                                                 |
| Akçam et al. (2003)                          | 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)                       | 10   | male  | MRA and cerebral angiography - ICA stenosis                              | Complete clinical and radiological resolution without steroids | Retro-orbital                                                |                                                 |
| Mormont et al. (2000)                        | 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)                         | 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)                           | 65   | female | Cerebral angiography - normal                                             | Partial clinical and complete radiological resolution   | Frontal headache + paresthesia                              |                                                 |
| Odabaşı et al. (1997)                        | 23   | male  | Cerebral angiography - decreased caliber of petrous and cavernous ICA    | Complete clinical and radiological resolution            | PO                                                          |                                                 |
| Hama et al. (1996)                           | 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)                           | 12   | female | MRA - narrowing of carotid siphon                                         | Radiological findings persisting, optic atrophy         | Retro-orbital                                                |                                                 |
| Zournas et al. (1995)                        | 54   | male  | Digital arteriogram - normal                                             | Complete clinical and radiological resolution            | Retro-orbital + frontal pain                                |                                                 |
| Drevelengas et al. (1993)                    | 49   | male  | Angiography - narrowed ICA                                               | Complete clinical and significant radiological resolution | Retro-orbital + bifrontal headache                         |                                                 |
| Thomas et al. (1988)                         | 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)⁹⁰       | 2 (pediatric)   | MRI - no evidence of ICA narrowing                     | Periorbital + temporal pain        |                                   |
| Akpinar et al. (2017)⁹¹          | 7               | All CTA normal                                        | Not available                      |                                   |
| Hung et al. (2013)⁹²             | 49 (28 benign)  | MRA/DSA - I had evidence of ICA narrowing              | Periorbital                        |                                   |
| Schuknecht et al. (2009)⁹³        | 15              | MRI - 7 had evidence of ICA narrowing                 | Periorbital in all                 |                                   |
| Jain et al. (2008)⁹⁴             | 7               | MRI - 1 had evidence of ICA narrowing                 | Complete resolution                | Retro-orbital in all              |
| Monzillo et al. (2005)⁹⁵         | 6 (5 benign)    | Angiography - no evidence of vessel malformations (query image suggestive of narrowed ICA caliber on MRI) | Complete resolution                | Periorbital in all                |
| Haque et al. (2004)⁹⁶            | 5               | Dynamic MRI - normal flow voids in ICA                 | Periorbital                        |                                   |
| Cakirer (2003)⁹⁷                 | 5               | MRI - 2 had mild narrowing of ICA                     | Complete or partial resolution at 8 weeks | Orbital + periorbital pain in all |
| Wasmeier et al. (2002)⁹⁸         | 2               | Cerebral angiography, MRI - both had narrowing of ICA | Periorbital + temporal headache, dysesthesia in V1 region | Periorbital |
| Tessitore and Tessitore (2000)⁹⁹ | 2               | MRA - 1 had compressed in ICA                         | Fronto-temporal headache           |                                   |
| Miwa et al. (1998)⁹⁰             | 10 (9 benign THS) | MRA/cerebral angiography - normal in all              | Periorbital                         |                                   |
| Takahashi et al. (1996)⁹¹        | 2               | Cerebral angiography - 1 had stenosis of ICA          | Significant radiological improvement at 7 weeks | Retro-orbital Headache |
| Imai et al. (1995)⁹²              | 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)⁹³                | 63/male | MRA - normal                                          | Complete resolution                | Retro-orbital                     |
| Ilgen Uslu and Özkan (2015)⁹⁴     | 45/female | MRA - normal                                        | Complete resolution                | Retro-orbital + periorbital       |
| Abdelghany et al. (2015)⁹⁷       | 60/female | MRA - normal                                        | Query extent of clinical resolution | Retro-orbital + periorbital + headache |
| Tsuda et al. (2012)⁹⁰            | 67/female | MRA - normal                                          | Complete resolution                | Periorbital                       |
| Itokawa et al. (2010)⁹⁷          | 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)⁹⁸             | 76/female | MRA - normal                                          | Complete resolution                | Retro-orbital                     |
| O’ Connor and Hutchinson (2009)⁹⁹| 39/female | MRA - normal                                          | Steroid resistant, complete resolution after infliximab | Orbital + frontal pain + numbness |
| Mendez et al. (2009)⁹⁰           | 19/female | MRA - normal                                          | Complete resolution                | Periorbital                       |
| Sugano et al. (2003)⁹¹           | 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 4: Tolosa Hunt Syndrome case reports with associated idiopathic hypertrophic pachymeningitis

| Author (year) | Age/sex | MRI | Biopsy | HP | Additional deficits |
|---------------|---------|-----|--------|----|---------------------|
| Yu (2020)     | 34/male | MRI - narrowing of ICA, clinoid, and ophthalmic artery. Incidental right MCA aneurysms-clipped | Complete resolution | Radiologically suggestive of HP | Hypopituitarism, DI |
| Madhavan et al. (2020) | 19/female | Abnormal enhancement involving the left cavernous sinus, Meckel’s cave, V2, V3, SOF, and temporal dura | Radiologically suggestive of HP | Biopsy proven HP | Sequential B/L facial palsy |
| Caçô et al. (2019) | 52/female | Dural thickening of CS | Radiologically suggestive of HP | Biopsy proven HP | B/L THS |
| Zečević Penić et al. (2017) | 47/male | Enhancement lesion in CS, extending to trigeminal cave and OA, dural enhancement in CS and along clivus dura | Radiologically suggestive of HP | Biopsy proven HP | B/L THS with HP, anterior hypopituitarism |
| Świątkowska-Stodulska et al. (2017) | 80/female | Infiltrate involving B/L CS, SOF, and sella turcica. Mild segmental thickening of right ICA | Radiologically suggestive of HP | Biopsy proven HP | B/L THS |
| Takasuna et al. (2016) | 53/female | MRI - enlarged bilateral CS, hypertrophied dura around sella | Granulomatous inflammation | Biopsy proven HP | B/L THS |
| Sánchez Vallejo et al. (2014) | 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 of HP | Biopsy proven HP | B/L THS |
| Kodera et al. (2013) | 59/male | Enhancing lesion in CS | Thickened dura with inflammatory infiltrate | Biopsy proven HP | B/L THS (sequential) |
| Slattery et al. (2013) | 17/female | Enhancement of CS, Meckel’s cave and petrous apex of affected side | Radiologically suggestive of HP | Biopsy proven HP | B/L THS |
| Beraldin et al. (2013) | 60/male | Enhancing mass in CS-suspected tumor | Nonspecific granulomatous inflammation | Biopsy proven HP | B/L THS |
| Sugie et al. (2011) | 54/male | Diffuse enhancement of bilateral CS with surrounding cranial base dural thickening | Radiologically suggestive HP in poorly controlled DM | Biopsy proven HP | B/L sequential THS |
| Wu et al. (2011) | 59/female | Bilateral CS and sellar enhancement with extension to right SOF | Radiologically suggestive of HP | Biopsy proven HP | B/L sequential THS |
| Kita et al. (2007) | 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) | 58/female | Enhancement of pituitary (enlarged) and bilateral CS R=L | Granulomatous inflammation | Biopsy-proven HP | B/L sequential THS |
| McKinney et al. (2006) | 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) | 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 | B/L sequential THS |

**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 3: Contd...

| Author (year) | Age/sex | MRI | Biopsy | HP | Additional deficits |
|---------------|---------|-----|--------|----|---------------------|
| Ozawa et al. (2001) | 47/female | MRA - narrowing of ICA, clinoid, and ophthalmic artery. Incidental right MCA aneurysms-clipped | Complete resolution | Periorbital | |
| Reference | Patient Details | Clinical Findings | Imaging Findings | Additional Details |
|-----------|----------------|------------------|-----------------|-------------------|
| 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 | Biopsy proven HP |
| Bosch et al. (2000)\(^{[43]}\) | 62/male | Extra-parenchymatous infiltrating lesion in MCF | HP |
| Tesitiore and Tessitore (2000)\(^{[44]}\) | 54/female | No evidence of enhancing tissue in CS, only compression of cavernous ICA | Radiologically suggestive of HP |
| Hatano et al. (1999)\(^{[45]}\) | 56/male | Linear enhancement of CS dura | Radiologically suggestive HP |
| Hama et al. (1996)\(^{[46]}\) | 54/female | Nonhomogeneous enhancement of CS extending to intrasellar region along edge of cerebellar tentorium | Radiologically suggestive HP |
| Drevelengas et al. (1993)\(^{[47]}\) | 60/male | Enlargement and enhancement of CS, and hypophysis, thickening of infundibulum, obstruction of ICA. Absent normal high intensity in posterior pituitary lobe | Biopsy proven HP |
| Okubo K., et al., 1992\(^{[48]}\) | 49/male | Enlarging mass in sphenoid sinus and CS, causing ICA stenosis, CT-demineralisation of sellar floor and left anterior clinoid process | Radiologically suggestive of HP |

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 2015;5:2324709616689478. doi: 10.1177/2324709616689478.
7. Świątkowska-Stodulska R, Stodulski D, Barman H, Baworaczkiewicz M. 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, Wakis D, Ito H, et al. Steroid-resistant Tolosa-Hunt syndrome with a de novo intracavernous aneurysm: A case report. Surg Neurol Int 2016;7:879-84.
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:
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, Özkam 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, Fukuji M, Yamanoto 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, Chen WC. Tolosa-Hunt syndrome with pituitary involvement. Endocr Pract 2020 Mar 11. doi: 10.4158/EP-2020-0049. Epub ahead of print. PMID: 32160047.
75. Madhavan AA, Delone DR, Verduo JM. Bilateral facial nerve involvement in a patient with Tolosa-Hunt syndrome. Neuroradiol J 2020;33:424-7.
76. Cação G, Calejo M, Alves JE, Medeiros PB, Vila-Cha N, Mendonça T, et al. Clinical features of hypertrophic pachymeningitis in a center survey. Neuroradiol J 2019;40:543-51.
77. Sanchez Vallejo R, Lopez-Rueda A, San Roman L. MRI findings in Tolosa-Hunt syndrome (THS). BMJ Case Rep 2014;2014:bcr2014206629.
78. Kodera T, Takeuchi H, Arishima H, Tsunetoshi K, Kaitai R, Arai Y, et al. Microsurgical findings of Tolosa-Hunt syndrome. World Neurosurg 2013;79:594.e1-4.
79. Cagenta G, Calejo M, Alves JE, Medeiros PB, Vila-Cha N, Mendonça T, et al. Clinical features of hypertrophic pachymeningitis in a center survey. Neuroradiol J 2019;40:543-51.
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, Kito 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, Tintore M, Rio J, Ferreira R, Rubio E, et al. Paquimeningitis hipertrofica. 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.