

Clinical insights on Tolosa Hunt syndrome: A multidisciplinary approach on neurological-related symptomatology in maxillofacial region

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BRIEF REPORT

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ABSTRACT

Background

Tolosa–Hunt syndrome (THS) related neurological symptoms are described in literature as “unilateral”, “recurrent”, “episodic”, “intense”, “severe”, “lancinating” or “stabbing” pain on the upper face and forehead and may be misdiagnosed due to the similarity of few symptoms and a significant number of common characteristics between both conditions.

Aims

The aim of this brief report is to indicate some important

clinical insights related to Tolosa Hunt syndrome, and to give a frank account on the multidisciplinary approach on neurological-related symptomatology in maxillofacial region.

Methods

We analysed a selection of patients with such clinical picture. To better describe the proper management of clinical cases, we report a 50-year-old female reporting an history of two years of recurrent, severe stabbing pain around the right eye, prominence of her cheek and forehead. Her general dentist first mistakenly diagnosed toothache and, thus, it was subsequently misdiagnosed the trigeminal neuropathy (TN).

Results

Reported exemplificative case presented a mild ptosis, diplopia of the right eye, corneal reflex loss, paresthesia and hyperesthesia of upper part of left side of face. Magnetic resonance imaging (MRI) findings were suggestive of THS. Complete resolution of symptoms was achieved with oral Prednisolone and constant monitoring of symptoms.

Conclusion

THS may be added to the long list of differential diagnosis of TN and general dentist and oral surgeons should be informed about such rare causes of facial pain through continued medical education programs.

Key Words

Tolosa–Hunt syndrome, trigeminal neuralgia, ocular diseases

Implications for Practice:

1. What is known about this subject?

Tolosa–Hunt syndrome (THS) related neurological symptoms are uncommon and they can be misunderstood and confused with Trigeminal neuralgia (TN).

2. What new information is offered in this report?

In this brief report we indicate some important clinical insights related to Tolosa Hunt syndrome, and we also give a frank account on the multidisciplinary approach on neurological-related symptomatology in maxillofacial region.

3. What are the implications for research, policy, or practice?

THS may be added to the long list of differential diagnosis of TN to avoid wrong diagnosis and treatments.

Background

Trigeminal neuralgia (TN) is a recurrent, sharp, superficial, sudden, severe, stabbing, pain in the distribution of one or more branches of the fifth cranial nerve more commonly affecting the maxillary and mandibular branches but rarely involving the ophthalmic division of the trigeminal nerve.¹⁻³ TN pain severity is often correlated with reduced measures of daily functioning, well-being, sleep, mood and overall health status, thereby making profound impact on quality of life (QOL) by preventing the patient from speaking, eating, drinking, touching or washing of the face and brushing teeth.^{3,4}

Despite the clarity of painful symptoms of TN, as defined by International Association of Study of Pain (IASP) and the International Classification of Headache Disorders (ICHD), there are significantly common characteristics between TN and other painful conditions of the maxillofacial region.⁵ As the pain of TN seems to be arising from jaws, dental or oral structures, most patients initially seek a general dentist for management.⁶ It has been reported that majority of patients presenting at tertiary care centers for treatment of various facial pain had previously been misdiagnosed and had undergone irreversible dental treatment.^{7,8} Paradoxically, most general dentists know very little about the other causes of facial pain and often tend to overdiagnose TN as it is often the only diagnosis apart from dental causes which they are familiar with.^{5,9}

TN pain has a long list of differential diagnoses as a number of pathological conditions affecting the sinuses, teeth, temporo-mandibular joints, eyes, nose, and the neck may

present with similar symptoms namely Cluster headache, SNUCT syndrome (Short lasting, unilateral, neuralgiform headache with conjunctival injection and tearing), Chronic paroxysmal hemicranias, Cracked tooth syndrome, Jabs and jolts syndrome, Post-herpetic neuralgia, Giant cell arteritis.¹⁰ Tolosa–Hunt syndrome (THS) an extremely rare disorder characterized by recurrent paroxysms of severe and unilateral periorbital or hemicranial pain in the distribution of the ophthalmic and maxillary division of the trigeminal nerve associated with ophthalmoplegia, ipsilateral ocular motor nerve palsies, oculosympathetic paralysis, and sensory loss in the first division of the 5th cranial nerve.^{11,12} THS may be misdiagnosed as TN due to the similarity of few symptoms and a significant number of common characteristics between both conditions.¹³

We report a case of THS as an addition to the long list of differential diagnosis of TN among patients presenting at oral medicine department of Khyber college of Dentistry Peshawar.

Case details

A 50-year-old female lady presented to our department in October 2014 with two years history of recurrent, severe stabbing pain around the right eye, prominence of her cheek and forehead. She consulted her general dentist for management when her symptoms initially developed two years ago, mistaking it for toothache. The general dentist performed a few dental procedures in the upper jaw to relieve her pain but without any success. Suspecting TN as a cause the patient was put on carbamazepine 200mg but that too did not provide any relief in symptoms. The patient was subsequently referred to an oral surgeon. Based on the history of her symptoms, the patient was labeled as having typical TN and was offered neurectomy and alcohol injection as treatment options since the pain was not responding to anticonvulsants. She declined to undergo these treatment options offered by the oral surgeon and continued live a life of pain and suffering while taking any and every over the counter analgesics to relieve her pain. Meanwhile there was a spontaneous remission in her symptoms and she remained pain free for more than six months. The patient presented to us after being referred by the oral surgeon for experiencing recurrence of her painful symptoms for a few months.

On clinical examination she had mild ptosis and diplopia of the right eye. The patient had a corneal reflex loss, and also paresthesia and hyperesthesia of upper part of left side of face which was significant of involvement of ophthalmic branch of trigeminal nerve. Ophthalmologist opinion was

taken to rule out any other cause of headache. Funduscopy examination was within normal range.

A Multiplanar MRI imaging through brain acquiring T1 and T2 weighted images with and without contrast was done, that revealed 1x1.2x1cm homogeneously enhancing extra axial lesion involving the right orbital apex with extensions into right cavernous sinus suggestive of Tolosa Hunt Syndrome (Figure 1).

The patient was treated with oral Prednisolone (Deltacortril 5mg tablets) and showed significant relief of symptoms within 48–72 hours. Complete resolution of her ptosis as well as the oculomotor nerve palsy was achieved within one week. Patient was followed-up for six months and showed no recurrence of symptoms till her last evaluation visit.

Discussion

THS is an extremely rare condition with an estimated annual incidence of one case per million per year.¹⁴ Originally reported by E Tolosa in 1954 in a (a 47-year-old man with self-limited left orbital pain. The pain recurred after several months and became associated with ptosis and subsequently total ophthalmoplegia.¹⁵ Later, on in 1961 W. E Hunt reported six similar cases and they concluded that the process was an inflammatory reaction limited to the cavernous sinus and that corticosteroid therapy was beneficial.¹⁶ Five years later in 1966, the condition was finally termed as “Tolosa-Hunt syndrome” by Smith and Taxdal as they described five more cases and stressed the importance of steroid administration as a diagnostic test.^{17,18}

According to Modified Revised IHS headache classification of 2004, THS is now described as “An episodic orbital pain associated with paralysis of one or more of the third, fourth and/or sixth cranial nerves which usually resolves spontaneously but tends to relapse and remit” with the following diagnostic criteria:¹⁸

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

Carotid-cavernous fistulae, pituitary adenomas, vasculopathic cranial neuropathy, aspergillus invasion, Wegener's granulomatosis, sarcoidosis, lymphoma and ophthalmoplegic migraine may be included in the extended list of differential diagnosis of any steroid responsive painful ophthalmoplegia.¹⁶⁻¹⁸ It is important to mention that meningiomas do not resolve with steroid therapy, sarcoidosis and lymphoma often have systemic symptoms whereas vascular abnormalities such as arteritides, carotid-cavernous fistulae, ophthalmoplegic migraines and aneurysms are not associated with masses in the cavernous sinus or orbital apex.^{15,20}

In 2006 Shim KW, Moon JC et al reported the first case of THS misdiagnosed as TN and Atypical facial pain. They emphasized that THS may be misdiagnosed as TN and atypical facial pain due to the similarity of few symptoms and a significant number of common characteristics between both conditions.¹³ To the best of our knowledge ours was probably the second case of THS misdiagnosed as TN due to similarity of presentation.

Despite the fact that THS and TN is usually described in literature as “unilateral”, “recurrent”, “episodic”, “intense”, “severe”, “lancinating” or “stabbing” pain on the upper face and forehead yet neither are mentioned in the long lists of differential diagnosis of either conditions.^{5,10,18}

Future therapies should be directed toward the immunomodulatory activity of mesenchymal stem cells (MSCs).¹⁹ Inflammation must be excluded from the potential causes of the described symptomatology, in fact, oxidative stress,²⁰⁻²³ tumor-related inflammation,^{24,25} and syndromic conditions affecting oral and perioral tissues²⁶ are an important cause of secondary TN. New treatments will be directed on local drug delivery functionalized scaffolds and active principles delivered on site.²⁷⁻³⁰

Conclusion

Lack of knowledge may lead to delayed or erroneous diagnosis and unsuitable or unnecessary treatment interventions as most general dentists know very little about the other causes of facial pain. It is recommended that THS may be added to the long list of differential diagnosis of TN and general dentist and oral surgeons should be informed about such rare causes of facial pain through continued medical education programs.

References

1. Zakrzewska JM. Differential diagnosis of facial pain and

- guidelines for management. *Br J Anaesth.* 2013;111(1):95–104.
2. Ali M, Ansari SR, Khan MP, et al. Microvascular decompression for idiopathic trigeminal neuralgia: Ultimate solution to the management dilemma. *Pak Oral Dent J.* 2009;29(2):193–196.
 3. Shah SA, Murad N, Salaar A, et al. Trigeminal neuralgia: Analysis of pain distribution. *Pak Oral Dent J.* 2008;28:37–41.
 4. Tolle T, Duke E, Sadosky A. Patient burden of trigeminal neuralgia: results from a cross-sectional survey of health state impairment and treatment patterns in European countries. *Pain Pract.* 2006;6:153–60.
 5. Zakrzewska JM, Padfield D. The patient's journey through trigeminal neuralgia. *Pain: Clinical Updates.* 2014;22(1):1–8.
 6. Baskaran K. A systemic review of patients appearing to dental professionals with trigeminal neuralgia arising from intracranial tumours. *Int J Sci Res.* 2017;6(5):72–76.
 7. Benoliel R, Eliav E. Neuropathic orofacial pain. *Oral Maxillofac Surg Clin North Am.* 2008;20:237–254.
 8. B. Perić, Zore IF, Vidaković B, et al. Trigeminal neuralgia – case and treatment analysis at the Department of Oral Surgery of the University Hospital Dubrava. *Coll Antropol.* 2014;38(2):685–689.
 9. Koopman JS, Dieleman JP, Huygen FJ, et al. Incidence of facial pain in the general population. *Pain.* 2009;147:122–7.
 10. Nurmikko TJ, Eldridge PR. Trigeminal neuralgia—pathophysiology, diagnosis and current treatment. *Br J Anaesth.* 2001;87:117–132.
 11. Colnaghi S, Versino M, Marchioni E, 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.
 12. Gladstone JP. An approach to the patient with painful ophthalmoplegia, with a focus on tolosa-hunt syndrome. *Curr Pain Headache Rep.* 2007;11:317–325.
 13. Shim KW, Moon JC, Yoon KB, et al. Hemifacial pain accompanied with delayed ipsilateral abducens nerve palsy: Tolosa hunt syndrome. A case report. *Korean J Pain.* 2006;19(1):104–106.
 14. Patel S, Sankhe P, Dave D, et al. Tolosa Hunt syndrome: a rare syndrome. *Int J Res Med Sci.* 2015;3:3914-6.
 15. Tolosa E. Periarteritic lesions of the carotid siphon with the clinical features of a carotid infraclinoid aneurysm. *J Neurol Neurosurg Psychiatry.* 1954;17:300–2.
 16. Hunt WE, Meagher JN, Le Fever HE, et al. Painful ophthalmoplegia. Its relation to indolent inflammation of the cavernous sinus. *Neurology.* 1961;11:56–62.
 17. Smith JL, Taxdal DSR. Painful ophthalmoplegia. The Tolosa-Hunt syndrome. *Am J Ophthalmol.* 1966;61:1466– 72.
 18. Kline LB, Hoyt WF. The Tolosa-Hunt syndrome. *J Neurol Neurosurg Psychiatry.* 2001;71:577-82.
 19. Tatullo M, Falisi G, Amantea M, et al. Dental pulp stem cells and human periapical cyst mesenchymal stem cells in bone tissue regeneration: Comparison of basal and osteogenic differentiated gene expression of a newly discovered mesenchymal stem cell lineage. *J Biol Regul Homeost Agents.* 2015;29(3):713–8. PMID: 26403412
 20. Tatullo M, Gentile S, Paduano F, et al. Crosstalk between oral and general health status in e-smokers. *Medicine (Baltimore).* 2016;95(49):e5589. doi: 10.1097/MD.0000000000005589
 21. Tatullo M, Simone GM, Tarullo F, et al. Antioxidant and antitumor activity of a bioactive polyphenolic fraction isolated from the brewing process. *Sci Rep.* 2016;6:36042. doi: 10.1038/srep36042
 22. Marrelli M, Gentile S, Palmieri F, et al. Correlation between Surgeon's experience, surgery complexity and the alteration of stress related physiological parameters. *PLoS One.* 2014;9(11):e112444. doi: 10.1371/journal.pone.0112444.
 23. Tatullo M, Marrelli M, Scacco S, et al. Relationship between oxidative stress and "burning mouth syndrome" in female patients: a scientific hypothesis. *Eur Rev Med Pharmacol Sci.* 2012;16(9):1218–21. PMID: 23047505
 24. Tatullo M, Marrelli M, Amantea M, et al. Bioimpedance detection of oral lichen planus used as preneoplastic model. *J Cancer.* 2015;6(10):976–83. doi: 10.7150/jca.11936. eCollection 2015.
 25. Inchingolo F, Tatullo M, Abenavoli FM, et al. Non-Hodgkin lymphoma affecting the tongue: unusual intra-oral location. *Head Neck Oncol.* 2011;3:1. doi: 10.1186/1758-3284-3-1.
 26. Inchingolo F, Tatullo M, Abenavoli FM, et al. Non-syndromic multiple supernumerary teeth in a family unit with a normal karyotype: case report. *Int J Med Sci.* 2010;7(6):378–84. doi:10.7150/ijms.7.378
 27. Aulino P, Costa A, Chiaravalloti E, et al. Muscle extracellular matrix scaffold is a multipotent environment. *Int J Med Sci.* 2015;12(4):336–40. doi: 10.7150/ijms.10761
 28. Perniconi B, Coletti D, Aulino P, et al. Muscle acellular scaffold as a biomaterial: effects on C2C12 cell differentiation and interaction with the murine host environment. *Front Physiol.* 2014;5:354. doi: 10.3389/fphys.2014.00354.
 29. Marrelli M, Pujia A, Palmieri F, et al. Innovative approach for the in vitro research on biomedical scaffolds

designed and customized with CAD-CAM technology. *Int J Immunopathol Pharmacol.* 2016;29(4):778–783. doi: 10.1177/0394632016646121

30. Paduano F, Marrelli M, Amantea M, et al. Adipose tissue as a strategic source of mesenchymal stem cells in bone regeneration: A topical review on the most promising craniomaxillofacial applications. *Int J Mol Sci.* 2017;18(10)2140. doi: 10.3390/ijms18102140.

PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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ETHICS COMMITTEE APPROVAL

This study was approved by internal committee of Department of Oral & Maxillofacial Surgery, College of dentistry, University of Hail, KSA.

Figure 1: A Multiplaner MRI imaging with contrast through brain acquiring T1 and T2 weighted images that revealed 1 x 1.2 x1 cm homogeneously enhancing extra axial lesion involving the right orbital apex with extensions into right cavernous sinus suggestive of Tolosa Hunt Syndrome

