J Nur Today

REVIEW ARTICLE

www.jolnt.com

e-ISSN 2456-1630

A Review on the Tolosa Hunt Syndrome

Krupa Patel[1] and Dharmendrasingh Rajput[2]*

[1]Student of Doctor of Pharmacy, Department of Pharmacy Practice, Indubhai Patel College of Pharmacy & Research Centre, Dharmaj Anand Gujarat, India

[2]Assistant Professor, Department of Pharmacy Practice, Indubhai Patel College of Pharmacy & Research Centre ,Dharmaj Anand Gujarat, India

ABSTRACT

Tolosa Hunt Syndrome(THS) is a rare disorder which is characterized by severe periorbital Unilateral Headache. It ispainful ophthalmoplegia caused by nonspecific inflammation of cavernous sinus or superior orbital fissure.Cranial Nerves involved are III, IV and VI. Symptoms of THS arepainful eye movements,Double vision worse at distance, Headache, photophobia, Neck Stiffness,chronic fatigue,blurred vision.The Hallmark of THS is painful Ophthalmoparesis or ophthalmoplegia.Estimated Incidence of THS is 1 per 1,000,000 people with an average age of 41 years with no sex predilection.The exact cause of THS is still unknown.In 2004, the International Headache Society (HIS) re-defined diagnostic criteria of THS specifying that granuloma demonstrated by MRI or Biopsy is essentially required for diagnosis

KEYWORDS *Cavernous Sinus, Periorbital Inflammation, Painful Ophthalmoplegia, Corticosteroids, Palsy, Unilateral Headache*

Date Received: 19 /10 /21 **Date Revised: 14/02/22** **Date Published: 15/02/2022**

INTRODUCTION

Tolosa- Hunt syndrome was first described by Tolosa in 1954 who found granulomatous inflammation in cavernous sinus during autopsy of a patient with severe trigeminal pain and total ophthalmoplegia.[1]Smith and Taxdal were first to apply the Eponym "Tolosa-Hunt Syndrome" to this rare disease in 1966. Similar cases were reported by Hunt in 1961.Synonyms of this disease are painful ophthalmoplegia,recurrent ophthalmoplegia, ophthalmoplegia syndrome, Nonspecific inflammation of cavernous sinus,superior orbital fissure etc. THS was first classified by International Headache Society (THS) in 2004[2,3].

The Syndrome of painful ophthalmoplegia consists of Periorbital or hemicranial pain, combined with ipsilateral ocular motor nerve palsies, oculosympathetic paralysis and sensory loss in the maxillary division of trigeminal Nerve. All three ocular motor cranial nerves may be involved with pupillary reaction may be normal or parasympathetic or sympathetic involvement[3].

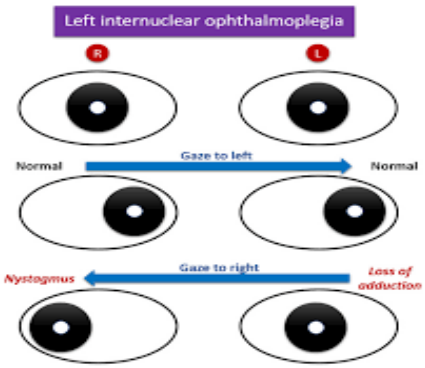

Figure 1 Normal vision[10]

Figure 2 Neuro-ophthalmologic examination showing ophthalmoplegia in a patient with Tolosa–Hunt syndrome, prior to treatment. The central image represents forward gaze, and each image around it represents gaze in that direction (for example, in the upper left image, the patient looks up and right; the left eye is unable to accomplish this movement). The examination shows ptosis of the left eyelid, exotropia (outward deviation) of the primary gaze of the left eye, and paresis (weakness) of the left third, fourth and sixth cranial nerves[11].

AETIOLOGY

Tolosa Hunt syndrome is usually Idiopathic and the exact cause of THS is still unknown. But some theory predicts that it may be linked with autoimmune disorders which produces abnormal autoimmune response linked with an inflammation in a specific area behind the eye. Inflammation may be due to clumping of certain type of cells. Other possible causes may include generalized

inflammation and constricted or inflamed cranial blood vessels, traumatic injuries, tumours or aneurysm could become possible potential triggers for THS[2,9].

SIGNS & SYMPTOMS

The Hallmark of THS is painful Ophthalmoparesis or ophthalmoplegia.

In most cases, affected individuals experience intense sharp pain and decreased eye movements. Symptoms may reoccur without a distinct pattern. Individuals may exhibit signs of paralysis(palsy) of certain cranial nerves such as dropping of upper eyelid (ptosis),double vision (diplopia),large pupil, facial Numbness[5,9].

CLINICAL PROFILE OF THS

THS affect people of virtually any age from first to eighth decades of life with no sex predilection.

The pain lasts for an average of 8 weeks if it is left untreated. Pain is usually described as "***intense***", "***stabbing***", "***boring***", "***lancinating***", "***severe***".

It is periorbital in location, frequently extending into the retro-orbital, frontal and temporal regions[2,3].

EPIDEMIOLOGY

THS is uncommon in united states and internationally too.There is one recorded case of THS in Australia, New South Wales. It is found Worldwide with no racial or geographical prevalence. Equally affected in females and males. Usually it is Unilateral, either side can be affected but bilateral involvement is also reported in approximately, 5% Cases. This disorder is rare in first 2 decades of life and in people older than 20 years of age and have even distribution[5,6].

PATHOPHYSIOLOGY

THS is Idiopathic, sterile Inflammation of cavernous sinus.

It mainly occurs due to Nonspecific Inflammation i.e. noncaseating granulomatous or nongranulomatous within the cavernous sinus or superior orbital fissure is the cause of constant pain, which is a characteristic of onset of this disorder .Cranial Nerves III, IV and VI are damaged by granulomatous inflammation which causes Ophthalmoparesis or Disordered Eye Movements. Involvement of Trigeminal Nerve may cause paraesthesia's of the forehead[3].

DIAGNOSIS

The diagnosis of THS is based upon presence of physical features like pain, Headache,ophthalmoplegia.

Diagnosis is confirmed by clinical evaluation,detailed patient history, radiological tests and many other tests[9].

Table 1 Diagnostic Evaluation of THS[3]

Haematological Tests	**Complete Blood Count (CBC)** **Erythrocyte Sedimentation Rate (ESR)** **Serum Chemistry (Glucose ,Electrolytes ,liver & Renal Function)** **Antinuclear Antibody Tests**
Cerebrospinal Fluid	Opening pressure Cell count and Differential cell count Serology Cytology Angiotensin Converting Enzyme(ACE) Culture: Bacterial, Fungal, Mycobacterial
Neuroradiological Studies	MRI CT Scan Cerebral angiography
Biopsy	Nasopharynx Cavernous sinus

The International Headache Society lays down diagnostic criteria for THS which have high sensitivity(Approx. 95%-100%) but with low specificity (Approx.50%).

- Unilateral Headache

1. Presence of granulomatous inflammation of cavernous sinus, superior orbital fissure or orbit as seen on MRI or Biopsy.
2. Palsies of one or more oculomotor Nerves(cranial Nerve III,IV and/or VI) on same side.

- Pain may precede the ophthalmoplegia by several days. It is not throbbing but a steady pain behind the eye which is described as “gawning” or “boring”.
- Symptoms lasts for days to weeks.
- Attacks reoccur at intervals of months or years.
- Exclusion of other conditions by neuroimaging and angiography[4].

Surgical procedures like Neuroimaging or CT scan and other tests helps in final diagnosis of THS.

Neuroimaging

Magnetic Resonance Imaging (MRI)

MRI of brain with contrast, especially coronal view is important for diagnostic study.

MRI helps in excluding other diseased condition which produces painful ophthalmoplegia other than THS .It may show evidence of inflammatory changes in anterior cavernous sinus, superior orbital fissure and orbital Apex also. Thickening of cavernous sinus occurs due to presence of abnormal soft tissue which is

T1 – Involved region is Isointense to Hyper intense

T2 – Involved region is Hyper intense and enhances with contrast.

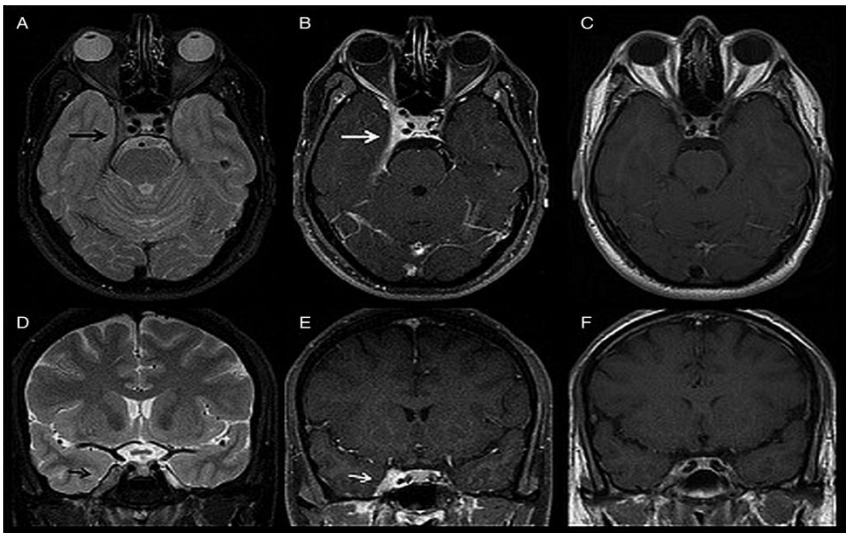

Figure 3 CT Scan

MRI finding of a 36-year-old male patient with right-sided Tolosa-Hunt syndrome. Axial (A) and coronal (D) T2-weighted images (WI) show an enlarged right cavernous sinus (CS) that is mildly hypo intense to grey matter (black arrow). Axial (B) and coronal (E) post contrast T1-weighted fat-suppressed images show the enhancement of the abnormal soft tissue extending through the superior orbital fissure into the orbital apex (white arrow). Also noted is the hyper enhanced thickening of the right temporal dura, tentorium and right orbital apex. Axial (C) and coronal (F) postcontrast T1-WI follow-up, performed one month later, show significant improvement of right-sided CS abnormal enlargement and enhancement[12].

CT Scan

May show asymmetrical enlargement in the region of cavernous sinus on the affected side with contrast enhancement[5].

Differential Diagnosis

It includes Anisocoric, cavernoussinus syndrome, Diabetic Neuropathy, Brain Metastasis ,Lyme Disease[5].

TREATMENT

Corticosteroids are treatment of choice which significantly provide pain relief within 24-72 hours of initiation of therapy. Steroids are used to treat inflammation of THS. Treatment continues at initial dose for 7–10 days after pain resolves. If patient is unable to tolerate steroid therapy, other

immunosuppressive therapy should be considered. Corticosteroids like **Prednisone (Sterapred)** decrease inflammation by reversing increased capillary permeability and Suppresses Polymorphonuclear (PMN)Activity. Immunosuppressive agents like **Methotrexate (Trexall), Azathioprine (Imuran)** decrease autoimmune reaction. They mainly work primarily on T cells[7].

PROGNOSIS

Dramatic Improvement is seen with Glucocorticosteroids.Improvement in symptoms mainly pain relief is 24-72 hours after starting steroids within one week.

Patients usually respond to corticosteroids and spontaneous remission occur.Relapse can occur in 40 % of patients successfully treated for THS.

Gimenez-Roldan have reported that relapses may occur as long as 13 years after diagnosis and treatment[2,5].

PATIENT EDUCATION

Patient should understand that this is an idiopathic condition and it is self-limiting and also it is non-fatal disease so it can be cured successfully with good recovery if appropriate course of treatment is maintained which is provided by physician or any other healthcare provider in treatment regimen. Relapses may occur in 30%-40% patients and they must know cause and course of relapse and may need to perform additional testing. The risk with use of high dose steroids should also be known by patient prior to treatment.

The above all information should be provided by pharmacist as they play key role in between physician and patient[6].

COMPLICATIONS

In patients withextra cavernoussinus, involvement affecting optic nerve, vision loss may occur[5].

AFFECTED POPULATIONS

THS is a rare-neuroimmunological disorder that occurs in males and females in equal numbers. The average age of onset is 41 years but there have been cases reported among people younger than age 30.

In rare cases,children under age of 10 years are affected by THS[7].

RELATED DISORDERS

Symptoms of following disorders can be similar to THS.

Orbital Cellulitis- Inflammation of tissues within the cavity which holds the eyeballs.

Cavernous Sinus Thrombosis- Ophthalmologic disorder caused by infection and clotting in veins behind eyeball.

Migraine headaches usually involve one side of THS[6].

CONCLUSION

Around 50 % of patients with THS can have Recurrence.Steroid-sparing agents appear to prevent recurrence.[8]

REFERENCES

1. NaderiA,AhmadiMA,EsmaeliMA,EsmaeliB.Tolosa Hunt Syndrome.In: NORD Guide to Rare Disorders.Philadelphia, PA : Lippincott Williams & Wilkins;2003 : 664.

2. Smith JL,Taxdal DS. Painful ophthalmoplegia.TheTolosa hunt syndrome.Jun; 61 1466 – 1472.

3. Hunt WE,MeagherJN,Le Fever HE (1961) painful ophthalmoplegia – Its relation to indolent inflammation of the cavernous sinus ,Neurology 1961 56-62.

4. Headache Subcommittee of the International classification of headache disorders,ICHDII.Cephalagia 2004;24 , 131.

5. Danette C Taylor,DO.” Tolosa – Hunt Syndrome” Medicine.Retrieved 2008-01-21.

6. KlineLB, Hoyt WB. The Tolosa Hunt Syndrome J NeurolNeurosurg psychiatry syndrome 2001.577-582577-582

7. AmrutkarC,Burtonev. Tolosa Hunt syndrome.

8. Cohn DF,CarassoR,streifler M (1979) painful ophthalmoplegia 373-381.

9. Adams RD,VictorM,RopperAA,Principles of neurology 6 th edition. New York ; 1997.

10. Pgblazer.com

11. Tolosa Hunt Syndrome National Organization For rare Disorders 2008 - 01-21.

12.SchuknechtB, sturmV, Huiman TA, THS: MRI features in 15 patients with 20 episodes of painful ophthalmology 2009 ; 69; 445-53.