Asian Journal of Research and Reports in Neurology

2(1): 61-66, 2019; Article no.AJORRIN.55185

Mortal Aneurysm Rupture in a Rare Case of Steroid-resistant Tolosa-Hunt Syndrome

Anthoula C. Tsolaki[1*], Galaktion Konstantinidis[1,2], Stavroula Koukou[1], Fotini Michali[1], Christina Manika[3] and Nikolaos D. Michalis[1]

[1]Department of Neurology, 1st General Hospital of Thessaloniki "Agios Pavlos", Thessaloniki, Greece.
[2]Department of Neurology (3rd), Aristotle University of Thessaloniki, Thessaloniki, Greece.
[3]Department of Radiology, 1st General Hospital of Thessaloniki "Agios Pavlos", Thessaloniki, Greece.

Authors' contributions

This work was carried out in collaboration among all authors. Author ACT wrote the manuscript, performed the literature research and made the submission and all the final corrections of the manuscript. Authors GK, SK, FM and NDM were all responsible for the patient's treatment and reviewed the final version of the manuscript. Author CM was responsible for the radiological diagnosis and chose the imaging pictures for the manuscript. All authors read and approved the final manuscript.

Article Information

Editor(s):
(1) Dr. Ekanem Eyo Philip-Ephraim, University of Calabar Teaching Hospital, Nigeria.
Reviewers:
(1) Arthur N. Chuemere, University of Port Harcourt, Nigeria.
(2) Harini Sarva, Weill Cornell Medicine, USA.
Complete Peer review History: http://www.sdiarticle4.com/review-history/55185

Case Study

Received 10 January 2020
Accepted 17 March 2020
Published 27 March 2020

ABSTRACT

Tolosa-Hunt Syndrome is a rare condition characterized by painful ophthalmoparesis and idiopathic granulomatous inflammation of the cavernous sinus, classically extremely responsive to corticosteroid administration. We present a rare case of a 27-year-old man with Tolosa-Hunt Syndrome who did not respond to corticosteroids and the rupture of the co-existing internal carotid artery aneurysm caused his death.

Keywords: Tolosa-Hunt syndrome; ophthalmoplegia; cavernous ICA aneurysm.

**Corresponding author: E-mail: tsolakianthoula@gmail.com;*

ABBREVIATIONS

ICA : Internal Carotid Artery
PO : Painful Ophthalmoplegia
THS : Tolosa- Hunt Syndrome
WBC : White Blood Cell
CICA : Cavernous Internal Carotid Artery
CNS : Central Nervous System
GI : Granulomatous Inflammation

1. INTRODUCTION

The differential diagnoses for painful ophthalmoplegia (PO) include aneurysms, thrombosis, para-sellar lesions, tumors, orbital pseudotumor, sarcoidosis, infection head, and neck trauma, and hypertensive or diabetic microvascular infarction. Tolosa- Hunt Syndrome (THS) was initially described in 1954 [1]. Current diagnostic criteria defined by the International Classification of Headache disorders 3rd Edition [2]. Consist a unilateral orbital pain, paresis of one or more of cranial nerves III, IV or VI with demonstrable inflammation of the cavernous sinus. THS remains a diagnosis of exclusion. THS is a rare condition characterized by painful ophthalmoparesis and idiopathic granulomatous inflammation of the cavernous sinus, classically extremely responsive to corticosteroid administration. Hence, unusual angiographic findings have been described, such as arterial narrowing and aneurysms of internal carotid artery associated with the inflammatory changes in the cavernous sinus.

2. CASE REPORT

A 27-year –old otherwise healthy man presented with severe left retro-orbital pain and diplopia. The retrobulbar discomfort had an onset 2-week before diplopia presentation. A neurological evaluation performed on admission in the emergency room of a local hospital revealed left abducens nerve palsy. The remainder of the neurological examination, including facial sensation except for a subjective warm feeling on the left side of his face, was unremarkable. He was afebrile, conscious, and oriented.

The ophthalmological evaluation, which performed right before his admission, showed an uncorrected visual acuity 8/10 in the right and 10/10 in the left eye. Intraocular pressures were normal at 12 mmHg in the right eye and 13mmHg in the left eye. The fundoscopic examination was normal without disc pallor or papilledema.

The patient was recently seen by his primary care provider and was given Amoxicillin/ Clavulanic acid for seven days and subsequently Cefuroxime for more seven days for suspected sinusitis. The patient completed the course of antibiotics without improvement of his symptoms.

On admission, the emergency computed tomography scan was read as normal with no evidence for intracranial bleeding, masses, or other findings that could explain his symptoms. His laboratory values shown leucocytosis (WBC 19.24% with neutrophil dominance 87.8%), elevated C-reactive protein 6.0 mg/dl, Erythrocyte sedimentation rate 30 mm/h and fibrinogen 506 mg/dl. A Magnetic Resonance Image (MRI) and Magnetic Resonance Angiography (MRA) revealed an enlargement of the left cavernous sinus with concurrent aneurysm of the internal carotid artery (ICA) about ~8 mm, Post-contrast T1W image showed enhancement of the lesion in the cavernous sinus (see Fig. 1 and Fig. 2a). Serological analysis for ANA, ANCA, ACE, serum protein electrophoresis, serum antibodies including SS-A, SS-B, Anti –Sm, were within normal limits. Blood and urine cultures were negative. The blood coagulation function, infection examinations, and tumor markers were normal. The Mantoux skin test was negative. A Thorax CT was also performed to exclude Tb and sarcoidosis as a systemic cause of cavernous sinus inflammation, which was normal. A presumptive diagnosis of THS was made, and he began iv treatment with iv prednisolone 60mg/day. A DSA was performed on the fourth day, confirming the previous finding of a rather big aneurysm ~1 cm of the left cavernous internal carotid artery (CICA) with anterior bend and pre-aneurysm stenosis of the left ICA (see Fig. 2b).

The patient's clinical condition had a progressive improvement of the pain till the seventh day. The excruciating pain returned with nausea and vomiting, resistant to analgesics such paracetamol and it was only relieved by opioid analgesics.

A subsequent neuroimaging with NECT excluded hemorrhage and the MRI performed on the tenth day revealed a partial aneurysm thrombosis beside the inflammation of the cavernous sinus. Despite the clinical deterioration, the laboratory findings were remarkably improved. We increased the I.V. Prednisone to 75 mg/ day with mild improvement of the pain. Gradually the arterial blood pressure was elevated, and the

inflammation markers were raised as well. The newly established nuchal rigidity made us perform a lumbar puncture revealing pathologic CSF values: Glu 48 mg/dl, LDH 52.0U/L, Albumin 122.5 mg/dl and 2.200 cells/μL 78% polynuclear type. We added empirical antibiotic treatment, although all the cultures (Blood, CSF, Urine) were eventually negative. Negative was the performed PCR in CSF for Neisseria meningitis, Streptococcus pneumonia, Listeria monocytogenes και Haemophilus influenzae type b, H. influenzae (non-b), Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus spp, and Mycobacterium tuberculosis. A new brain MRI performed showing inflammation spreading in sphenoid sinus and the posterior ethmoidal air cells, and a high-MR- a signal of the posterior part of the left gyrus rectus with abnormal diffusion. There was also intense meningeal enhancement of the frontal cranial fossa, on either side of the medial longitudinal fissure, in cavernous sinuous bilaterally and the falx cerebri. The patient had partial pain relief but soon presented a clinical deterioration with centrally induced fever, sustained and resistant to antipyretics, complete ophthalmoplegia on the left side with a dilated pupil, and a partial ophthalmoparesis on the right side with a satisfying response to the light, and a spastic paraparesis. The aneurysm rupture was induced during a fever attack, with concurrent elevated arterial blood pressure and the recurrence of the excruciating pain. The patient was intubated immediately, and a NECT was performed, showing a large intracranial hemorrhage, especially in the posterior cranial fossa. He died in the ICU a week later.

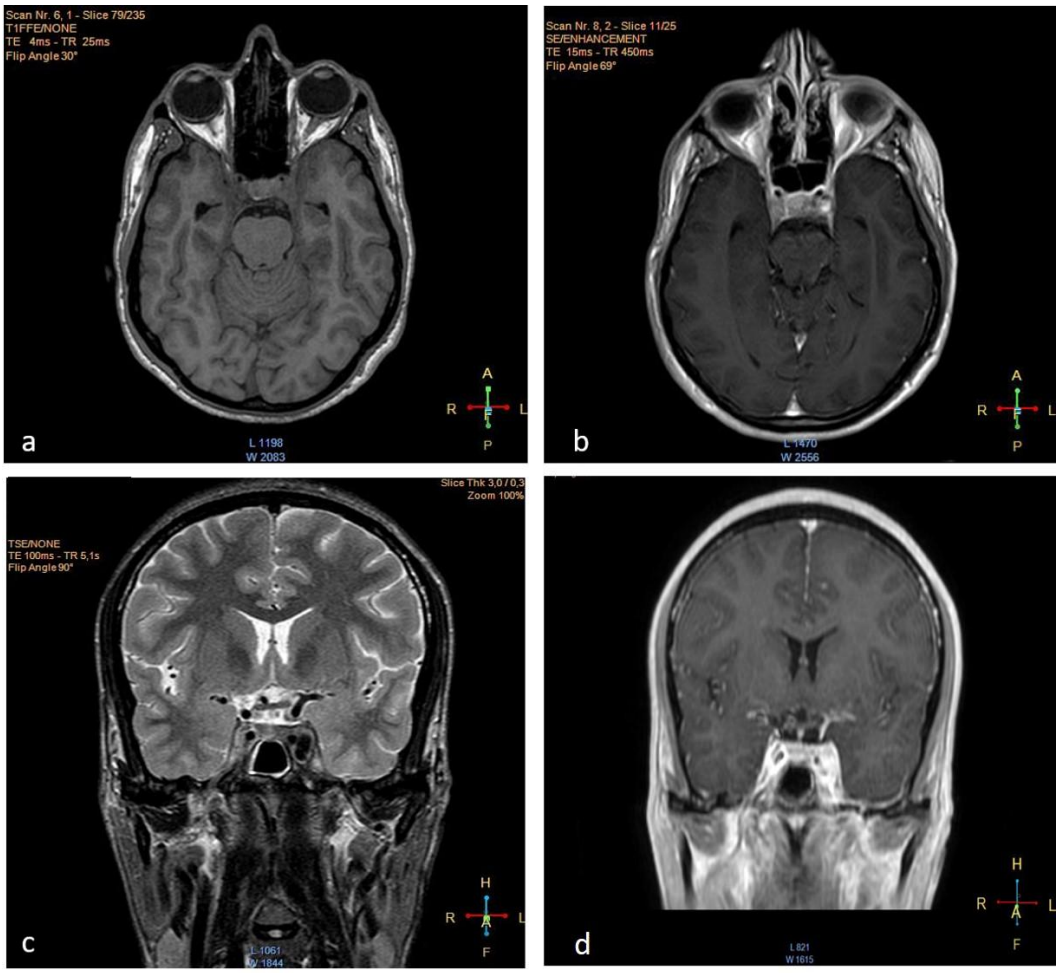

Fig. 1. Pre (a) and post-contrast (b) T1 weighted MRI demonstrating inflammatory homogeneously enhancing changes within the left cavernous sinus and an internal carotid artery aneurysm about 8mm. Coronal T2 weighted (c) and coronal T1 weighted post-contrast (d)

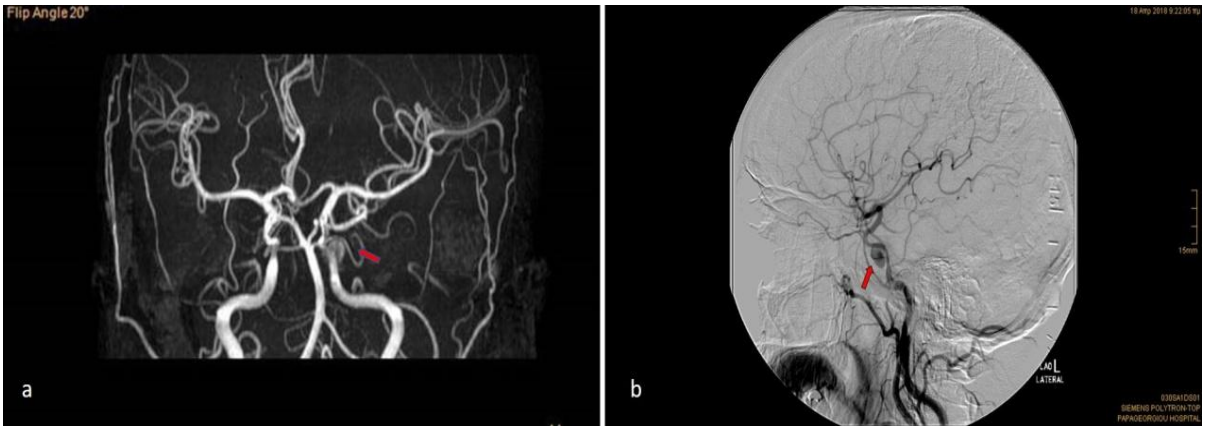

Fig. 2. MRI angiography (a) demonstrating an intracavernous aneurysm of the left internal carotid artery (red arrow). Cerebral angiogram (b) lateral projection after contrast injection into the left internal carotid artery demonstrating a large (~1 cm) aneurysm of the left cavernous internal carotid artery (CICA) with anterior bend and pre-aneurysm stenosis of the left ICA (Red arrow)

3. DISCUSSION

THS is a benign, steroid-responsive nonspecific granulomatous inflammation of the cavernous sinus that should be suspected in a case of painful ophthalmoplegia**.** Although corticosteroids persevere as a cornerstone therapy for THS [3–6], infliximab (300 mg infusion) [7], azathioprine [8], methotrexate [9] and acupuncture exist as alternative therapies. Lately, surgical techniques have been employed, although permanent CN VI palsy and risk of late malignancy have been stated [5]. In some cases, long-term immunosuppression is necessary, and even radiotherapy [10] has also been applied successfully in some patients [6].

IHS 2018 diagnostic criteria require MRI demonstration of CS or SOF/OA granulomatous inflammation (GI) ipsilateral to the presenting headache a confirmatory diagnostic technique for THS, as it can distinguish this from its mimics [2]. Notion supported by many published cases [4,5,11,12]. However, MRI findings before and after systemic corticosteroid therapy are critical diagnostic criteria to put the definitive diagnosis of THS and to differentiate it from other cavernous sinus lesions that simulate THS both clinically and radiologically [12].

There are only four other reported cases in the literature presenting aneurysm arising from the internal carotid artery in the cavernous portion with Tolosa- Hunt syndrome [9,13], one of them with bilateral ICA aneurysms. From those only in one performed coil embolization. Two aneurysms decreased in size after corticosteroid treatment, while the other two were stable. Angiographic findings in THS present focal narrowing of the cavernous ICA and ICA aneurysms in limited cases. It is speculated that the inflammation process is responsible for these findings due to local vasculitis [13]. However, the possibility of aneurysm pre-existence cannot be ruled out.

Despite the classic syndrome onset in our case with the retrobulbar discomfort and it's 2-week before diplopia presentation due to left abducens nerve palsy, it did not have a favorable response to steroid treatment. In our case, the inflammation was gradually extended after the tenth day, causing a rise of intracranial pressure, and hemodynamic load with “central” fever and hypertension (the Cushing Response) leading to aneurysm rupture and death before the scheduled neurosurgery intervention. There is one more reported case of steroid-resistant THS forming a pituitary abscess and finally responded to methotrexate [9]. In our case, the 48-72 hours waiting to exclude possible infectious causes of the clinical deterioration, before escalating the immunosuppressive therapy, drove to irreversible damage.

The cavernous ICA aneurysms are generally characterized by a benign course according to the literature [14]. This is the reason why the neurosurgery department did not suggest an emergency operation. However, in our case, the size of the aneurysm, the probably impaired vessel wall integrity, and the inflammation spread, led to the intracranial pressure increase and caused the mortal aneurysm rupture.

4. CONCLUSION

THS has been considered as a diagnosis of exclusion after excluding other known causes of painful ophthalmoplegia with proper clinical and laboratory evaluation. Although it is a benign, steroid-responsive inflammation, immunosuppression has been employed in some cases. Despite the usefulness of MRI to exclude other causes and demonstrate the offending inflammatory lesion itself, it is suggested that MRI before and after systemic corticosteroid therapy should be performed to put the definitive diagnosis of THS and to differentiate it from other cavernous sinus lesions that simulate THS both clinically and radiologically. In our case, the clinical and radiological findings supported the diagnosis of THS. However, the steroid-resistant course in line with the ICA aneurysm and the unfavorable end did not allow the necessary timeframe to investigate and exclude definitively an alternative underlying cause such a paraneoplastic syndrome or a CNS neoplasm. THS remains a diagnostic challenge necessitating multi-specialization consultations.

HIGHLIGHTS

- Tolosa-Hunt Syndrome is a rare condition of an idiopathic granulomatous inflammation of the cavernous sinus, which may be related to arterial narrowing and aneurysms of the internal carotid artery.
- Rarely Tolosa-Hunt Syndrome may not respond to corticosteroids.
- The cavernous ICA aneurysms have a benign course in general, but in case of a concurrent inflammation may lead to death due to intracranial haemorrhage.

CONSENT

As per international standard or university standard, patient's consent has been collected and preserved by the authors.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Tolosa E. Periarteritic lesions of the carotid siphon with the clinical features of a carotid infraclinoidal aneurysm. J Neurol Neurosurg Psychiatry. 1954;17:300–2.
2. International Headache Society. The International Classification of Headache Disorders, 3rd Edition. Cephalalgia 2018; 38:1–211.
   DOI: 10.1177/0333102417738202
3. Amrutkar C, Burton EV. Tolosa-hunt syndrome. Statpearls Publishing; 2020.
4. Olsen K, Johnson A, Castillo-Jorge S, Bennett J, Ryan Mf, Olsen K, Et Al. Diagnosis and treatment of tolosa-hunt syndrome in the emergency department. Open J Emerg Med 2017;05:1–7.
   DOI: 10.4236/Ojem.2017.51001
5. Msigwa Ss, Li Y, Cheng X, Msigwa Ss, Li Y, Cheng X. Tolosa hunt syndrome: Current diagnostic challenges and treatment. Yangtze Med. 2020;04:140–56.
   DOI: 10.4236/Ym.2020.42014.
6. Evers S. Facial Pain: Overlapping Syndromes. Cephalalgia. 2017;37:705–13.
   DOI: 10.1177/0333102417703761
7. Halabi T, Sawaya R. Successful Treatment of tolosa-hunt syndrome after a single Infusion of infliximab. J Clin Neurol 2018; 14:126–7.
   DOI: 10.3988/Jcn.2018.14.1.126
8. Mazzotta G, Alberti A, Ps-Ha. Undefined. a case of tolosa-hunt syndrome responsive to azathioprine treatment. Cliggott Publ N.D; 2004.
9. Takasuna H, Sasaki R, Shiraishi M, Doi M, Wakui D, Ito H, Et Al. Steroid-resistant tolosa-hunt syndrome with a de novo intracavernous aneurysm: A case report. Surg Neurol Int. 2016;7:S779–84.
   DOI: 10.4103/2152-7806.193925
10. Furukawa Y, Yamaguchi W, Ito K, Hamada T, Miyaji H, Tamamura H, Et Al. The Efficacy of radiation monotherapy for tolosa-hunt syndrome. J Neurol 2010;257: 288–90.
    DOI: 10.1007/S00415-009-5335-8.
11. Wani Na, Jehangir M, Lone Pa. Tolosa-hunt syndrome demonstrated by constructive interference steady state magnetic resonance imaging. J Ophthalmic Vis Res 2017;12:106–9.
    DOI: 10.4103/2008-322x.200171
12. Cakirer S. Mri findings in tolosa-hunt syndrome before and after systemic

corticosteroid therapy. Eur J Radiol 2003;45:83–90.
DOI: 10.1016/S0720-048x(02)00012-8

13. Ravindran K, Schmalz P, Torun N, Ronthal M, Chang Y-M, Thomas Aj. Angiographic findings in the tolosa–hunt syndrome and resolution after corticosteroid treatment. Neuro-Ophthalmology. 2018;42:159–63.
DOI: 10.1080/01658107.2017.1365268

14. Kupersmith Mj, Stiebel-Kalish H, Huna-Baron R, Setton A, Niimi Y, Langer D, Et Al. Cavernous carotid aneurysms rarely cause subarachnoid hemorrhage or major neurologic morbidity. J Stroke Cerebrovasc Dis. 2002;11:9–14.
DOI: 10.1053/Jscd.2002.123969

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/55185