

# Tolosa-Hunt syndrome associated with Coronavac / Sinovac vaccination against Covid-19

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## Abstract

Tolosa-Hunt syndrome consists of unilateral or periorbital headache, paresis of the III, IV, and/or VI cranial nerves ipsilateral to the headache; along with image evidence of pathology in the cavernous sinus or superior orbital fissure. We present the case of a 76 YO woman who developed Tolosa-Hunt syndrome posterior to the application of Sinovac vaccine against Covid-19.

**Keywords:** Covid-19, Tolosa-Hunt, Sinovac, Coronavac.

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## Introduction

Tolosa-Hunt syndrome (THS) – originally described by Tolosa and later by Hunt in the mid-20th century consists of unilateral painful ophthalmoplegia, with involvement of the cranial nerves responsible for eye movement and ipsilateral facial sensory loss. This syndrome can occur due to multiple causes at the cavernous sinus or the superior orbital fissure. However, it has been acknowledged as a unilateral inflammatory process of unknown etiology.<sup>1</sup> This case report intends to address a new etiology for Tolosa-Hunt syndrome as well to inform of a new possible side effect of the Covid-19 vaccination.

## Clinical case

We present the case of a 76 YO woman, resident of Mexico City, with the following personal history: quinolones allergy, systemic arterial hypertension, non-insulin-dependent diabetes mellitus, and irritable bowel syndrome. The patient completed Coronavac / Sinovac vaccination scheme (1st dose March 21, 2021, 2nd dose May 5, 2021) and came to the emergency department due to oppressive headache of mild intensity and pain at the puncture site on the day of application of the first dose. The patient presented to the emergency room four more times after the application of the second dose; all of them

were diagnosed as hypertensive emergencies and the patient was discharged with adjustment of her antihypertensive medications. On June 07, 2021, she went to the emergency department for the 5th time due to oppressive headache 9/10 visual analogue scale (VAS), phonophobia, and right ear pain, she was then assessed by the neurology service, and a computed tomography scan of the skull was performed, which reported as normal, ruling out structural causes. On June 09, 2021, she came again presenting photophobia, right ptosis, and right eye pain which exacerbated with movement; laboratory exams showed severe hyponatremia (116 mmol / l) and for this reason she was admitted at the internal medicine department for treatment and diagnostic protocol.

During her hospitalization, she was evaluated again by the neurology service. On physical examination, she presented pain facies, hyporexia, right oppressive-stabbing hemicranial headache, 7/10 VAS, photophobia – which conditioned her to wear an eye mask –, incomplete palsy of the right third cranial nerve without pupillary involvement, palsy of the right IV cranial nerve, as well as diplopia – which improved with the Bielschowsky maneuver –, pain on right eye movement and hypoesthesia in right V1 and V2. Palsy of right VI nerve was also noted (Figure 1).



Laboratory studies and a lumbar puncture were performed, which only showed a unique alteration in previously known sodium levels (Table 1). Magnetic resonance imaging (MRI) was requested, which exhibited right cavernous sinus enhancement (Figure 2). With the clinical data obtained through physical examination and imaging studies, as well as the absence of alterations in laboratory studies, the diagnosis of Tolosa-Hunt syndrome was established.

Management started with high doses of corticosteroids (dexamethasone 8 milligrams intravenously every 8 hours), with improvement of the previously described symptoms, and she was discharged with prednisone at a dose reduction scheme. The patient had a last consultation on June 28, 2021, in which an improvement in her symptoms was observed, and no extraocular movements deficit were registered (Figure 3).

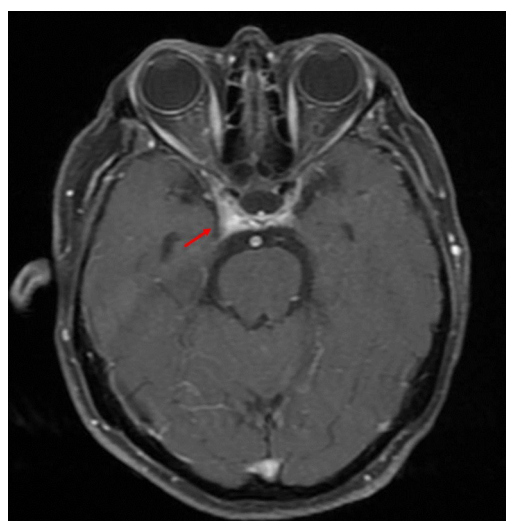
**Figure 1.** Extraocular eye movements pre-treatment



**Table 1.** Laboratory tests

Laboratory test	Result
Leucocytes	8.82 103/ul
Hemoglobin	15.30 gr/dl
Hematocrit	41.80 %
Platelets	363 103/ul
Glucose	116 mg/dl
Glycosylated hemoglobin	6.5 %
Urea	19.9 mg/dl
Creatinine	0.64 mg/dl
Aspartate aminotransferase	26 u/l
Alanine aminotransferase	14 u/l
Lactate dehydrogenase	164 u/l
Total bilirubin	0.53 mg/dl
Sodium	121 mol/l
Potassium	4.6 mmol/l
Chloride	86 mmol/l
Prothrombin time	17.2 seconds (70% activation)
Partial thromboplastin time	36.9 seconds
INR	1.28
Lumbar puncture	
Aspect	Clear
Total cells	2 cells/ul
Leucocytes	2 cells/ul
Total protein	21.2 mg/dl
Glucose	99.5 mg/dl
Gram stain	negative
Ziehl-Neelsen stain	negative

**Figure 2.** Magnetic resonance image. Axial view, T1 weighted. Enhancement of the right cavernous sinus is noted (red arrow)



**Figure 3.** Extraocular eye movements post-treatment

## Discussion

The International Headache Society presents in the third edition of its classification (ICHD-III) the criteria for the diagnosis of Tolosa-Hunt syndrome. These correspond to unilateral or periorbital headache with evidence by MRI or biopsy of granulomatous inflammation of the cavernous sinus, superior orbital fissure or orbit, as well as paresis of the III, IV, and/or VI cranial nerve ipsilateral to the headache, not attributable to another diagnosis of ICHD-III.<sup>2</sup>

The diagnosis of Tolosa-Hunt syndrome is one of exclusion. Regarding this case, chronic hyponatremia was diagnosed as a result of long time medication with diuretic. Tolosa-Hunt syndrome has also been associated with poorly controlled diabetes mellitus; a previous clinical case has been reported, however, the registered glucose level was higher compared to that of our patient<sup>3</sup> (glycosylated hemoglobin of 12.4% vs. 5.6%). Another case of painful ophthalmoplegia and ipsilateral ptosis was reported in Papua New Guinea regarding a non-previously diagnosed diabetic patient; clinical diagnosis of supraorbital syndrome was made, nevertheless, the patient did not respond to prednisolone, thus not supporting the diagnosis of Tolosa-Hunt syndrome.<sup>4</sup> Sarcoidosis is one of the leading causes of Tolosa-Hunt syndrome, however our patient did not have a previous medical history that suggested she had experienced such disease prior to vaccination: her medical examination did not concur with clinical findings of sarcoidosis.

The inactivated SARS-CoV-2 vaccine by Sinovac has been previously reported to cause neurological disorders such

as acute disseminated encephalomyelitis, headache, and myalgia.<sup>5</sup> A case of complete paralysis of the oculomotor nerve was reported in January 2021, two weeks after the application of the vaccine against influenza – which is similar to Sinovac as both are inactivated in Vero cells. This vaccine is known to cause Guillain-Barre syndrome, demyelinating polyneuropathy, and disseminated encephalomyelitis, among others.<sup>6</sup>

A case of Tolosa-Hunt syndrome was reported most recently, however, this was with mRNA-based Covid-19 vaccine.<sup>7</sup> This continues the discussion on the side effects of vaccines against Covid-19, whether exacerbating previously acquired unknown conditions, or being the cause of such.

We strongly believe that the benefits of vaccination outweigh its possible side effects. However, proper documentation of side effects – whether from the vaccine itself or from conditions attributed to the patient – must be conducted and investigated.

## Conclusion

The diagnosis of Tolosa-Hunt syndrome is one of exclusion. The absence of risk factors, as well as the lack of clinical, laboratory, and/or image supporting the diagnosis of another type of pathology, along with the onset of symptoms after its application, leads to consider vaccination against Covid-19 as a possible cause of Tolosa-Hunt syndrome, which must be included in the differential diagnosis of such disease.

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Artículo sin conflicto de interés

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