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# Temporal arteritis, Sjögren's syndrome and mixed pain components as manifestations in a diabetic older adult: systematic review based on a case report

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Abstract

Temporal arteritis (TA) is an inflammatory vascular disease common in the European population. It is mainly characterized by sudden onset headache. TA is rarely associated with other autoimmune diseases, such as Sjögren's syndrome (SS). We present the case of a Peruvian 71 year-old man with SS history, who was admitted to the emergency department due to severe headache evolved in 4 days, periocular pain and right ptosis. The authors also performed a systematic review of case reports or case series of patients diagnosed with both TA and SS. This temporal arteritis case is an atypical presentation because headache was characterized by mixed nociceptive and neuropathic pain components. Despite the infrequency, new studies should be carried out to identify comorbidities in TA patients.

**Key words:** giant cell arteritis, headache, Sjögren's syndrome, chronic pain.

## Introduction

Temporal arteritis (TA), or giant cell arteritis, is an inflammatory vasculopathy of medium and large caliber arteries, which is mediated by an autoimmune mechanism [1]. It has a worldwide incidence of 15–25 cases per 100,000 people per year. It is more frequent in the European population, over 50 years old, and in women [2]. It is rarely reported in Hispanic, Asian or Afro-descendant populations [1].

Frequent clinical manifestation are sudden onset headache, scalp pain, mandibular claudication, abnormal temporal arteries and ocular symptoms (pain, diplopia or irreversible visual loss) [1]. Severe complications are vision loss and stroke [3]. TA is rarely associated with autoimmune diseases, such as Sjögren's syndrome (SS).

Although headache is frequent in patients with TA, there are cases without headache or painful eye vision loss [3, 4]. This neuropathic pain is caused by vascular inflammatory changes that result in alteration of the sensory transduction, causing recurrent activity [5]. Likewise, this pain could have atypical manifestations, such as being diffuse [6].

## Material and methods

The aims of this case-based review were:

- to report the case of a diabetic patient who was diagnosed with both TA and SS,
- to perform a systematic review of similar case reports (patients with TA and SS).

The authors performed a systematic search of case reports or case series of patients with both TA and SS in PubMed, Scopus and LILACS from the onset until January 2020. We excluded other publication types. We did not exclude any paper by language or publication date. We followed the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA, 2009) [7].

## Results

### Systematic review

After removal of duplicates, we identified 173 records, and selected seven records for full-text assessment. Two case reports did not report Sjögren's syndrome. We in-

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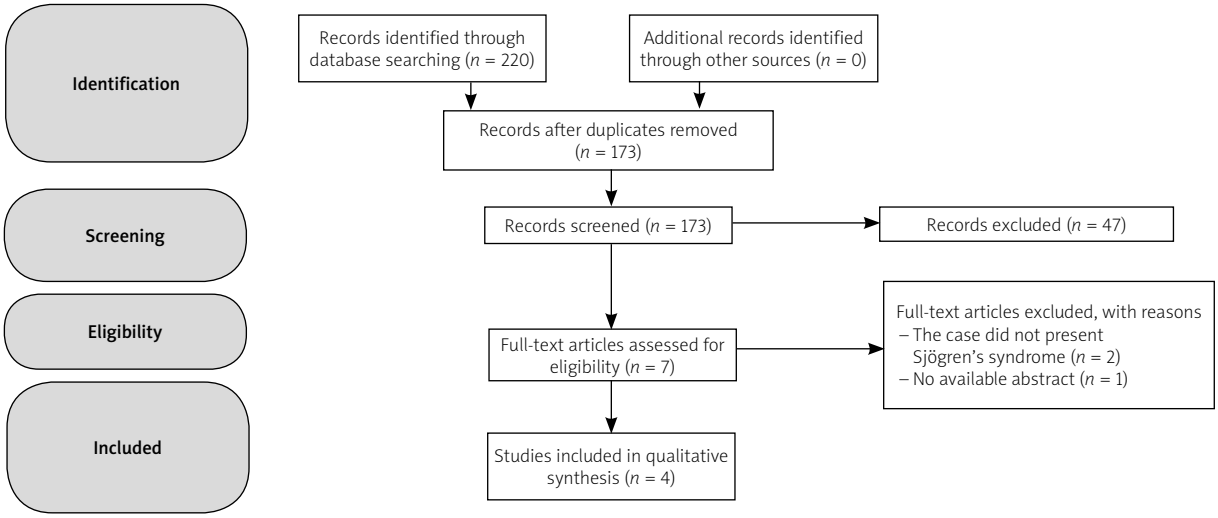


**Fig. 1.** Flow diagram of the systematic search.

cluded four case reports whose abstracts clearly stated that the patient had both TA and SS, but we could not open the full-text version of any of these articles (Fig. 1) [8–11].

All case reports were published between 1985 and 1997. Webster et al. [9] reported a patient with TA, SS, follicular lymphoma and polymyalgia rheumatica. Berthelot et al. [10] reported an older adult with rheumatoid arthritis, lupus, SS and TA, whose symptoms promptly resolved upon enalapril discontinuation with no recurrence at five-year follow-up, except the arthropathy of hands. Kohriyama et al. [11] reported an older adult with TA, SS and polymyalgia rheumatica, whose symptoms were headache, fever, and thickening of left temporal artery with tenderness. The temporal artery biopsy was positive for TA and the SS was subclinical. The CRP was elevated and rheumatoid factors were not detected.

**Table I.** Laboratory/imaging findings

| Laboratory/imaging findings | Results |
|---|---|
| At admission | |
| Brain tomography (with and without contrast) | No significant findings |
| Venous glycemia | 157 mg/dl |
| C-reactive protein (qualitative) | +/+++ |
| Blood count | No significant findings |
| Urea | No significant findings |
| Creatinine | No significant findings |
| Arterial gases | No significant findings |
| Urinary sediment | No significant findings |
| Potassium | No significant findings |
| Chlorine | No significant findings |
| On 17$^{th}$ day | |
| IgG/IgM anticardiolipin antibodies | No significant findings |
| Antiphospholipid antibody | No significant findings |
| Lupus anticoagulant | No significant findings |
| Anti β2-IgM/IgG glycoprotein | No significant findings |

## Case report

We report the case of a Peruvian 71-year-old man. The patient was diagnosed with SS and type II diabetes mellitus (four years before admission). Sjögren's syndrome was diagnosed 10 years before admission using the American College of Rheumatology/European League Against Rheumatism Classification Criteria [12].

Medication for SS was cyclosporine-ophthalmic (type A), pilocarpine, non-steroid anti-inflammatory drugs (associated-pain) and corticosteroids (associated-pain). Additionally the patient was diagnosed with diabetic retinopathy and neuropathy two years before admission. The patient reported other comorbidities: chronic gastritis, venous insufficiency and prostatic hypertrophy. His usual medications were metformin, glibenclamide, pregabalin, tolterodine, ranitidine and calcium dobesilate.

The patient was admitted to the emergency department with symptomatology evolution of four days, which was characterized by new-onset diffuse headache, right periocular pain, right palpebral ptosis and diplopia. The patient reported a pain intensity of 10/10 according to the visual analog scale (VAS), and it had been being aggravated by eye, neck and jaw move-

ments. His blood pressure was 155/85 mm Hg, but the other vital functions were normal.

The patient did not present disorientation or meningeal signs. The patient was evaluated by an ophthalmologist and a neurologist, who supported the diagnosis of diabetic retinopathy with normal intraocular pressure and cranial mononeuropathy III.

At admission, we only found high venous glycemia; the rest of laboratory/imaging findings did not show significant results (Table I). Treatment with intravenous dimenhydrinate and ketoprofen was initiated, added to isotonic serum hydration.

After 24 hours, pain was not controlled, so the patient started to receive intravenous tramadol (50 mg every eight hours) associated with intravenous saline replacement. Brain nuclear magnetic resonance was performed: no significant findings. At this point, the diagnosis was trigeminal neuralgia.

Within the first four days of hospitalization, pain severity according to the VAS fluctuated between 8 and 9/10. The patient began to show tramadol intolerance, presenting hypotension, nausea and vomiting, so treatment was rotated to intravenous lysine clonixinate and ketoprofen associated with oral pregabalin, reducing pain down to 7/10 (VAS). An ophthalmology reevaluation was requested since both pain severity and diplopia intensified, and right visual acuity decreased. Cerebral and ophthalmic angiography was performed: without alterations.

On the 17$^{th}$ day of hospitalization, a Geriatrics interconsultation was performed, concluding a mild functional dependence (baseline: independent), intact cognition, depressive disorder and malnutrition. This delay of Geriatrics interconsultation was associated with the delay in the diagnosis in the internal medicine ward where the patient was hospitalized added to the atypical symptoms.

Pain analgesic and semiology treatment was evaluated using the VAS, Douleur Neuropathique 4 items validated in Spanish (DN4) and the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) scale to discriminate the presence of the neuropathic component, yielding positive results and evidencing ineffective analgesic management (VAS: 8–10, DN4: 6, LANSS: 17). Additionally the patient reported overall loss of vision in the right eye and partial loss in the left eye.

Physical examination showed bilateral pain in the temporomandibular joint, right eye twitching and pulsatile headache in the temporal region. In addition, the pain was predominantly nocturnal with the presence of paresthesias in the right hemiface and bilateral upper maxilla, and allodynia in the right temporal region. Therefore, temporal arteritis was suspected. While studies were being completed, the pregabalin dose was increased and morphine hydrochloride was started due to severe pain. Rheumatology reassessment was requested. Rheumatologic tests are presented in Table I. Moreover, temporal artery Doppler ultrasound was performed (Fig. 2).

The patient reported pain relief, but the patient had an intestinal sub-occlusion, so it was rotated from morphine to fentanyl. Analgesic treatment with pregabalin and fentanyl successfully reduced pain (VAS: 3/10, DN4: 2, LANSS: 4). Next, treatment with prednisone at 0.70 mg/kg was initiated, completely relieving pain on the third day, and the patient was discharged. The patient was treated with prednisone (40 mg/d orally) until the seventh day after discharge (ambulatory visit).

The patient was followed for four months. The patient was re-hospitalized twice for respiratory infections. During the second admission, the patient suffered sepsis and died of cardiovascular complications, the pathological diagnosis being acute myocardial infarction. Figure 3 shows the postmortem biopsy of the right temporal artery, confirming the temporal arteritis. The patient had been treated without prednisone when the patient died.

## Discussion

Temporal arteritis is a panarteritis that affects the extracranial branches of the carotid artery, and the most important risk factor is aging. The mean age of presentation is 72 years [2].

However, it is infrequent in men and the Latin American population. One of the largest case series in Latin America concerns 22 Mexican patients in 20 years, demonstrating the low frequency in populations similar to ours [13]. No cases of TA have been reported in Peru,

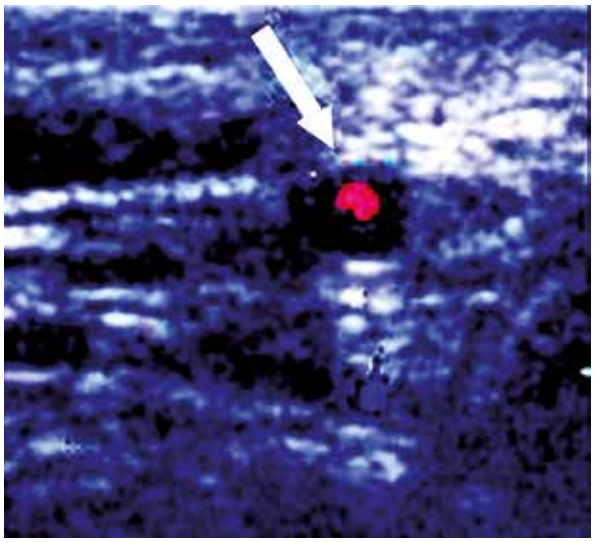

**Fig. 2.** Doppler ultrasound of the temporal artery.

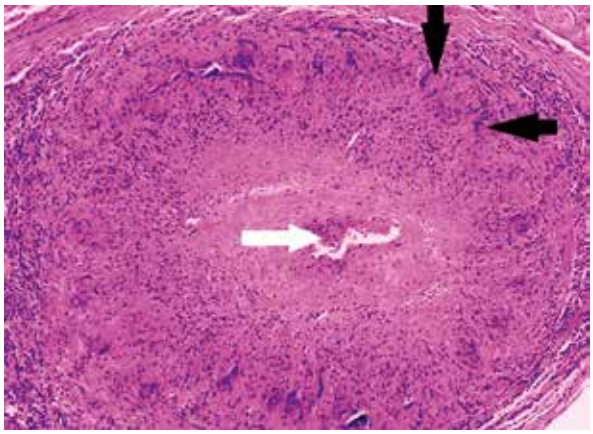

**Fig. 3.** Postmortem biopsy of temporal artery. White arrow: mononuclear infiltration in the inner layer of the temporal artery. Black arrow: multinucleated giant cell infiltration.

and there are very few case reports in Latin America, so there may be a genetic factor. It is evidenced that the associated genes are the antigens of the major histocompatibility complex HLA-DR1, HLA-DR3, HLA-DR4 and HLA-DR5, with expression of the HLA-DRB1*04 allele in the majority of patients [14].

The American College of Rheumatology recommends the diagnosis using three of five criteria: age > 50 years, recent onset headache, temporal pain, erythrocyte sedimentation rate (ESR) greater than 50 mm and temporal artery biopsy with predominant mononuclear inflammation or multinuclear giant cell infiltration; however, it should be noted that they are not diagnostic criteria for cases with atypical presentation [14]. In this case report, the patient met the following criteria: age ≥ 50 years, new-onset headache and pain (diffuse). Additionally the postmortem biopsy of temporal artery was positive for TA [3].

It was ruled out that the symptomatology was due to the history of Sjögren's syndrome. The patient had pain at the right periocular level accompanied by diplopia, which has been found to be a rare but serious consequence of TA. Moreover it occurs due to muscular or nerve ischemia [15]. The patient presented palpebral ptosis; therefore we considered cranial mononeuropathy III as the differential diagnosis, although it also occurs in TA [1]. We requested the qualitative CRP and the result was +/+++. It has been reported that ESR and CRP are sensitive tests of TA screening, but they could be normal in 17% of cases since they are not specific [14].

The prevalence of ocular complications is high (70%), and patients may present loss of vision (20%) with a range of time of 1–14 days of both eyes. In this case, there was an irreversible loss of vision, and this is mainly explained by an ischemic optic neuropathy [1, 3]. We also observed involvement of the temporomandibular joint, which is described in TA patients [1].

Although headache is the most frequent symptom of temporal arteritis, the intensity and location could vary, simulating other diseases. In this case, the headache was intense with both nociceptive and neuropathic characteristics; consequently, it was confused with trigeminal neuralgia or multifactorial otalgia. Due to the mixed-component pain caused by vasculitis, we managed this symptom using fentanyl and pregabalin, which significantly reduced pain intensity (VAS: from 8 to 4). The application of corticosteroids, which is the first-line treatment, totally eliminated the pain [3].

## Conclusions

This case prompted us to reflect on a disease that affects older adults who usually have a delayed diagnosis with disabling consequences owing to their pluripathological status, frailty and atypical disease presentation.

Likewise, we recommend focusing on studying risk factors of temporal arteritis in specific populations, such as Latin American, through case-control studies or cohorts. Moreover, Sjögren's syndrome and other comorbidities should be taken into account to avoid making mistakes in the differential diagnosis assessment [16].

*The authors declare no conflict of interest.*

### References

1. Chacko JG, Chacko JA, Salter MW. Review of Giant cell arteritis. Saudi J Ophthalmol 2015; 29: 48-52, DOI: 10.1016/j.sjopt.2014.10.001.
2. Ponte C, Rodrigues AF, O'Neill L, Luqmani RA. Giant Cell Arteritis: Current Treatment and Management. World J Clin Cases 2015; 3: 484-494, DOI: 10.12998/wjcc.v3.i6.484.
3. Gossman W, Peterfy RJ, Khazaeni B. Temporal (Giant Cell) Arteritis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing 2017.
4. Kornberg MD, Ratchford JN, Subramaniam RM, Probasco JC. Giant Cell Arteritis Mimicking Infiltrative Leptomeningeal Disease of the Optic Nerves. BMJ Case Rep 2015; 2015: bcr2014209160, DOI: 10.1136/bcr-2014-209160.
5. Malcangio M. Role of the Immune System in Neuropathic Pain. Scand J Pain 2019; 20: 33-37, DOI: 10.1515/sjpain-2019-0138.
6. Gabr A, El Kholy K, Crotty J, et al. Giant Cell Arteritis Presenting with Bilateral Subdural Haematomas of Arterial Origin. Eur J Case Rep Intern Med 2016; 3: 000411, DOI: 10.12890/2016_000441.
7. Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA statement. Int J Surg 2010; 8: 336-341, DOI: 10.1016/j.ijsu.2010.02.007.

8. Semble EL, Agudelo CA, Challa VR, Heise ER, Pisko EJ. Temporal Arteritis in Sjögren's Syndrome. Clin Exp Rheumatol 1985; 3: 345-347.
9. Webster E, Corman LC, Braylan RC. Syndrome of Temporal Arteritis With Perivascular Infiltration by Malignant Cells in a Patient With Follicular Small Cleaved Cell Lymphoma. J Rheumatol 1986; 13: 1163-1166.
10. Berthelot JM, Moreau A, Glémarec J, et al. Enalapril-induced vasculitis resembling rheumatoid arthritis, lupus, sicca syndrome, and giant cell arteritis. Rev Rhum Engl Ed 1997; 64: 421-423.
11. Kohriyama K, Kohno A, Arimori S. [A Case of Temporal Arteritis Associated With Polymyalgia Rheumatica and Subclinical Sjögren's Syndrome]. Ryumachi 1990; 30: 272-280.
12. Shiboski CH, Shiboski SC, Seror R, et al. 2016 ACR-EULAR Classification Criteria for primary Sjögren's Syndrome: A Consensus and Data-Driven Methodology Involving Three International Patient Cohorts. Arthritis Rheumatol 2017; 69: 35-45, DOI: 10.1002/art.39859.
13. Alba MA, Mena-Madrazo JA, Reyes E, Flores-Suárez LF. Giant Cell Arteritis in Mexican Patients: J Clin Rheumatol 2012; 18: 1-7, DOI: 10.1097/RHU.0b013e31823e2e35.
14. Acosta-Mérida A, Hernández FFM. Diagnóstico y tratamiento de una arteritis temporal en urgencias. Semin Fund Esp Reumatol 2012; 13: 134-141.
15. Ross AG, Jivraj I, Rodriguez G, et al. Retrospective, Multicenter Comparison of the Clinical Presentation of Patients Presenting With Diplopia From Giant Cell Arteritis vs Other Causes. J Neuroophthalmol 2019; 39: 8-13, DOI: 10.1097/WNO.0000000000000656.
16. Goodman BP. Immunoresponsive Autonomic Neuropathy in Sjögren Syndrome – Case Series and Literature Review. Am J Ther 2019; 26: e66-71, DOI: 10.1097/MJT.0000000000000583.