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Cogan's syndrome

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ABSTRACT

Cogan's syndrome is a disease characterized by ocular and audiovestibular signs and symptoms that can present anachronistically in less than 2 years and its atypical form es usually accompanied by systemic symptoms , being responsible for these vascular inflammatory commitment .

Because to the low specificity of the symptoms associated with a low incidence of the disease , the diagnosis is usually late, which requires a high clinical suspicion to initiate management and avoid irreversible sequelae .

KEYWORDS: Cogan syndrome, audiovestibular, vasculitis.

INTRODUCTION

Cogan syndrome is an autoimmune disorder that should be suspected in those patients who present ocular and audiovestibular symptoms in the context of fever of unknown origin, are usually young and have no gender predilection [1] ; It is frequently related to a previous infection by bacteria of the genus *Chlamydia,* with molecular mimicry being the immunological mechanism to trigger it [2] .

It is a disease that was described for the first time in 1945 and since then there have been more than 300 cases reported in the literature worldwide with an incidence whose figure may be underestimated due to the difficulty in making the diagnosis. [3]

To date, it is a disease that is part of the group of variable vessel vasculitis and it is essential to per-

form a differential diagnosis between diseases such as Meniere's disease. [3]

CASE PRESENTATION

Male patient, 81 years old, mixed-race, with no documented pathological or pharmacological history upon hospital admission.

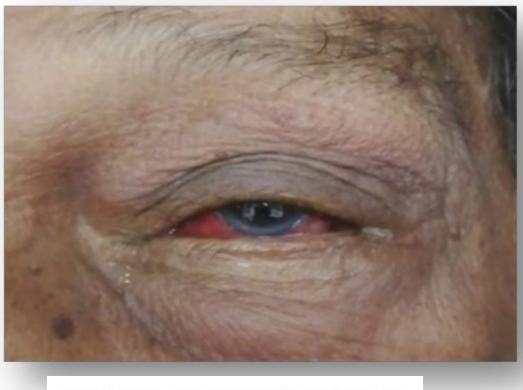

Figura 1. Quemosis izquierda.

He was consulted for symptoms of asthenia and adynamia of progressive onset accompanied by left chemosis, conjunctival and scleral erythema, epiphora, bipalpebral edema.

(figure 1) and limitation for spontaneous ocular opening of the left eye, without pain or changes in visual acuity, which is why he is evaluated by ophthalmology on an outpatient basis where paralysis of the 3rd cranial nerve is suspected, which indicates hospitalization, documenting his moderate thrombocytopenia admission. During his hospital stay, he developed peripheral vertigo, fever quantified up to 38.4°C for 2 weeks with no apparent focus of infection, no signs of hemodynamic instability, exhaustible horizontal nystagmus with rapid movement to the right, bilateral hearing loss with a sudden onset of predominance on the right.

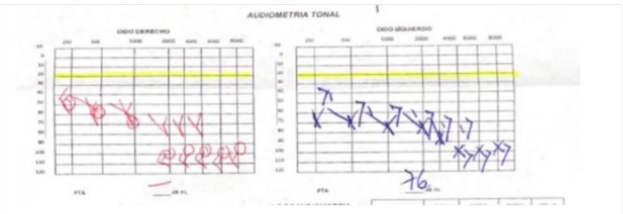

Figura 2. Oído derecho: Hipoacusia neurosensorial profunda solo respuesta de 250 – 1000 Hz; Oído izquierdo: Hipoacusia Neurosensorial severa.

(figure 2) , increase in angle of support and right lateralization when walking, so studies were expanded for fever of unknown origin, finding moderate thrombocytopenia upon admission and anemia without transfusion requirement, ruling out central involvement or lesion of the brain by MRI of the brain and orbit. cranial nerves, lymphadenopathy in the non- adenomegalic range is documented mediastinal and retroperitoneal, so studies are expanded to rule out an infectious or neoplastic cause, resulting in negative results, negative blood and urine cultures, echocardiogram without data of endocarditis, negative serology for leptospirosis , hepatotropic viruses , subsequently progressing to PET- Scan without evidence of cause solid neoplastic , drawing attention to findings of irregular uptake in the aortic arch and descending aorta compatible with an inflammatory process (Aortitis).

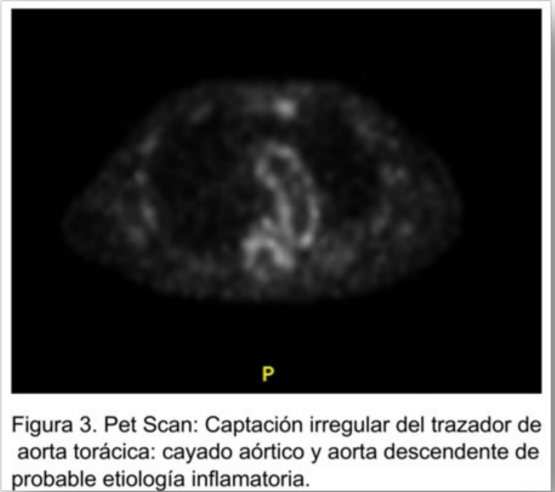

Figura 3. Pet Scan: Captación irregular del trazador de aorta torácica: cayado aórtico y aorta descendente de probable etiología inflamatoria.

(figure 3) , which added to the acute onset of hearing loss, vertigo and ocular damage guides us due to systemic compromise , considering etiologies immunological, autoimmunity studies were sent, finding anti-nuclear antibodies with negative reports for Anti DNA, P-ANCA C-ANCA, which due to a negative autoimmune profile is limited to clinical diagnosis with a high clinical suspicion of Cogan syndrome due to keratitis, sudden severe hearing loss. , vertigo and large vessel vasculitis, deciding to extend the study for chlamydia IgG and IgM with a positive report, giving greater weight to the suspected diagnosis due to their association, which is why starting pulses with corticosteroids for 3 days is indicated, with a favorable clinical response. With disappearance in PET control uptake of presumed inflammatory origin.

DISCUSSION

Cogan syndrome is a rare autoimmune disorder characterized by involvement of the eye and inner ear, the most representative findings being interstitial keratitis and audovestibular dysfunction. [1] To date, it is a disease that is part of the group of variable vessel vasculitis and it is essential to perform differential diagnosis between diseases. [2]

It is a disease that was described for the first time in 1945 and since then there have been more than 300 cases reported in the literature worldwide with an incidence whose figure may be underestimated due to the difficulty in making the diagnosis. [2] At an international level, this disease usually has a peak incidence in the third and fourth decade of life, without having a predilection for gender. [1] Regarding national epidemiology, in Colombia, the latest sociodemographic characterization shows 6 cases for the year 2013, classifying it as an orphan disease. [3]

It has been shown that the main trigger of this entity is the infectious cause, especially those related to the upper respiratory tract that usually precede the onset of the disease in 50% of cases. [4] In particular, *Chlamydia* infection has attracted a lot of attention , but no direct link between the different *Chlamydia* species has been demonstrated . A research group discovered that patients with Cogan syndrome had higher antibody titers against Chlhamydia [5] species as was the case in the case previously reported.

Antibodies have been demonstrated against the Cogan peptide (also called peptide antigen, which shares a sequence with CD148 and connexin 26, which are expressed on endothelial cells and in the inner ear, the latter protein of which results in hearing loss when is absent in the organ of Corti and which also has similarity with Connexin 43 and 50, which are present in corneal fibroblasts) cross-react with structural proteins of *Reovirus* type III, which suggests that molecular mimicry is the main mechanism of pathogenesis of the disease. [4.7]

In recent years, markers have emerged that suggest autoimmune etiology, such as anti-Hsp70 antibodies in patients with hearing loss; antineutrophil cytoplasmic antibodies (ANCA) in patients who present systemic expression of the disease and more than five cases have been found with these antibodies positive. [5]

Cogan syndrome is characterized by variability in the clinical presentation given by ocular and audiovestibular manifestations , the first manifestation is usually ocular in 41% of cases and the ear in 43% of cases, the interval of appearance of symptoms between both organs It is usually from 3 months to

11 years. [6]

the main ocular manifestations are usually [6,7]: Conjunctival hyperemia 74%, photophobia 50%, ocular pain 50%, temporary decrease in visual acuity 42%. Interstitial keratitis, although very common, is not diagnosed and can be associated with conjunctivitis 26%, uveitis 26%, episcleritis or scleritis 25% and corneal ulceration 11%. [6]

Audiovestibular manifestations frequently present as vestibular syndrome : Vertigo , instability, nausea, vomiting, tinnitus , nystagmus and ataxia may be evident, as well as hearing loss that in most cases can be irreversible. [6]

Regarding systemic manifestations, fever can be found in 39% of patients, with cardiovascular involvement in 28% (aortic insufficiency), gastrointestinal (diarrhea, rectal bleeding or melena, abdominal pain) and neurological involvement (paresis , plegia , aphasia) in 26%. %, weight loss in 26%, skin involvement (erythematous rash , vascular purpura) in 19%, urogenital (ulcers) 16% and lymphadenopathy in 8%.[6]

	Typical Cogan Syndrome	Atypical Cogan syndrome
Appearance time between ocular and audio-vestibular symptoms	Less than two years.	Greater than 2 years.
Eye symptoms	Non-syphilitic interstitial keratitis	Scleritis , uveitis, episcleritis , keratitis, retinal hemorrhages, papilledema , exophthalmos.
Audio-vestibular symptoms	Vertigo, tinnitus , hearing loss, nausea, vomiting	Progressive hearing loss

Clinically it is divided into two groups, [4.8] Typical Cogan Syndrome (TCS) or Atypical (ACS) as shown in the following graph:

The diagnosis of this clinical entity is currently based on the presentation of clinical manifestations mainly in audio-vestibular and ocular symptoms and with the exclusion of differential diagnoses of infectious or inflammatory origin, mainly syphilis, Behcet 's Syndrome , vasculitis associated with ANCA, polyarteritis. nodosa and sarcoidosis . (eleven).

There is no highly sensitive or specific marker to determine the diagnosis of Cogan syndrome ; it is recommended that all suspected patients should have a complete blood count, erythrocyte sedimentation rate (ESR), which increases during active disease (4,8), serological tests to rule out infectious agents such as syphilis and Chlamydia, given the relationship between confirmed cases and confirmation of infection by this etiological agent (9).

Despite being an autoimmune pathology, there is currently no biomarker or antibody that provides a definitive diagnosis. Research began on antibodies directed against antigens of the inner ear, cornea and endothelium given the greater involvement of these organs, where Antibodies were established against the Cogan peptide , which is an antigen that shares sequence homology with CD148 and Connexin 26 with great similarity to autoantigens such as SSA/ Ro (7,10). And in addition, antibodies against heat shock protein 70 (Hsp 70) are available mainly in patients with sensorineural hearing loss , with prevalence rates in Cogan syndrome between 45% to 50%, and a prevalence in comparison of Cogan syndrome typical versus atypical of 66.7%, 37.5% respectively. (10)

On the other hand, the diagnosis can be supported

with tests that detect organic involvement and if the suspicion is involvement of vasculitis in other sites, it must be complemented with angiography or positron emission tomography combined with computed tomography (11).

The basis of treatment for this syndrome is symptomatic and immunosuppressive management. First-line glucocorticoids are used at doses of 1 mg/kg/day for 2-4 weeks depending on the patient's clinical evolution (11); However, given the organic compromise of our patient, we decided to start with intravenous pulses before starting oral doses of glucocorticoids.

There is evidence of clinical benefit, although scarce, with the use of methotrexate , cyclophosphamide , rituximab , anti-IL-6, anti-TNF drugs and even JAK inhibitors, but the use of these medications should be regulated according to the patient's clinical context . level of evidence from clinical studies and their safety profile. (11, 12)

Depending on the severity and refractoriness to medical therapy, plasmapheresis could provide benefit. These patients could also be candidates for surgical treatments depending on the degree of involvement and organic compromise. (eleven)

Conclusion

Cogan syndrome , given its low incidence, can be a disorder that could easily go unnoticed by doctors. Due to the still experimental therapy, it is essential that studies be initiated that lead to greater knowledge of this entity in order to advance in both diagnostic tools. as therapeutic.

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