Atypical Cogan syndrome; case report

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Abstract: Cogan syndrome is a rare disease characterized by the concomitance of non-syphilitic interstitial keratitis with Meniere-like vestibulo-auditory symptoms. There are criteria for the diagnosis of both typical and atypical Cogan syndrome. We present the case of a 40 years old woman with sudden onset of hearing loss, tinnitus, intense vertigo, instability associated with kerato-conjunctivitis. The concomitance of the symptoms, the onset, and the evolution under treatment are consistent with the diagnosis of atypical Cogan syndrome.

Keywords: Cogan syndrome, atypical Cogan syndrome; vertigo; hearing loss

INTRODUCTION

Cogan syndrome is a disorder characterized by the association between the Meniere-like vestibulo-auditory symptoms and ocular symptoms (interstitial keratitis). Although the first to describe a disorder associating ocular and inner ear symptoms were Morgan RF, Baumgartner in 1934 [1], the name of the disease comes from Dr. David Cogan who published in 1945 a series of 4 cases of patients with non syphilitic interstitial keratitis and vestibulo-auditory symptoms [2]. In 1980 Haynes et al proposed the enlargement of the criteria for the diagnosis, defining typical and atypical Cogan syndrome. They proposed that other ophthalmologic inflammatory manifestations such as episcleritis, uveitis, conjunctivitis, can be considered as disease criteria for atypical syndrome. [3]

For a disease described such a long time ago there is very little knowledge about the etiology of the disorder. Until now, approximately 250 cases have been published but we still don’t understand the etiopathogeny of the disease. It is considered an autoimmune disorder. This disease seems to affect young Caucasian adults with ages ranging between 25 to 35 years old, in most of the cases. [5]

CLINICAL FEATURES

Ocular manifestations: The main characteristic of the disease is the ocular involvement. Usually patients have red eye, eye pain and photophobia. The typical Cogan syndrome is defined by the presence of the non syphilitic interstitial keratitis. The examiner might notice granular and irregular infiltrate on the posterior part of the cornea. Neovascularization is also a possibility. Blindness and amaurosis can happen but usually the lesion regresses and the loss of visual acuity is moderate. In the majority of the cases both eyes are affected, the unilateral disease is infrequent [6]. In the atypical Cogan syndrome the vestibulo-cochlear manifestations can be associated with scleritis, episcleritis, uveitis, optic neuritis, conjunctivitis or glaucoma. [7]

Vestibulo-cochlear symptoms: Cogan syndrome is classically characterized by sensory-neural hearing loss, vertigo and...
Tinnitus in an association that resembles Meniere’s disease. The hearing loss might be profound, leading to cophosis in almost 52% of cases and usually it is bilateral. The auditory deficit is installed in days, months, too slow for a sudden nerosensorial hearing loss and too quick for a presbyacusys. The speech discrimination scores are poor. The hearing loss is associated with tinnitus. [4]

The vertigo can be important causing marked instability, ataxia, sometimes associated with nausea and vomiting. The nystagmus can be observed at the ocular examination. In most of the cases, complains are similar to Meniere’s disease.

Other signs and symptoms

General manifestations of the disease are not rare, fever has been reported in many cases, weight loss and extreme asthenia can be found in patients with Cogan’s.

Cardiac involvement, especially aortic insufficiency is present in as much as 15% of cases. Large vessels can also be affected causing heart murmur, abdominal pain, claudication of the members.

Musculo-skeletal involvement manifests as myalgia or arthritis (mono, oligo or polyarthritis).

Neurological signs appear in ¼ of cases [8], patients might have paresis, hemiplegia, aphasia, cerebellar syndrome, pyramidal syndrome, spinal cord disorders, epilepsy, and vigilance disorders. MRI can sometimes detect lesions of the white matter consistent with cerebral vasculitis.

Cutaneous lesions might appear during attacks taking the form of urticarial rash, vascular purpura, ulcerations or nodules.

Some patients might have gastro-intestinal or pulmonary symptoms.

Laboratory investigations

Biologic parameters can be modified in Cogan syndrome, especially during the attacks, but no laboratory test in pathognomonic for the disease. Leukocytosis, elevated ESR, anemia, hyperfibrinemia may appear. Several immunological modifications also can be noticed: rheumatoid factor, antinuclear antibodies, cryoglobulins, lupus anticoagulant but none of these are specific or relevant for the disease. [9]

In small series of patients, some authors determined the presence of specific antibodies for the inner ear or cornea but these studies were not relevant and could not be reproduced by other authors so cannot be used to support the diagnosis of Cogan.

Differential diagnosis

The first differential diagnosis one should bear in mind when facing a rapid onset hearing loss with vestibular symptoms and interstitial keratitis is syphilis. Another important differential diagnosis is Meniere’s disease but in this case the ocular manifestations are absent.

Another diagnosis to be differentiated from Cogan is Susac syndrome, a retino-cochleo-cerebral vasculopathy involving the arterioles, manifested by central neurological disorders, visual acuity loss, and hearing loss.[10] Vogt- Koyanagi-Harada syndrome is characterized by uveitis, alopecia, vitiligo and audio-vestibular symptoms.[11]. Other systemic diseases such as Wegener granulomatosis, PAN, relapsing polychondritis, Behcet disease, and Sjogren syndrome can associate vestibulo-auditory symptoms with ocular involvement.

Evolution, prognosis

In some cases, the onset of the disease is preceded by upper respiratory tract viral infection.

The vestibular and auditory symptoms can be the first manifestations of the disease in 41% of cases. in 43 % of cases the Cogan syndrome debuts with the ocular symptoms. The involvement of the two organs is usually done in approximately 3 months [8]. In cases of atypical Cogan syndrome the complete symptomatology might be installed in a long period, even years.

Usually, after the first attack the disease enters a phase of remission without evident symptomatology. There is a possibility that there are recurrent episodes that repeat at variable intervals. Once installed the hearing loss is not remissible. The vestibular symptoms diminish as a result of the compensation mechanisms. The ocular symptoms have a variable evolution, but usually respond favorably to treatment.

Treatment

As the etiology and the pathogenic mechanisms are not known, there is not yet available a codified treatment for Cogan’s syndrome.

Usually the first line of treatment is represented by corticosteroids. [12] In cases where the corticoderpendence is installed or in cases of corticoresistance there is the possibility of using other therapeutic agents such as immunosuppressants (cyclophosphamide, azathioprine, and methotrexate). [13] The corticotherapy should be prescribed in high dosage (1-1.5 mg prednisone or equivalent) and interrupted in two weeks in cases where it is ineffective. Studies show that the vestibulo-cochlear symptoms respond
to treatment only in one third of the cases (orphanet). Once the deafness is installed, it is usually non-reversible.

In the last years there were attempts to treat Cogan syndrome with TNF alfa blockers but there are not enough evidence based results [14, 15]

**CASE REPORT**

We present the case of a 40 years old woman with no remarkable medical history who presented at the emergency department of our hospital accusing sudden onset intense vertigo and dizziness, tinnitus and hearing loss in the right ear. The patient was admitted in the ENT department.

The physical examination of the patient yielded no relevant data, the ENT exam was within normal limits.

The vestibular examination pointed out to an important instability, the patient was unable to maintain orthostatic position or walk without support, no spontaneous nystagmus.

The cerebral IRM examination did not reveal any vascular or tumoral lesions. The neurologic examination did not discover any motor or sensorial deficit, no signs of localization.

The audiogram performed initially can be visualized in Figure 1. We diagnosed a profound sensoryneural hearing loss for the right ear and a medium sensory-neural hearing loss for the left ear.

![Figure 1: Initial audiogram](image)

The rheumatologic examination revealed no remarkable findings: no arthritis, no cutaneous lesions, and no ocular symptoms.

The blood hematological and biochemical parameters were modified showing a slight leukocytosis with a white blood count of 11000/mm$^3$, the ESR also slightly elevated 25 mm/hour and the CRP had the value of 5. The modifications were interpreted as a reaction to an acute dental infection the patient had at that moment.

All the immunologic tests we performed were in normal limits, IgA, IgG, IgM, ANA, antibodies anti beta 2 glycoprotein, antibodies antiphospholipid were tested and the values were normal. Antibodies Ig M and Ig G for Epstein Bar virus, Toxoplasma, HIV, herpes virus, cytomegalovirus were all negative.

The ophthalmologic examination did not find any modifications of the anterior ocular pole at that initial moment.

The computerized posturography we performed at admission showed a severe vestibular deficiency pattern (Figure 2).

The videonystagmography with caloric testing evidenced a total right areflexia and an extremely important left hyporeflexia (Figure 3).

We started a treatment with high dose corticotherapy (solumedrol), antiemetic (osetron), vestibular suppressant (diazepam), vasoactive agent (pentoxyphilin), vitamin (B1 and B6), plasma expander(dextran 40).

During the treatment, the patient presented a fluctuating evolution. The hearing level fluctuated especially on the left ear with PTA between 30 and 60 and on the right ear with PTA between 60 to 90.

In Figure 4 it can be noticed the aspect of two audiograms we performed during the treatment in which we could observe the fluctuant hypoacusis in both ears.

The dizziness also fluctuated with episodes of severe vertigo. In these episodes, the direction of the nystagmus varied. We recorded horizontal rotatory nystagmus beating to the left but also to the right (Figure 5) alternating with periods of lack...
of nystagmus.

**Figure 2: Computerized posturography**

**Figure 3: Videonystagmography**

**Figure 4: Audiograms during the treatment**
After 10 days of treatment in the hospital, the patient was discharged with an improvement of the hearing loss in the left ear, no vertigo and only a mild dizziness.

One month after this episode, the patient presented once again at the emergency department accusing intense vertigo, nausea, vomiting, tinnitus and aural fullness in the left ear. The audiogram evidenced a bilateral severe hearing loss (Figure 6).

The rheumatologic examination did not reveal any modifications. The second day of hospitalization the patient suddenly presented eye pain with intense redness of the conjunctive. The ophthalmologic examination established the diagnosis of kerato-conjunctivitis (Figure 7).

In this moment, we were able to diagnose an atypical Cogan syndrome taking into account the association between the audio-vestibular symptoms with an inflammatory ocular disease.

We repeated the same treatment as in the first episode associating local eye topical corticosteroids and artificial tear solution with a major improvement of the hearing loss for the left ear PTA 10 (Figure 8).

After 10 days of treatment in the hospital, the patient was discharged with an improvement of the hearing loss in the left ear, no vertigo and only a mild dizziness.

The patient was discharged with a prescription of prednisone in low dose for a period of three months.

One year later, in the follow up, we noticed that the hearing in the right ear did not improve at all but the instability improved a lot so the patient was able to continue with everyday life. In this year she did not have any attack, no audiovestibular or ocular symptoms.

**DISCUSSION**

Haynes et al described atypical Cogan syndrome for the first time in 1980. The typical Cogan syndrome was described as an association between Meniere–like audio-vestibular symptoms and non-syphilitic interstitial keratitis with an
interval between the onsets of the symptoms of less than two years.

The atypical Cogan syndrome consists in an association of symptoms in which the disease criteria are grouped as follows:
- Inflammatory ocular manifestations with or without interstitial keratitis
- Typical ocular manifestations associated with audio-vestibular symptoms different from Meniere’s
- A delay of more than 2 years between the onset of typical ocular and audio-vestibular manifestations.

The atypical Cogan syndrome with ocular manifestations other than interstitial keratitis tends to have a higher rate of systemic involvement with aortitis and has a worse prognosis. [3, 16]

It is the case of a 40-year-old woman with acute onset of intense audio-vestibular symptoms with no remarkable medical history and no other general manifestations. At the first presentation the diagnosis of presumption was Meniere disease but there were characteristics of the evolution that did not entirely correspond. The disease was rapidly onset with bilateral and unequal involvement. The right ear had a profound hearing loss from the very beginning and practically did not respond to treatment. The left ear had a minor amelioration in the first episode and quite a good response in the second episode of the disease although the treatment was similar. During the admission we performed multiple audiograms evidencing the fact that the thresholds at both ears were in a continuous modification, not respecting the classical pattern of Meniere’s. The videonystagmography with calorics showing bilateral vestibular lesion from the beginning of the disease, was also atypical for Meniere.

The onset and evolution of the disease made us believe that there is a autoimmune disorder of the inner ear but we did not have any disease criteria to classify. The laboratory tests were within normal limits, the minor leukocytosis and the slight elevated ESR were not noticeable. No other immunologic tests were modified or virus infections detected.

At the second episode of disease, the concomitance with the kerato-conjunctivitis was consistent with the diagnosis of atypical Cogan syndrome. We consider that this is the only disorder that can be taken into account for the diagnosis of this patient. Another remark is the fact that the patient is over the age of typical onset of the disease, but there are many reports of atypical Cogan with patients in the same age group. [17, 18]

The response to corticotherapy, was partial as the right ear did not recover, but the final result was considered satisfactory by the patient who could continue her daily activities.
CONCLUSION

Although Cogan syndrome is a rare disease, we must bear in mind that there is always a possibility of diagnosing it in the case of a patient with both vestibule-auditory symptoms and ocular manifestations.

Typical and atypical Cogan syndrome are diagnosed mainly based on clinical criteria as there are no laboratory tests able to evidentiate the disease.

The treatment consists mainly in corticotherapy. Immunosuppressants are an option in cases where corticotherapy is inefficient.

References:

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