

## Cogan's syndrome with left main coronary artery occlusion

Tim Weyn<sup>1</sup>, Steven Haine<sup>2</sup>, Viviane Conraads<sup>2</sup>

<sup>1</sup>Department of Cardiology, ZNA Hospital Middelheim Antwerp, Belgium

<sup>2</sup>Department of Cardiology, University Hospital Antwerp, Belgium

### Abstract

*Cogan's syndrome is a rare idiopathic chronic inflammatory disease of the eye and the inner ear in young adults. Cogan's syndrome can be associated with large vessel vasculitis.*

*We report a young female, with a history of interstitial keratitis and audiovestibular disease, who presents with large vessel vasculitis with left main coronary artery occlusion and develops heart failure.*

*Cogan's syndrome was diagnosed on the basis of the presence of large vessel vasculitis with the typical inner ear and ocular involvement. (Cardiol J 2009; 16, 6: 573–576)*

**Key words: Cogan's syndrome, large vessel vasculitis, left main coronary artery occlusion, heart failure**

### Case report

A 30 year-old female of Indonesian origin was admitted to the Department of Neurology complaining of right side amaurosis fugax and diminished exertional tolerance.

She was known to have a history of progressive hearing loss, tinnitus and vertigo since 2003 due to an autoimmune inner ear disease. At that time, audiometry testing demonstrated sensorineuronal hearing loss. Magnetic resonance imaging (MRI) showed enhancement of vestibular and cochlear structures with gadolinium. She tested negative in autoimmune (ANA, ENA, RF, ANCA, complements, smooth muscle antibody, anti-gliadin and anti-endomysial antibodies) tests and negative in serological tests (Syphilis, Lyme, HIV, Chlamydia, Tuberculosis, Epstein-Barr virus, Herpes simplex virus, Cytomegalovirus).

Although she was treated with corticosteroids and azathioprine, she became deaf in 2005 and had a cochlear implantation. In 2006 she developed bi-

lateral interstitial keratitis. No systemic disease could be revealed. Autoimmune and serological tests were again negative.

On admission in May 2007 there was a bilateral bruit over the carotid arteries. Neurological examination was normal. A diminished pulsation of the brachial arteries was present. Cardiac examination showed a systolic murmur at the apex. Ultrasonography (Doppler) revealed diminished velocities in the right vertebral artery and in the left and right internal carotid artery. There was flow reversal in the left vertebral artery (subclavian steal).

Computer tomography of the brain showed no signs of bleeding or ischemia.

Angiography demonstrated an occlusion of the left subclavian artery, a significant stenosis of the left common carotid artery and a moderate lesion in the innominate artery (Fig. 1).

Laboratory tests revealed an erythrocyte sedimentation rate of 26 mm/h (0–19 mm/h) and a C-reactive protein of 3 mg/dL (< 0.5 mg/dL)

**Address for correspondence:** Tim Weyn, MD, Department of Cardiology, ZNA Hospital Middelheim Antwerp, Lindendreef 1, 2020 Antwerp, Belgium, tel: +32 32 803 255, fax: +32 32 306 511, e-mail: tim\_weyn@hotmail.com

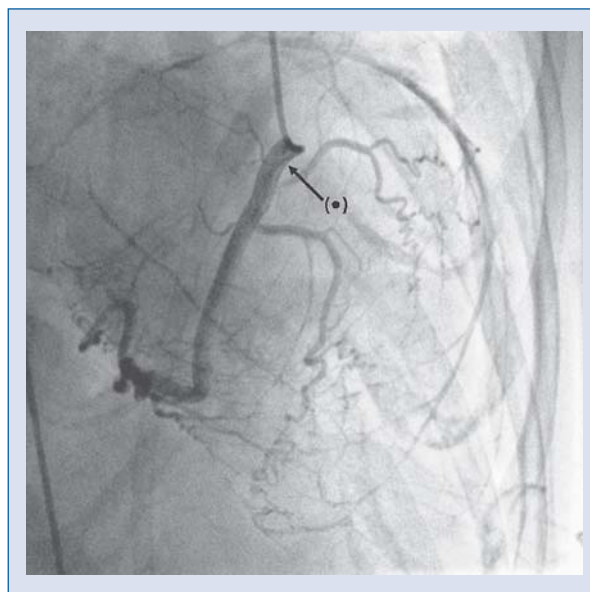
Received: 19.03.2009

Accepted: 9.04.2009



**Figure 1.** Angiography: occlusion of the left subclavian artery, a significant stenosis of the left common carotid artery (▲) and a moderate lesion in the innominate artery (●).

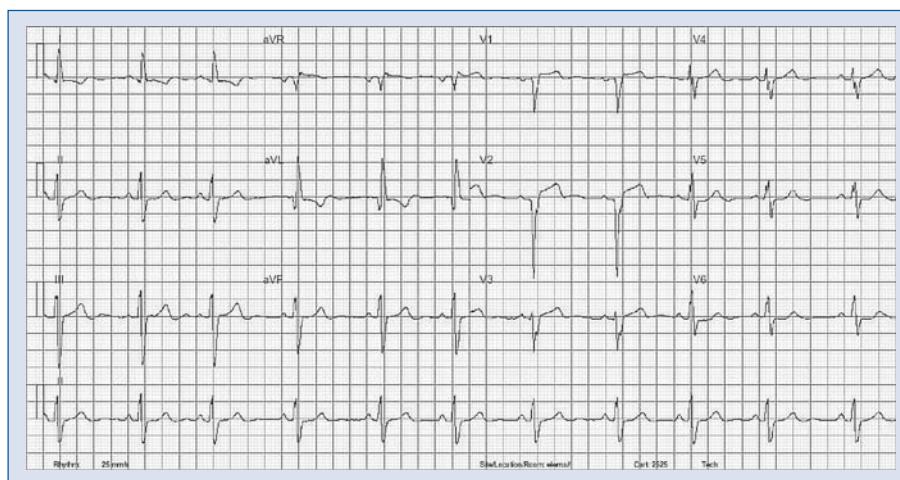
During her stay at the hospital, the patient developed chest pain. Electrocardiography showed anteroseptal myocardial loss and high lateral repolarization disturbances (Fig. 2). Troponin I was



**Figure 3.** Coronary angiography: right coronary artery (●) with collateral circulation to the left anterior descending and circumflex artery due to an occlusion of the left main coronary artery.

elevated 2 ng/mL ( $< 0.04$  ng/mL). Cardiac catheterisation showed a total occlusion of the left main coronary artery with collateral circulation out of the right coronary artery (Fig. 3), severe mitral valve regurgitation and a decreased left ventricular function.

Echocardiography revealed a dilated left ventricle with a severe diminished systolic function due to an antero-apical aneurysm. There was severe mitral valve regurgitation (regurgitant volume of 70 mL,



**Figure 2.** Electrocardiography: anteroseptal myocardial loss and high lateral repolarisation disturbances.

regurgitant fraction of 60%) due to dilatation of the left ventricle and retraction of the posterior mitral valve leaflet.

Nuclear investigation (99m-technetium MIBI) revealed a reversible perfusion defect in the lateral wall of the left ventricle.

The concomitant presence of large blood vessel vasculitis, interstitial keratitis and progressive vestibuloauditory dysfunction resulting in deafness resulted in the diagnosis of Cogan's syndrome (CS). The hallmarks of CS are progressive inflammatory involvement of ocular and audiovestibular organs, which results in interstitial keratitis and audiovestibular dysfunction. There is an association between CS and systemic vasculitis. The large vessel vasculitis associated with CS may resemble Takayasu's arteritis.

The patient was treated with high dose glucocorticoids and pulse therapy of cyclophosphamide.

Later on, she underwent coronary bypass surgery (venous jump bypass to the left anterior descendens and circumflex artery), a mitral valve repair (Carpentier Edwards Physio annuloplasty ring 26) and a Dacron 6 mm bypass from the aorta to the left carotid artery.

After the surgery, the patient recovered well. There was a minor persistent mitral valve leak. Left ventricular function improved. She was further treated with angiotensin-converting enzyme-inhibition, beta-blockers and anticoagulants.

Currently the immunosuppressive treatment consists of prednisolone and methotrexate.

## Discussion

In 1945 the ophthalmologist David Cogan [1] described a syndrome consisting of interstitial keratitis and audiovestibular symptoms. CS is a rare idiopathic chronic inflammatory disease of the eye and the inner ear in young adults [2]. There is no predisposition for race or gender. The etiology of CS is unknown and less than 250 cases have been reported.

The characteristics of CS are non-syphilitic interstitial keratitis and audiovestibular dysfunction resembling Ménière's disease [3]. The ocular symptoms are pain, photophobia, blurred vision and eye redness. During examination a corneal granular infiltrate is observed, and secondary neovascularization frequently occurs. In most cases both eyes are affected.

Audiovestibular manifestations are characterized by sensorineuronal hearing loss, vertigo and

tinnitus [4], complaints similar to those of Ménière's disease. The hearing loss is progressive and often leads to deafness.

Medical imaging with MRI scan (gadolinium) shows calcification or narrowing and soft tissue obliteration of the vestibular labyrinth, semicircular canals and the cochlea [5].

CS is not associated with autoantibodies or other specific immune abnormalities that are unique for this disorder.

Ophthalmological examination, audiometry and vestibular tests are the basis of the diagnosis of CS. Differential diagnosis of CS includes diseases that cause similar eye and inner ear manifestations: sarcoidosis, polyarteritis nodosa, Wegener's granulomatosis and rheumatoid arthritis. Moreover, possible infectious causes of interstitial keratitis (such as congenital syphilis, tuberculosis, chlamydia and viral infections) should be excluded.

In 15–20% of patients with CS, there are overt signs of systemic vasculitis [6]. The vasculitis mainly involves the large and medium-sized vessels. The large vessel vasculitis associated with CS may resemble Takayasu's arteritis [7].

Aortitis is described in 10% of patients and can lead to proximal aorta dilation, aortic valvular regurgitation, ostial coronary artery involvement and thoracoabdominal aneurysms.

Furthermore, non-specific systemic symptoms are described in CS: fever, fatigue, weight loss, lymphadenopathy, arthritis and urticaria.

Medical treatment of CS depends on how extensive the disease is.

In cases with only a mild eye involvement, the treatment of choice is the application of topical glucocorticoids. When there is evidence of an inner ear pathology, a severe infection of the eye or systemic vasculitis, the treatment consists of immunosuppressive therapy.

The first choices in immunosuppressive therapy are glucocorticoids (prednisolone 1 mg/kg). In case of treatment failure or corticosteroid-sparing therapy, other immunosuppressive drugs can be used such as cyclophosphamide [8], azathioprine, methotrexate [9], cyclosporine, mycophenolate mofetil and tumor necrosis factor-alpha blockers [10].

Bypass surgery or aortic valve replacement may be necessary where there are severe ischemic symptoms or heart failure.

Because of the progressive hearing loss in Cogan's syndrome, a cochlear implant [11] is often indicated, whereas the ophthalmological prognosis is mostly favourable.

## Acknowledgements

The authors do not report any conflict of interest regarding this work.

## References

1. Cogan D. Syndrome of nonsyphilitic interstitial keratitis and vestibuloauditory symptoms. *Arch Ophthalmol*, 1945; 33: 144–149.
2. Chynn EW, Jakobiec FA. Cogan's syndrome: Ophthalmic, audiovestibular, and systemic manifestations and therapy. *Int Ophthalmol Clin*, 1996; 36: 61–72.
3. Haynes BF, Kaiser-Kupfer MI, Mason P, Fauci AS. Cogan syndrome: Studies in thirteen patients, long-term follow-up, and a review of the literature. *Medicine*, 1980; 59: 426–441.
4. McDonald TJ, Vollertsen RS, Younge BR. Cogan's syndrome: Audiovestibular involvement and prognosis in 18 patients. *Laryngoscope*, 1985; 95: 650–654.
5. Casselman JW, Majoor MH, Albers FW. MR of the inner ear in patients with Cogan syndrome. *Am J Neuroradiol*, 1994; 15: 131–138.
6. Gluth MB, Baratz KH, Matteson EL, Driscoll CL. Cogan syndrome: A retrospective review of 60 patients throughout a half century. *Mayo Clin Proc*, 2006; 81: 483–488.
7. Raza K, Karokis D, Kitis GD. Cogan's syndrome with Takayasu's arteritis. *Br J Rheumatol*. 1998; 37: 369–372.
8. Allen NB, Cox CC, Cobo M et al. Use of immunosuppressive agents in the treatment of severe ocular and vascular manifestations of Cogan's syndrome. *Am J Med*, 1990; 88: 296–301.
9. Riente L, Taglione E, Berrettini S. Efficacy of methotrexate in Cogan's syndrome. *J Rheumatol*, 1996; 23: 1830–1831.
10. Touma Z, Nawwar R, Hadi U, Hourani M, Arayssi T. The use of TNF-alpha blockers in Cogan's syndrome. *Rheumatol Int*, 2007; 27: 995–996.
11. Pasanisi E, Vincenti V, Bacciu A et al. Cochlear implantation and Cogan syndrome. *Otol Neurotol*, 2003; 24: 601–604.