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Case Report

Acute ischemic stroke in a patient with Cogan's syndrome

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Cogan's syndrome is a rare disorder characterized by inflammatory eye and inner ear/vestibular disease. In some cases patients may present medium and large vessel vasculitis which may produce neurological manifestations. We present the case of a patient who was admitted with clinical manifestations of stroke. After intense study, Cogan's syndrome was diagnosed and treated.

Keywords

Stroke; Cogan's syndrome; Vasculitis; Critical care

1. Introduction

Vasculitides are defined by the presence of inflammatory leukocytes in vessel's walls with reactive damage to its structure. The central nervous system (CNS) can be either affected by primary or secondary vasculitis. It is considered secondary when it occurs in the context of a systemic inflammatory disease, such as systemic vasculitis or an infectious process like varicella-zoster virus infection [1]. Patients suffering from systemic vasculitis are at higher risk of developing acute ischemic stroke [2] and vasculitides may be an important etiology in younger patients [3]. Diagnosis and treatment of acute ischemic stroke may be challenging especially when it's not related to thrombosis. A detailed medical history must be made and an interdisciplinary approach is frequently needed.

2. Case report

A 62-year-old female patient, with medical history of left parietal and left frontal ischemic stroke, weight loss, bilateral keratitis punctata superficialis and severe hearing loss (Fig. 1) was suspected of an inflammatory disease, for which a positron emission tomography was obtained (Fig. 2) observing defuse 18F-fluorodeoxyglucose staining of the thoracic aorta standardized uptake value (SUV) 4.2. Treatment with methylprednisolone 40 mg/day and cyclophosphamide 1 gram/month was started, completing just one pulse before she was readmitted.

Serologic screening, including HIV and syphilis, was negative and a complete hemostatic, immunologic and rheumatologic panel was performed (Table 1).

Two months after the symptoms started, she was admitted to the emergency department with an 8-hour plegia of both upper limbs and aphasia. Physical examination revealed blood pressure 140/90 mmHg, heart rate of 60 beats/minute, Glasgow coma scale 12/15, anacusia, unable to follow commands, plegia of both upper limbs with reflexes present and isochoric reactive pupils with preserved nauseous reflex. The rest of the physical examination was unremarkable. Laboratory results showed hematocrit 38%, leukocytes 12,300 cells/mm^3, platelet count 228,000/mm^3, sodium 136 mEq/L, potassium 4.2 mEq/L, creatinine 0.63 mg/dL and lactic acid 2.9 mmol/L.

Magnetic resonance imaging of the brain (Fig. 3) demonstrated an ischemic left fronto-temporal ischemic lesion in the territory of the middle left cerebral artery and a right frontal ischemic lesion together with hypodense right putamen, showing affection of the territory of right anterior and middle cerebral arteries. The magnetic resonance angiography showed no evidence of blood flow from both internal carotid arteries in their petrous and cavernous segments on both sides, neither in the left supraclinoid segment and in the left middle cerebral artery. Carotid parietal enhancement could be observed suggesting vasculitic mechanisms.

Diagnosis of acute ischemic stroke secondary to a large vessel vasculitis in the context of Cogan's syndrome was made. High dose corticosteroids were started. She evolved with neurological deterioration after an episode of generalized tonic-clonic seizures. Orotracheal intubation was performed and the patient was connected to mechanical ventilation. Anticonvulsive therapy with Levetiracetam was started. After this, a physical exam revealed paraplegia with hyperreflexia of both upper and lower limbs. A new cerebral computed tomography was performed discarding new structural complications. Assuming refractoriness to steroid therapy, plasmapheresis was initiated as a rescue therapy. She received a total of three corticosteroid pulses and two plasmapheresis sessions. Despite medical efforts, she had a bad neurological outcome, developing refractory intracranial hypertension. After communication to the patient's family, no further invasive measures were decided and she finally died.

3. Discussion

Cogan's syndrome is a rare disorder characterized by inflammatory eye and inner ear/vestibular disease. Ophthalmologic involvement include interstitial keratitis, uveitis and scleritis while ear and vestibular manifestations include sen-

Table 1. Laboratory results of hemostatic, immunologic and rheumatologic parameters.

		Result	Standard values
Hemostasia	Fibrinogen (mg/dL)	590	200–400
	Factor V (%)	102	70–120
	Factor VII (%)	71	65–120
	Factor VIII (%)	258	50–150
	Hepcidin (ng/mL)	87.9	1.49–41.46
	Protein C (%)	93	65–140
	Protein S (%)	82	60–140
	G20210A Factor II Prothrombin mutation	Not present	–
	Factor V Leiden G1691A mutation	Not present	–
	PAI-1 polymorphism	Normal Homozygous	–
Immunology	Seric IgA (mg/dL)	490	70–400
	IgG Subtypes (1–4)	Normal	–
	Anticardiolipin antibodies IgG (GPL)	9	Negative: <20
	Anticardiolipin antibodies IgG (MPL)	16	Negative: <20
	Electrophoretic proteinogram	Normal	–
Rheumatology	ANA	Negative	–
	Complement C3 (mg/dL)	143	83–177
	Complement C4 (mg/dL)	43	10–40
	Anti DNA Antibodies	Negative	–
	Anti Ro	Negative	–
	Anti La	Negative	–
	Anti Smith	Negative	–
	ANCA	Negative	–
	Anti ribonucleoprotein antibodies	Negative	–
	Lupic anticoagulant	Negative	–
	Beta 2 glycoprotein	1	–
	Beta 2 glycoprotein antibody	2	–

ANCA, Anti-neutrophil cytoplasmic antibody; PAI-1, plasminogen activator inhibitor-1; IgA, immunoglobulin type A; IgG, immunoglobulin type G; ANA, anti-nuclear antibody.

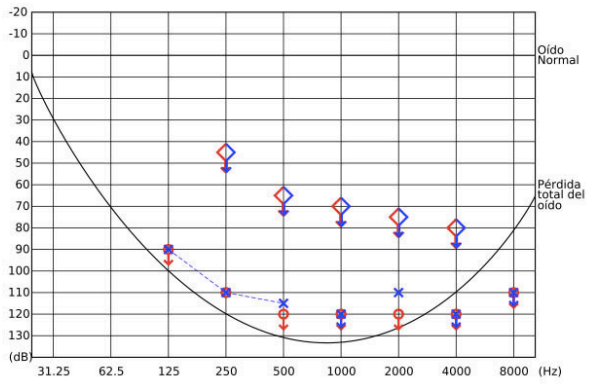

Fig. 1. Audiological test showing hearing loss.

sorineural hearing loss, tinnitus, and meniere-like symptoms. 15% of affected patients may present vasculitis, mostly large vessel disease with some medium-vessel manifestations [4]. The large vessel disease in Cogan's syndrome is similar to that of takayasu's arteritis and includes aortitis, stenosis of the carotid and subclavian and other aortic branch arteries, and even coronary artery disease. Involvement of the aortic branch may cause upper and lower limb claudication [5]. Stoke might be another manifestation of Cogan's syndrome vasculitis. Central nervous system involvement was first described in 1978 from a series of 79 patients with the illness, showing that more than half of the patients presented with neurologic manifestations, among which we could find stroke as one of them [6]. In 1991, Karni *et al.* [7] reported the case of a 32 year old woman with lacunar brain infarcts and in 2001 cerebral angiographic findings were described by Albayram *et al.* [8] revealing areas of severe occlusive disease. Due to the extremely low number of cases of this association between Cohan's syndrome and stroke, experience is limited.

The diagnosis of Cogan's syndrome is challenging and done on the basis of clinical inflammatory findings and after ruling out other medical conditions that might have similar presentations, such as Granulomatous polyangiitis, Panarteritis Nodosa and Behçet disease. Infectious diseases such as Varicella zoster virus and human immunodeficiency virus should also be considered and excluded with serologic testing and cultures.

Upper limb paraparesis might have been secondary to the external bilateral frontal motor cortex involvement following the distribution of the Penfield homunculus [9]. This sign

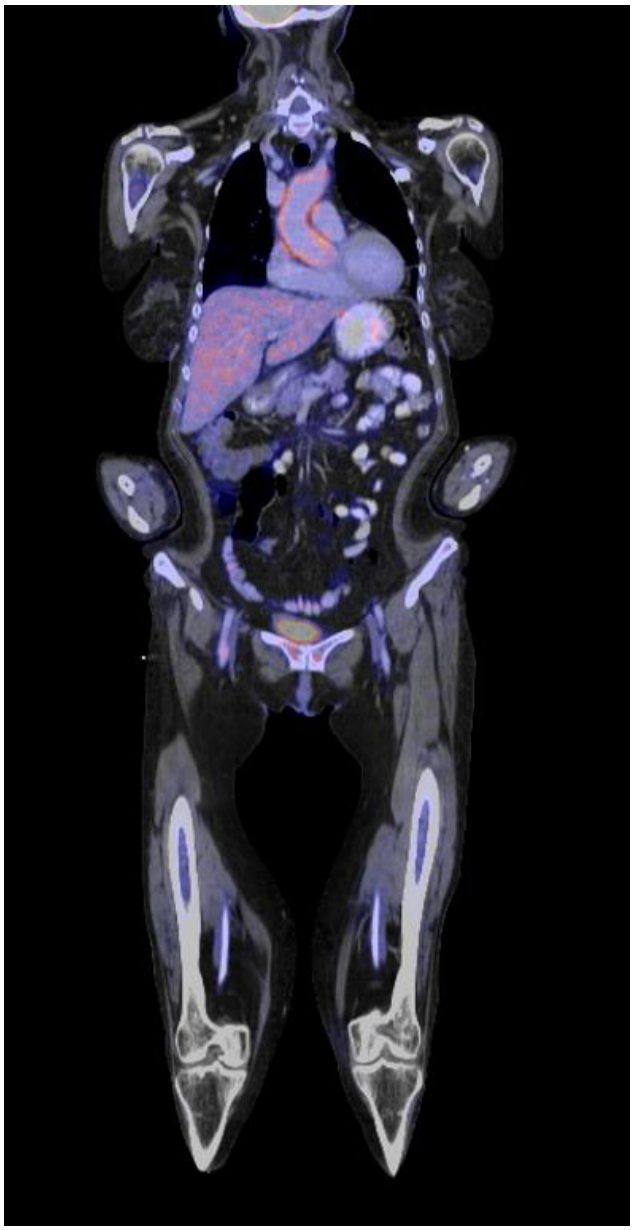

Fig. 2. Positron Emission Tomography (PET-TC) showing a diffuse 18F-fluorodeoxyglucose staining of the thoracic aorta (SUV 4.2). Study performed 2 months before de ischemic stroke.

might have been confused with bilateral upper limb claudication due to aortic branch involvement.

The treatment of Cogan's syndrome includes both glucocorticoids and immunosuppressive drugs such as methotrexate or cyclophosphamide depending on systemic involvement [10]. In some refractory cases, monoclonal antibodies might be an option [11]. Our patient had been treated with a course of corticosteroids and cyclophosphamide after which she had her first stroke.

Although the pathogenesis of Cogan's syndrome is not yet fully understood, there are articles suggesting the presence of autoantibodies, like anti-Hsp70, that could not only be involved in the pathogenesis, but could also serve as a serological marker of the disease [12]. There are reports [10, 13] that propose the combination of available treatment with plasmapheresis as a valid option for the removal of blood elements that could account for a persistent, progressive or critical illness. Therefore, plasmapheresis may be an option to consider in non-responders or under critical conditions.

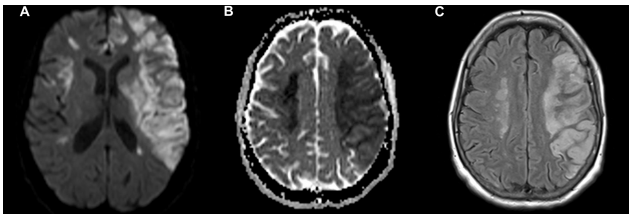

Fig. 3. Brain magnetic resonance imaging (MRI), axial view. (A) hyperintense signal in diffusion weighted sequence showing restriction in diffusion in the territory of both middle cerebral arteries. (B) Apparent diffusion coefficient (ADC) map with hypointense signal showing diffusion restriction in the territory of both middle cerebral arteries. (C) Flair sequence with hyperintensity in the territory of both middle cerebral arteries.

To our knowledge, this is the first critical patient with central nervous system involvement treated with plasmapheresis. Unfortunately, we didn't have a favorable outcome. Further investigation is still needed to better understand the role of different treatments, the timing of therapy initiation and the behavior of this complex and potentially lethal condition.

Author contributions

All authors have equally contributed to this work. SG was mainly involved in the conceptual framing and supervision. NAG and NCR were responsible for the manuscript production, translation and conceptual framing.

Ethics approval and consent to participate

Informed consent was obtained from the patient included in the study. Ethics approval is not applicable.

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Conflict of interest

The authors declare no conflict of interest.

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