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Ross' Syndrome: A Case Report

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Abstract

Introduction: Ross syndrome is characterized by the triad of diffuse anhidrosis, myotatic hyporeflexia, and tonic pupil of Adie, with compensatory hyperhidrosis. The evolution of the disease is benign and chronic, its etiology is not well defined, and the pathophysiology involves denervation of autonomic fibers. Approximately 60 cases have been reported worldwide. Therefore, we believe it is relevant to share this case with the medical community, given its characteristics.

Clinical Case: A 39-year-old female started two years ago with profuse diaphoresis, erythema on the left hemibody of insidious onset, progressive, accompanied by contralateral hypohidrosis. On neurological examination with mydriatic right pupil, photo motor and consensual reflex absent; however, accommodation reflex was preserved. On motor examination with preserved strength and global myotatic reflexes abolished. A diagnostic protocol is performed to rule out primary differential diagnoses, which, when excluded, is concluded with Ross' syndrome diagnosis. In addition, a complete laboratory workup was done to rule out systemic problems, nerve conduction studies for radicular-neuropathies, immunological to rule out lupus and other autoimmune diseases, and imaging studies both CT and MRI.

Conclusions: Ross' syndrome thoroughly presents in most patients with the characteristic triad; it is usually progressive and associated with autonomic symptoms. Its importance lies in evaluating and ruling out possible differential diagnoses and the timely treatment of the symptomatology that becomes disabling and has a social impact on the patient.

Keywords: Adie tonic pupil, anhidrosis, Ross' syndrome,

Introduction:

Ross syndrome was described in 1958 by Alexander Ross as a degenerative disease of the autonomic nervous system characterized by the triad of diffuse anhidrosis, myotatic hyporeflexia, and tonic pupil of Adie accompanied by compensatory hyperhidrosis and heat intolerance. The development of the disease is chronic and benign, its etiology is not well defined, and the pathophysiology involves denervation of autonomic fibers. Its prevalence approaches 60 reported cases worldwide. The following is a case of a patient diagnosed with Ross' syndrome and a subsequent literature review. Given the rarity of the case, we set out to

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understand the problem and differentiate it from other syndromes with similar characteristics and what were the key points to differentiate it from them.

Clinical Presentation:

A 39-year-old female was referred to neurology for a disorder that began two years ago with profuse diaphoresis in the left half face and hemithorax at the level of the T2 dermatome, with insidious and progressive onset, exacerbated by physical exertion, accompanied by contralateral hypohidrosis and ipsilateral erythema. There is no heredofamilial or chronic degenerative history of importance. On neurological examination with preserved cognitive functions, anisocoria with a mydriatic left pupil with absent photo motor and consensual reflex (Figure 1), but preserved accommodation reflex, the rest cranial nerves examination without evident alterations. On motor system examination with preserved mass and strength, global myotatic reflexes were abolished, sensory analysis with no apparent alterations.

General laboratory tests were performed, such as blood biometry, blood glucose, renal and liver function tests, thyroid and lipid profile, coagulation time, acute phase reactants, as well as antibodies against human immunodeficiency virus and viral hepatitis, VDRL, complement determination, and antinuclear antibodies, all of which were normal. In addition, Neuroconduction studies were performed with average results. A simple cranial tomography and magnetic resonance of the skull and spine were also performed, in which no alterations were evidenced.

Ross Syndrome is associated with a clinical picture with the classic triad and the exclusion of differential diagnoses.

Treatment was based on hygienic-environmental recommendations and beta-blocker, with follow-up in Neurology outpatient clinic. Since a differential diagnostic approach had been made to rule out the systemic, peripheral nervous system, and autoimmune diseases that could give us similar manifestations and require specific management.

Discussion

Ross' syndrome is a rare autonomic disorder that is diagnosed with the characteristic clinical findings of segmental anhidrosis, hyporeflexia, and tonic pupil of Adie.[1]

The tonic pupil is characterized by little or no response to light reflex with preserved accommodative reflex, with cholinergic hypersensitivity manifested by the 0.125% pilocarpine test, with increased miosis observed in the affected pupil following application.[2]

It occurs in any age group and is mainly diagnosed in the third decade of life, with no gender predominance and ethnic predisposition.[3]

Its etiology is not defined. Loung et al. described cases of Ross syndrome that were associated with positivity for SSA antibody and BSS in a patient with Sjogren's syndrome. Besides, Vasudevan et al. reported the syndrome in the presence of positive antinuclear antibodies.[4]

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Nolano et al. have described a case of monozygotic twins with Ross syndrome, giving rise to the suspicion of a possible genetic basis.[5]

Regarding clinical features, in addition to the characteristic triad, incomplete Ross syndrome in which there is the absence of Adie's pupil and hypo, or areflexia has been published.[4]

Other changes in the autonomic nervous system, such as orthostatic hypotension, tachycardia, intestinal alterations, bladder and sexual dysfunction, esophageal reflux, and even psychiatric disorders, may occur.[5] Cases of chronic cough related to the syndrome have been reported in probable relation to damage to the efferent and afferent fibers of the vagus nerve.[6] There are also dermatological alterations such as skin discoloration changes in half of the face and trunk affected.[1]

As for the pathophysiology of the alterations, they are based on modifications of the nerve fibers belonging to the autonomic nervous system; in the case of Adie's pupil, there is damage to cholinergic postganglionic fibers between the ciliary ganglion and the muscular sphincter of the iris, which can be unilateral and progress to bilateral.[1]

Hyporeflexia is explained by degeneration of dorsal root fibers and loss of medullary interneurons,[8] with the most affected reflexes being the patellar, Achilles, brachioradialis, tricipital, bicipital, and supinator reflexes.[3]

Hypohidrosis results from damage to postganglionic sympathetic fibers innervating the sweat glands, which eventually leads to anhidrosis. Whereas compensatory hyperhidrosis is secondary to early loss of presynaptic cholinergic inhibitors.[1]

Also, Nolano et al. described an absence of cholinergic (vasoactive intestinal peptide) and adrenergic (dopamine beta-hydroxylase) markers in sweat gland fibers in anhidrotic areas that may be related to the pathophysiology.[9] and hyperhidrosis is due to loss of presynaptic inhibitory cholinergic-type (M2) autoreceptors that may precede anhidrosis.[10]

The loss of sudomotor and vasomotor fibers that affect sweating and blood flow regulation, in addition to the loss of thermoreceptors, produce alterations in temperature control.[4]
The course of the condition is chronic with possible expansion of the affected area. Natural history is often slowly progressive, lasting up to 50 years.[7] The average time to diagnosis varies, with the average being six years, in most cases in the third stage.[4]

The iodine solution test with rice starch powder is performed, where the color changes from white to black are observed in the presence of sweat, and the skin biopsy has shown a lack of postganglionic sympathetic fibers and sudomotor cholinergic fibers.[11]

Differential diagnoses to consider in Adie's pupil are diabetes, systemic diseases such as sarcoidosis, infections, syphilis, and Guillain-Barre. We must rule out diabetes and systemic diseases and less common diseases such as congenital insensitivity to pain with anhidrosis for

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sweating disorders.[1] In addition, the tonic pupil may occur in infections (herpes zoster) or orbital surgery.[12]

Holmes-Adie syndrome is characterized by tonic pupils, accommodation palsy, and hyporeflexia, differentiated from Ross syndrome by alterations in sweating.[13] Another similar disorder is Harlequin syndrome which is composed of segmental hypohidrosis without pupillary abnormalities.[11] and Horner syndrome presents with anhidrosis, ptosis, miosis, and enophthalmos.[6]

Treatment is based on nonpharmacologic measures in terms of appropriate clothing and exercise recommendations. Anticholinergic and anxiolytic drugs such as beta-blockers, tricyclic antidepressants, and selective serotonin reuptake inhibitors are used but are necessary to monitor adverse effects. Glycopyrrolate cream is also recommended, which acts with anticholinergic effects by reducing heat production.[1]

The botulinum toxin type A and iontophoresis are other options, which have partial and transitory improvement. The former has a lasting effect of 2 to 6 months, and iontophoresis requires a weekly application. Thoracic sympathectomy is the definitive treatment, which has been shown to have excellent results.[14]

Conclusions

We present a rare condition called Ross syndrome.
It is characterized by a combination of segmental anhidrosis, tonic pupil, and myotatic areflexia.
Its presentation is due to ganglion cell loss and its cholinergic postganglionic modulatory action.
It may be associated with other dysautonomic manifestations.
Although it shares characteristics, it must be differentiated from Adie-Holmes syndrome, Harlequin syndrome, and Horner syndrome.
Treatment can be with botulinum toxin or thoracic sympathectomy, although it is considered to have a benign course.

Conflicts of interest: There are no conflicts of interest.

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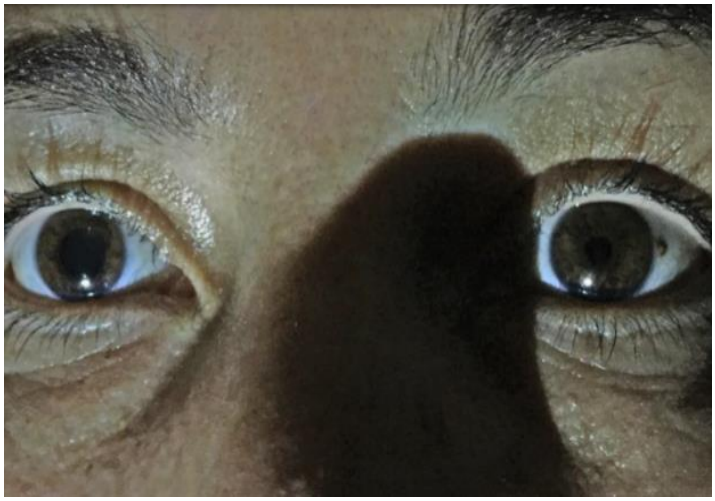

Figure 1. This photograph shows the pupil of Adie in the patient's right eye.