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Cyclic vomiting syndrome plus accompanying Ross syndrome: More than a peripheral autonomic dysfunction

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Abstract

Ross syndrome is a rare syndrome consisting of areflexia, tonic pupil and segmental anhidrosis. It has been shown to accompany neuropsychiatric diseases such as psychiatric disorders, headache, and epilepsy. We report here a 19-year-old female who was the first case in which cyclic vomiting syndrome plus was shown to accompany Ross syndrome.

Keywords: Ross syndrome, Adie's tonic pupil, cyclic vomiting syndrome plus, hypohidrosis, areflexia

INTRODUCTION

Ross syndrome was first described as partial autonomic dysfunction in 1958.[1] Its classical triad consists of hyporeflexia or areflexia, tonic pupil, and segmental anhidrosis with or without compensatory hyperhidrosis.[2]

Cyclic vomiting syndrome is an idiopathic syndrome with a prognosis of severe episodes of nausea, vomiting and lethargy where the patients recover their health completely between the attacks.[3] Due to being commonly accompanied by headaches, having prodromes, and photophobia, cyclical vomiting has been suggested to be associated with migraine, and even interpreted as a form of abdominal migraine in children.[4]

CASE REPORT

A 19-year-old female patient was referred to our Neurology clinic following a bilateral motor seizure accompanied by impaired consciousness. She has been treated as an inpatient in the Psychiatry ward for intermittent attacks of nausea, vomiting, and loss of appetite since the age of 14; depression and anxiety from at the age of 15 years. The nausea-vomiting attacks, which recurred every 2-3 months since the age of 7, has become more frequent from the age of 14. She noticed that it was triggered by stress. She experienced nausea-vomiting for about 15 days in a month before the hospitalization. She has past history of an episode of generalized convulsive status epilepticus at the age of 9 followed by the use of antiepileptic drugs for a year; migraine, sensory polyneuropathy syndrome, scoliosis, gastroesophageal reflux, and bronchial asthma. She mentioned that she had noticed her lack of pupillary light reflex but had not felt the need to see a doctor about it. There was no history of similar illness in her family.

In the neurological examination, the patient was conscious, cooperative and well-oriented. The pupils were located medially to the irises and there was no direct or indirect pupillary light reflex. Other cranial nerve examinations were normal. While the patient had no motor weakness, she had bilateral hypoesthesia with glove-and-stocking distribution. Her joint position sense and vibration sense were also impaired. Deep tendon reflexes (DTRs) could not be elicited except for triceps. The patient had bilateral non-responsive plantar reflex, normal cerebellar coordination examination and a positive Romberg test. There was no skin lesions on sun-exposed areas.

No abnormality was found in the routine hemogram and biochemical tests and there were no abnormality to indicate an active infections. VDRL (Venereal Disease Research

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Laboratory) and TPHA (Treponema pallidum hemagglutination) were negative. The patient's cranial imaging, and the electroencephalography (EEG) recorded three times during wakefulness were normal. The electrocardiography (ECG) revealed an incomplete right bundle branch block. Echocardiography was normal.

As for the tests for autoimmune diseases, anti-nuclear antibody (ANA), anti-Jo, anti- Scl 70, anti-Sm, anti-SSA, and anti-SSB were negative, and rheumatoid factor (RF) was within the normal range. Lactate was not detected in the arterial blood gas and there was no color change in urine.

In the eye examination using pupillometry, the right pupil was 5.52 mm while the left pupil was 5.90 mm. After the administration of 0.1% dilute pilocarpine, the right pupil constricted to 3.36 mm and the left one to 3.01 mm, and the patient was diagnosed with Adie's tonic pupil (Figure 1, 2).

The sympathetic skin response could not be elicited in the palmar or plantar regions. Although the patient had no symptoms, hypohidrosis in the medial side of the left thigh and in the left lower leg were elicited by the iodine-starch test (Figure 3).

Based on the findings of Adie's tonic pupil, areflexia and hypohidrosis, the patient was diagnosed as having Ross syndrome.

DISCUSSION

Ross syndrome is a rare disease first described in 1958 by Ross consisting of a triad of areflexia, tonic pupil, and segmental anhidrosis; the first two of which define Holmes-Adie syndrome while the last defines the Harlequin syndrome.[2,5] Although there is no clear distinction between these three syndromes, they have been suggested to be different presentations of the same pathology.[6] Skin biopsies in this syndrome with the peripheral autonomic dysfunction indicated selective loss in sudomotor, vasomotor and pilomotor fibers. Additional criteria have been suggested, such as heat intolerance, absence of sympathetic skin response, and the absence of vasoactive intestinal peptide-immunoreactive nerve fibers in the skin.[5,7] While the underlying cause of this syndrome has yet to be fully understood, pathological α-synuclein deposits have been detected in the autonomic nerve terminals and it has been suggested that Ross syndrome may be an α-synucleinopathy.[8]

Approximately 60 Ross syndrome cases aged from 3 to 60 years have so far been reported in the medical literature. A review study of 11 patients showed that only 45% of the patients met the triad criteria and those presented with the triad were diagnosed in average of 8.3 years after symptom onset. The most common clinical symptoms reported in the study were hyperhidrosis, hypohidrosis, and heat intolerance, respectively.[9] Our patient initially had sensory complaints, and the hypohidrosis was elicited in her visit to our center.

The presence of headaches, psychiatric disorders and abnormal heart rate response has been shown in patients with Ross syndrome. In 1975, it was shown in 2 patients that Holmes-Adie and Ross syndromes may be accompanied by psychiatric disorders, as was the case in our

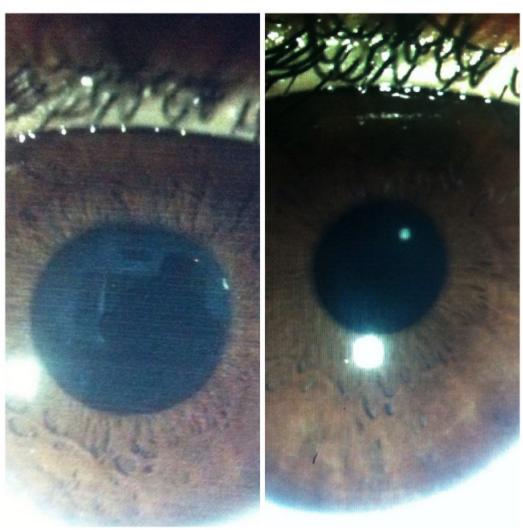

Figure 1. Before and after the administration of 0.1% dilute pilocarpine of right pupil

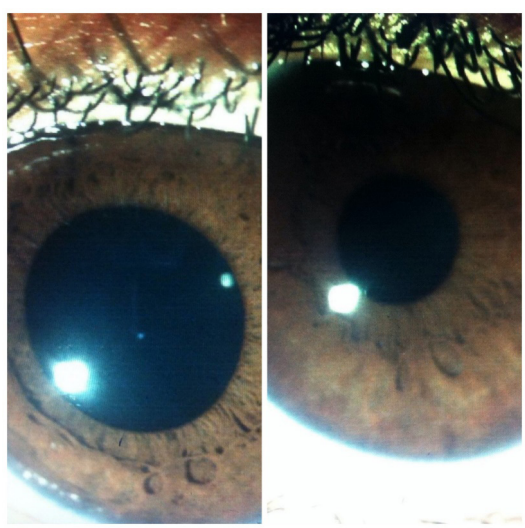

Figure 2. Before and after the administration of 0.1% dilute pilocarpine of left pupil

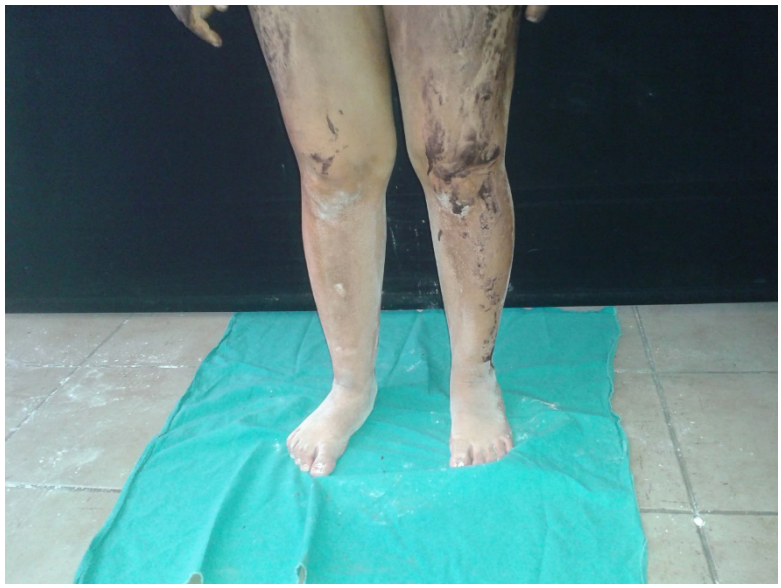

Figure 3. Hypohidrosis in the medial side of the left thigh and in the left lower leg

patient. Also, previous investigators tried to explain the coexistence of the peripheral and central nervous system dysfunctions in the same patients with the fact that acetylcholine was an important neurotransmitter for the peripheral nervous system as it was for the brain.[10] It was reported that the autonomic dysfunctions detected in Adie syndrome could be associated with the damage to the autonomic and dorsal root ganglions, and eventually a 1968 autopsy study aiming to reveal the pathophysiology of this syndrome showed the presence of degeneration in the dorsal root ganglions.[11]

"Cyclic vomiting syndrome" is considered as a migraine variant and it shares some common features with the migraine headache, such as auras, photophobia and response to antimigraine treatment.[3] Genetic studies investigated mitochondrial DNA polymorphism and showed that the polymorphisms 16519T and 3010GA were associated with migraine and cyclic vomiting syndrome.[12] Another study with the pediatric population showed that the cyclic vomiting syndrome concurred with the sympathetic autonomic dysfunction where vasomotor and sudomotor systems are affected in particular.[3] Approximately 25% of the cyclic vomiting syndrome cases were found to have additional neurological disease symptoms and they were diagnosed with "cyclic vomiting syndrome plus". Neurological disease symptoms, such as cognitive disorders, myopathy, cranial nerve involvement and seizure disorders, were found to cluster together among the same patients. Furthermore, patients with cyclic vomiting syndrome with these additional findings had an earlier age of onset for vomiting attacks and a three- to eightfold increased prevalence for dysautonomia-related disorders, such as migraine, neurovascular dystrophy, chronic fatigue, and for constitutional disorders, such as growth retardation and birth defects.[13]

In conclusion, we report here a patient of Ross syndrome plus with epilepsy, migraine, sensory and autonomic neuropathies, and other neuropsychiatric disorders such as anxiety disorder, as well as cyclic vomiting syndrome. This may be the first case report of the association of cyclical vomiting syndrome plus with Ross syndrome.

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DISCLOSURE

Consent: Writing consent was obtained from the patient for this publication.

Conflict of interest: None.

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