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Case Series

Ross syndrome: a case series of five patients

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ABSTRACT

Ross syndrome, a rare neurological disorder, is characterized by the combination of three primary features: segmental anhidrosis, tonic pupils, and areflexia. The exact aetiology remains unclear, but it involves dysfunction in the autonomic nervous system, specifically affecting the sympathetic pathways. Patients often experience reduced sweating, particularly in specific body regions, alongside pupillary abnormalities and diminished reflex responses. Due to its rarity, further research is needed to understand its pathophysiology, optimize treatment strategies, and improve patient outcomes. In our case series of five patients, a diagnosis of 'complete' Ross syndrome was made for two patients, while the remaining patients were diagnosed with 'incomplete' Ross syndrome. The rarity of Ross syndrome underscores the importance of detailed clinical reporting, as it may lead to improved patient care and outcomes.

Keywords: Ross syndrome, Anhidrosis, Tonic pupil, Autonomic nervous system, Reflexes

INTRODUCTION

Ross syndrome, initially described by Ross in 1958, is a rare peripheral autonomic nervous system disorder.[1] The condition is marked by three main features: segmental hypohidrosis or anhidrosis, areflexia, and Holmes-Adie's tonic pupil. Harlequin syndrome represents the first two component of this triad, while Holmes-Adie syndrome includes the latter two features, posing challenges in differentiation from Ross syndrome due to their shared pathogenesis.[2] Etiological factors include autoimmunity, viral infections, genetic factors, autonomic denervation, and nuclear synuclein deposition. The exact cause of selective cholinergic denervation remains under research. Approximately 60 cases worldwide exhibit the classical triad of symptoms and signs.[3] Here, we report five cases with clinical and histological features of Ross syndrome.

CASE SERIES

Case 1

A middle-aged female homemaker presented with an absence of sweating on the left side of the body with increased heat tolerance and left-sided headache for 1 year. She also had increased sweating over the right side. Past- history revealed multiple episodes of seizures in 2017. There was no history of palpitations, orthostatic

hypotension, syncope, urinary or bowel complaints or trauma to the spine. Clinical examination revealed anhidrosis on the left side with hyperhidrosis on the right side predominantly involving C3-7 and T6-10 dermatomes. Starch iodine test reflected the clinical findings (Figure 1 A-C).

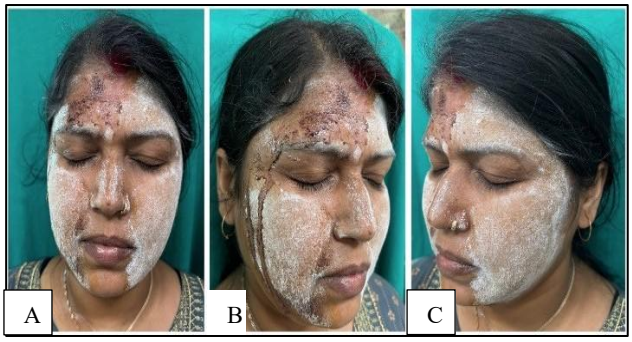

Figure 1: Starch iodine test: (A) anhidrosis on the left side of body with hyperhidrosis on the right side predominantly involving c3-7 and t6-10 dermatomes, (B) hyperhidrosis on the right side of face and (C) anhidrosis on the left side of face.

Deep tendon reflexes were absent. Ophthalmological examination revealed mid-dilated left pupil with the absent pupillary light reaction but reacting better to accommodation was noted suggesting a tonic pupil with light-near dissociation.

Case 2

A middle-aged male construction worker presented with an absence of sweating on the right side of the body with increased heat tolerance for 10 years. He also had increased sweating over the left side (Figure 2 A and B).

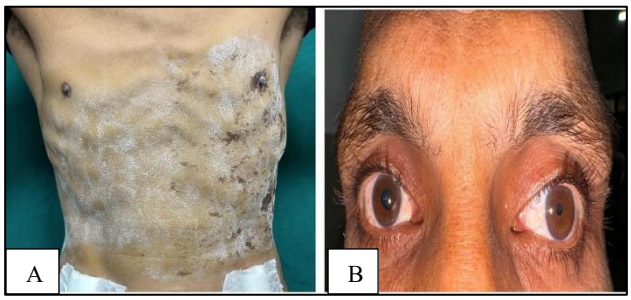

Figure 2: Starch iodine test: (A) Anhidrosis on the right side of the body with hyperhidrosis on the left side predominantly over t3-9 dermatomes; ophthalmological examination and (B) Atonic pupil in the right with normal size and normal reaction in the left eye.

Case 3

A middle-aged female homemaker presented with an absence of sweating on the left side of the body with increased heat tolerance and increased sweating over the right side for six years (Figure 3 A-D). There was history of palpitations, tingling and numbness, easy fatiguability, epigastric pain and discomfort. The patient had been on beta-blockers for the past three years.

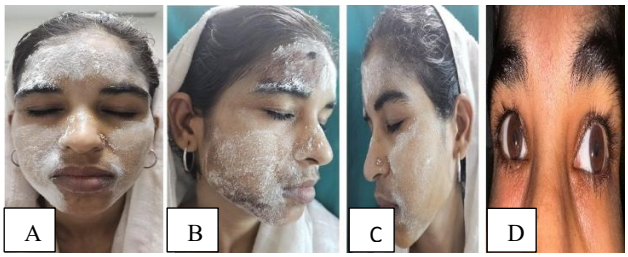

Figure 3: Starch iodine test: (A) anhidrosis on the left side of the body with hyperhidrosis on the right side predominantly involving the c2-7 and t3-9 dermatomes, (B) hyperhidrosis on the right side of face, (C) anhidrosis on the left side of face, ophthalmological examination and (D) tonic pupillary near response with light-near dissociation in the left eye with normal reaction in the right eye.

Case 4

A middle-aged female homemaker presented with an absence of sweating on the right side of the body with increased heat tolerance and increased sweating over the left side for two years (Figure 4 A-C).

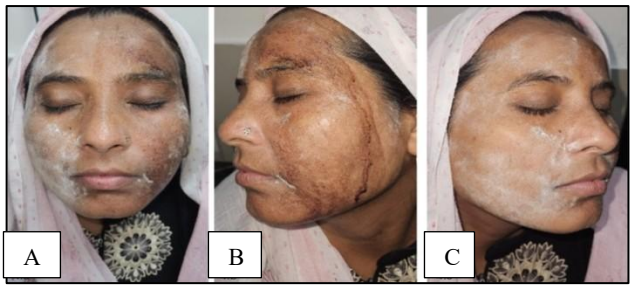

Figure 4: Starch iodine test: (A) anhidrosis on the right side of body with hyperhidrosis on the left side predominantly involving c2-7 dermatomes, (B) hyperhidrosis on the left side of face and (C) anhidrosis on the right side of face.

Case 5

A young male student presented with an absence of sweating on the right side of the body with increased heat tolerance for three years. He also had increased sweating over the left side (Figure 5A and B).

In all five patients, there was no history of spine trauma, family history was insignificant, blood pressure was normal in both supine and standing positions, sensory examination was normal, and peripheral nerves were not thickened.

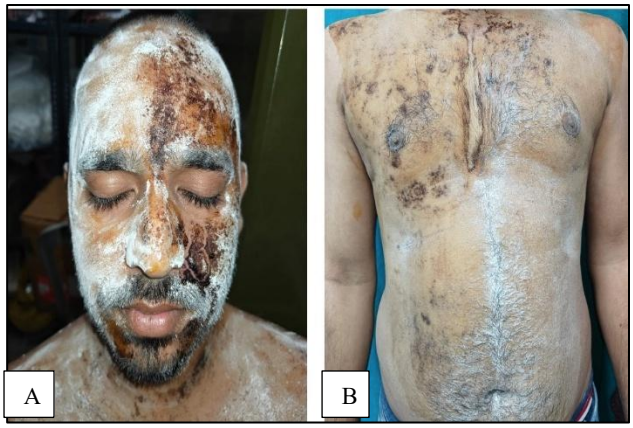

Figure 5: Starch iodine test: (A) anhidrosis on the right side with hyperhidrosis on the left side of face predominantly involving c3-7 dermatomes and (B) anhidrosis on the left side with hyperhidrosis on the right side of body predominantly t5-t10 dermatomes.

Histopathology was done in all the patients which has been mentioned in Figure 6, 7 and Table 1.

Based on the findings mentioned above and in Table 1, Ross syndrome was diagnosed in all five patients. They were advised to avoid heat exposure and to wear damp clothing during household chores or other physical activities to prevent episodic hyperthermia.

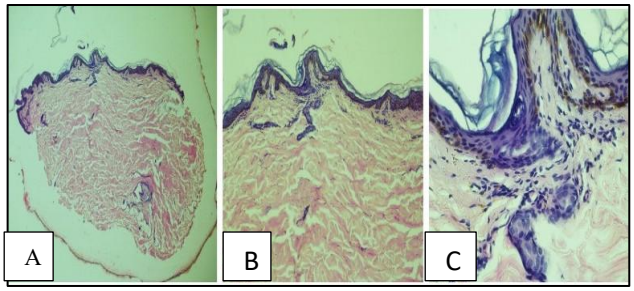

Figure 6: (A) (40x): H and E section shows thinned out keratinised stratified squamous epithelium with reduced number of sweat ducts, (B) (100x): high power showing similar findings, (C) (400x): 1-2 sweat ducts can be appreciated.

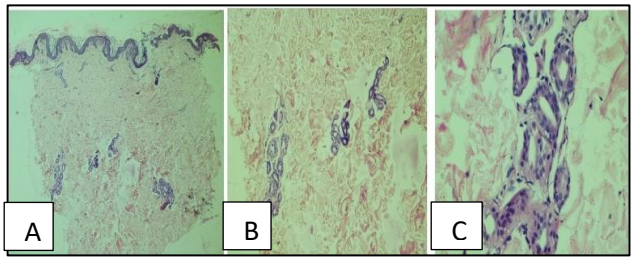

Figure 7: (A) (40x): H and E section shows keratinised stratified squamous epithelium with multiple sweat ducts and glands in fibrocollagenous stroma, (B) (100x): multiple sweat glands in clusters can be appreciated, (C) (400x): further high power with similar findings.

Table 1: Clinical examination and investigations of all five patients.

Investigations	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Cutaneous examination	Anhidrosis on the left side with hyperhidrosis on the right side predominantly involving c3-7 and t6-10 dermatomes. Starch iodine test reflected the clinical findings (Figure 1 A-C).	Anhidrosis on the right side of the body with hyperhidrosis on the left side predominantly over t3-9 dermatomes. Starch iodine test reflected the clinical findings (Figure 2A)	Anhidrosis on the left side of the body with hyperhidrosis on the right side predominantly involving the c2-7 and t3-9 dermatomes. Starch iodine test reflected the clinical findings (Figure 3A-C).	Anhidrosis on the right side with hyperhidrosis on the left side predominantly involving c2-7 dermatomes. Starch iodine test reflected the clinical findings (Figure 4 A-C).	Anhidrosis on the right side with hyperhidrosis on the left side of face predominantly involving c3-7 dermatomes (Figure 5A) and anhidrosis on the left side with hyperhidrosis on the right side of body predominantly t5-t10 dermatomes. Starch iodine test reflected the clinical findings (Figure 5B).
Deep tendon reflexes	Absent	Absent	Present	Absent	Present

Continued.

Investigations	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Ophthalmological examination	Mid-dilated left pupil with the absent pupillary light reaction but reacting better to accommodation was noted suggesting a tonic pupil with light-near dissociation.	Atonic pupil in the right with normal size and normal reaction in the left eye (figure 2B).	Tonic pupillary near response with light-near dissociation in the left eye with normal reaction in the right eye (figure 3D).	Normal	Normal
Complete hemogram	Normal	Normal	Normal	Normal	Normal
Liver function tests	Normal	Normal	Normal	Normal	Normal
Renal function tests	Normal	Normal	Normal	Normal	Normal
Thyroid function tests	Normal	Normal	Normal	Normal	Normal
ANA	Negative	Negative	Negative	Negative	Negative
VDRL	Non-reactive	Non-reactive	Non-reactive	Non-reactive	Non-reactive
X-ray spine	Normal	Normal	Normal	Normal	Normal
Nerve conduction velocity	Normal	Normal	Normal	Normal	Normal
EEG	Cerebral dysrhythmia	Normal	Normal	Normal	Normal
MRI brain	Granulomatous lesion with surrounding oedema in the left frontal lobe, possibly indicative of neurocysticercosis	Normal	Normal	Normal	Normal
CT brain	Ring-enhancing lesion in the left frontal region, also suggestive of neurocysticercosis	Normal	Normal	Normal	Normal
Skin biopsy	Anhidrotic site: Thinned out stratified squamous lining. Sparse to absent eccrine sweat glands in dermis. Hyperhidrotic site: Keratinized stratified squamous lining with increased number and size of sweat glands.	Anhidrotic site: Thinned out stratified squamous lining. Underlying dermis showing a single sweat duct only. Hyperhidrotic site: Keratinized stratified squamous lining with multiple sweat ducts in a fibrocollagenous stroma.	Anhidrotic site: Keratinised stratified squamous epithelium with few eccrine coils in the dermis. Hyperhidrotic site: Keratinized stratified squamous epithelium with the focal areas in deep dermis showing increased density of eccrine coil with surrounding fatty tissue.	Anhidrotic site: Thinned out stratified squamous lining. Sparse to absent eccrine sweat glands in dermis. Hyperhidrotic site: Keratinized stratified squamous lining with increased number and size of sweat glands.	Anhidrotic site: Keratinised stratified squamous epithelium with few eccrine coils in the dermis. Hyperhidrotic site: Keratinized stratified squamous epithelium with the focal areas in deep dermis showing increased density of eccrine coil with surrounding fatty tissue.

DISCUSSION

Ross syndrome is a rare disorder of the peripheral autonomic system, characterized by segmental hypohidrosis/anhidrosis, areflexia, and Holmes-Adie's tonic pupil. In our case series of five patients, two had the complete triad, while three had incomplete forms with varying combinations of symptoms.

The condition results from primary impairment of postganglionic sudomotor and pupillary fibers, affecting both genders and typically presenting between ages 3 and 50. The tonic pupil and decreased sweating are linked to dysfunction of cholinergic fibres innervating the iris and sweat glands.[4] Extensive anhidrosis can trigger compensatory hyperhidrosis, which may be severe and require treatment. This could be due to compensatory mechanisms or early loss of presynaptic M2 cholinergic receptors.[5]

Differential diagnoses include Shy-Drager disease, multiple sclerosis, diabetes, leprosy, and polyneuropathies.[6] Hyporeflexia arises from involvement of neurons in the dorsal root ganglia and spinal interneurons and may be accompanied by other autonomic dysfunctions, including orthostatic hypotension and cardiac dysautonomia.[7,8]

No specific treatment exists for Ross syndrome, and management focuses on symptom control. Hyperhidrosis can be treated with botulinum toxin, iontophoresis, or anticholinergics, while hypohidrosis is managed by avoiding hot environments and damp clothing.[9,10]

CONCLUSION

Ross syndrome is a rare disorder of peripheral nervous system characterized by segmental hypohidrosis/ anhidrosis, areflexia, and Holmes-Adie's tonic pupil. In our case series of five patients, a diagnosis of 'complete' Ross syndrome was made for two patients, while the remaining patients were diagnosed with 'incomplete' Ross syndrome. Although Ross syndrome is benign, it can significantly impact social interactions, making proper patient counselling essential. The discovery of five cases from a single centre suggests that Ross syndrome may be more common than previously reported in the literature.

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