Complete heart block in Ross syndrome

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Introduction

Ross syndrome, initially described in 1958, is a rare, poorly understood syndrome traditionally characterized by a triad of hyporeflexia, tonic pupil, and segmental anhidrosis.[1,2] At the time of publication there have been fewer than 100 reported cases of Ross syndrome worldwide. While its pathophysiology remains unclear, it is hypothesized to be due to degeneration of the autonomic nervous system, resulting in both hypoactive and hyperactive responses. Ross syndrome is a clinical diagnosis; however, a thermoregulatory sweat test, an iodine starch test, and a skin biopsy can all be used to support the diagnosis. Thought to be a benign disease, Ross syndrome has adverse effects, including non-life-threatening hyperthermia and visual impairment. No autonomic cardiovascular dysfunction has been described in the literature. We present the first published case of complete heart block in the setting of Ross syndrome.

KEY TEACHING POINTS

- Ross syndrome is a rare disease thought to alter the autonomic nervous system, resulting in areas of increased parasympathetic activity. It traditionally presents with a triad of hyporeflexia, tonic pupil, and segmental anhidrosis. Effects on cardiac innervation have yet to be identified.
- Our case presents the first documented case of third-degree heart block in the setting of Ross syndrome.
- Although Ross syndrome remains exceedingly rare, cardiology should be included in a multimodality team if symptoms of weakness, presyncope, or syncope arise.

Case report

A 61-year-old female patient presented to the emergency department for an episode of bright red blood per rectum, severe abdominal pain, nausea, vomiting, and episodes of syncope at home. She has had a prior history of Ross syndrome (phenotypical tonic right pupil, segmental anhidrosis, and hyporeflexia) diagnosed 20 years prior by 2 independent neuro-ophthalmologists. In addition, she had several unexplained episodes of presyncope and syncope, and an unexplained ischemic colitis.

She reported experiencing several presyncopal and syncopal events in 2017, accompanied by nausea. Following each episode she had noticeable bright red blood in her stool. She underwent abdominal computed tomography angiography and colonoscopy, resulting in biopsy-proven ischemic colitis without evidence of any significant major vessel obstruction by angiographic evaluation. She was seen by cardiology and placed on a 30-day event monitor without evidence of tachyarrhythmia or bradyarrhythmia. However, she did not have any syncopal events during the recording time. Following those events, she was lost to follow-up until 2022.

In 2022, upon arrival to the emergency department, she was hypertensive with blood pressure of 187/94, pulse of 80 beats per minute, and respiratory rate of 18 breaths per minute with 100% saturation on room air. Twelve-lead electrocardiogram showed normal sinus rhythm with no conduction abnormalities. She received a dose of 10 mg intravenous (IV) labetalol and was admitted to a telemetry floor for further evaluation.

Over the next 24 hours, while on telemetry, she was noted to have 4 discrete episodes of 7–13 seconds of third-degree heart block accompanied by syncope (Figure 1). Laboratory values were unremarkable at the time. Beyond the 1 dose of 10 mg IV labetalol in the emergency department, she otherwise was on no home or hospital atrioventricular (AV) nodal blockade. She was emergently taken for a temporary transvenous pacer, and a dual-chamber pacemaker was placed the following day.

Discussion

Ross syndrome is a rare, benign, autonomic degenerative disease affecting both parasympathetic and sympathetic physiological response with varied phenotypical variation.[1–3] Pathology remains unclear but is attributed to mixed

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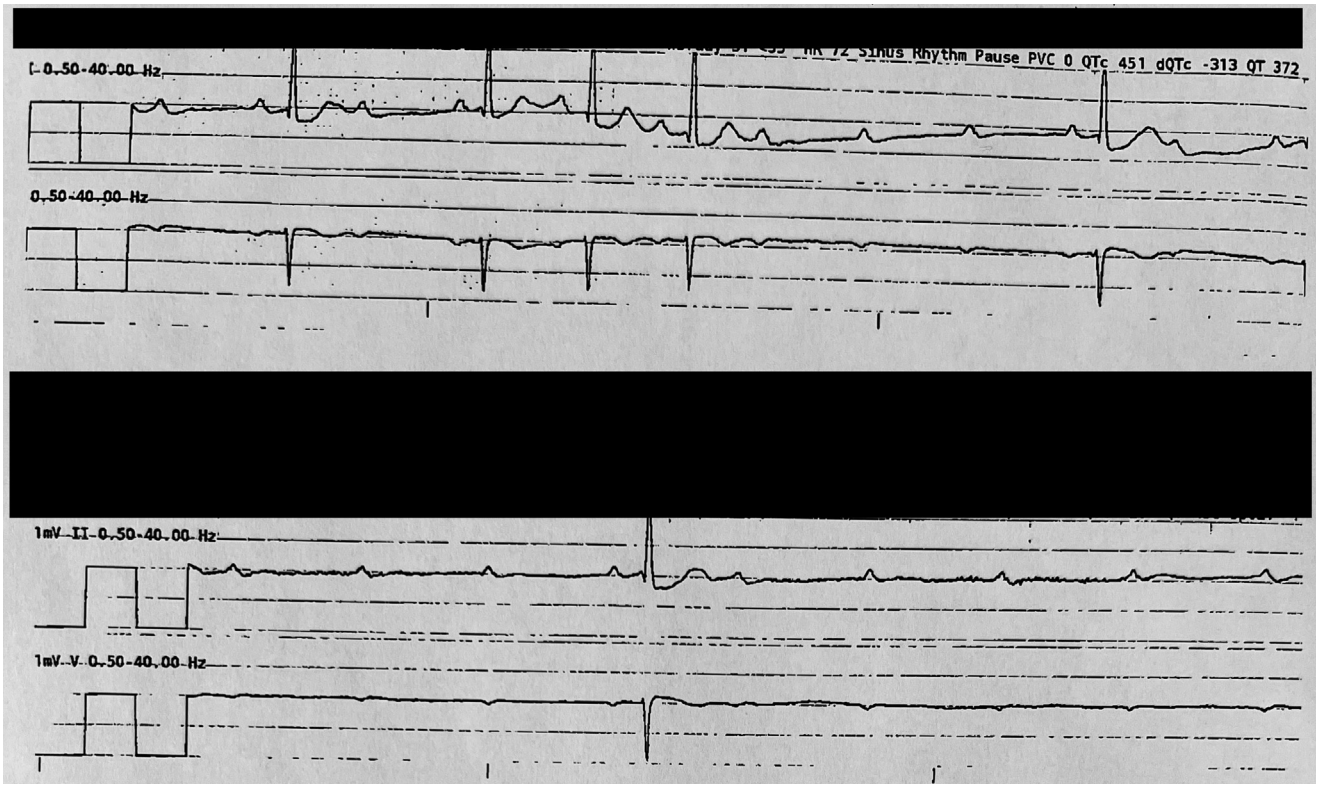

Figure 1 Episode of third-degree heart block with occasional conducting p wave.

denervation of cholinergic and adrenergic nerve fibers, resulting in areas of enhanced sympathetic and parasympathetic responses. Limited data suggest denervation differences among organs, with skin biopsies predominantly showing selective loss of cholinergic fibers, while gastrointestinal and bladder biopsies show downregulation of adrenergic fibers.[3]

The heart is a richly innervated organ with areas of cholinergic and adrenergic foci, such as the AV node and His bundle.[4] Cholinergic stimulation is predominantly mediated by left and right vagal nerves and adrenergic activity is mediated by the left and right stellate ganglion. Even among highly innervated areas, the heart displays asymmetric areas of innervation in which right-sided autonomic innervation has a dominant effect on the sinoatrial node and left-sided autonomic fibers preferentially affect the AV node.

Increased right-sided stellate ganglion innervation causes sinus tachycardia with little effect on the AV node. Left-sided stellate innervation causes an increase in cardiac sympathetic tone, resulting in ectopic pacing with sufficiently elevated sympathetic tone. Left vagal nerve innervation has a negative dromotropic response, resulting in decreased AV nodal conduction and increased refractoriness. At high levels this may cause high-degree and third-degree heart block. Right-sided vagal innervation results in sinoatrial nodal slowing and sinus bradycardia.

Owing to the autonomic nature of Ross syndrome, cardiovagal dysfunction has been investigated, but investigation is limited to small cohorts and case reports owing to its scarcity. Researchers have employed electrocardiogram monitoring in conjunction with different modalities, such as tilt table, Valsalva, deep breathing, cold face, and isometric handgrip, to interrogate vagal tone. No significant cardiovagal abnormalities were noted.[1,2,5–8] One case report used MIBG-SPECT in 1 Ross syndrome patient without cardiovagal symptoms, showing a decreased iodine-123 meta-iodobenzylguanidine uptake in the posterior lateral aspect of the heart, but its significance remains unclear.[9]

This case represents the first documented case of AV nodal dysfunction in the setting of Ross syndrome. While the patient did received a singular dose of IV labetalol, her symptoms both predated and postdated the half-life of the drug. Furthermore, her diagnosis of biopsy-proven ischemic colitis without evidence of vascular obstruction supports chronic transient episodes of high-degree AV block as the probable etiology. The authors acknowledge that Lyme disease markers were not sent, but she did not have Lyme exposure risk. Cardiac magnetic resonance imaging was deferred at the time given the newly placed device.

Conclusion

Although Ross syndrome is considered a benign disease process, our case illustrates potentially life-threatening cardiovascular manifestation not yet captured owing to the low prevalence of the disease. Close attention to cardioinhibitory abnormalities should be taken into consideration, and cardiology should be included in the multidisciplinary approach

if patients present with signs of unexplained syncope or other cardioinhibitory sequelae. Further research is required to delineate and stratify the different presentation of autonomic dysfunction in Ross syndrome and to determine patients at risk for developing cardioinhibitory symptoms.

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