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A Rare Neurological Presentation of Noonan Syndrome and Its Management—A Case Report

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Abstract

Although Noonan syndrome is a relatively common congenital disorder with autosomal dominant inheritance, its association with cerebrovascular anomalies is rare. We report a case of a 20-year-old with Noonan syndrome with cerebrovascular aneurysm, who underwent successful endovascular coiling. Only four cases of cerebrovascular aneurysms in Noonan syndrome have been reported in the literature so far. To the best of our knowledge, this is only the fifth reported case and the first one that has been treated successfully with endovascular coiling. We hereby discuss the management of this case, which had several comorbidities like congenital heart disease and craniovertebral junction anomaly.

Keywords
- cerebrovascular aneurysm
- craniovertebral junction anomaly
- endovascular coiling
- Noonan syndrome

Introduction

Noonan syndrome (NS) is a congenital disorder with a frequency of one in 1,000 to 2,500.[1] The syndrome is associated with multiple congenital anomalies including dysmorphic facies, cardiac defects, coagulopathies, craniovertebral junction anomalies, and skeletal malformations. Cerebrovascular anomalies are not a common feature but have been reported in association with NS.[2] Only four cases of intracranial aneurysms in association with NS have been reported in the literature so far.[3] To the best of our knowledge, this is only the fifth reported case. We discuss the management of this case for which endovascular coiling was done successfully.

Case Report

A 20-year-old male known to have NS presented to our emergency department with a history of sudden onset severe headache and transient loss of consciousness 4 days prior. He was known to have pulmonary stenosis and atrial septal defect (ASD) with a right to left shunt. Percutaneous balloon dilatation of the pulmonary valve had been done 2 years ago due to worsening dyspnea following which the gradient across the pulmonary valve improved from 78 to 41 mm Hg and the shunt across the ASD reduced. His medication history included tablet propranolol 20 mg twice daily.

The patient had distinctive triangular facies common with NS with torticollis, flat chest, kyphoscoliosis, and webbed neck. He was 150 cm tall and weighed 59 kg. He was conscious and oriented, with World Federation of Neurosurgical Societies (WFNS) grade 1. His pulse rate was 60/min, noninvasive blood pressure was 130/80 mm Hg, and room air oxygen saturation was 92%.

A head computed tomography (CT) was done that showed a hyperdensity in the anterior interhemispheric fissure

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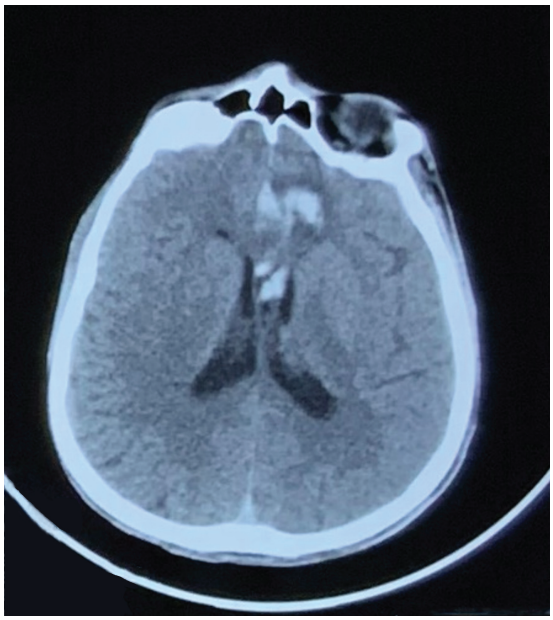

Fig. 1 Head computed tomography showing subarachnoid hemorrhage with blood in the anterior interhemispheric fissure.

suggestive of subarachnoid hemorrhage of modified Fisher grade 3. (►**Fig. 1**). CT angiography of the brain revealed an 8.4 × 3.5 mm aneurysm in the anterior communicating artery. Head CT also revealed complex craniovertebral junction anomaly—bilateral atlantooccipital assimilation with hypoplastic right atlas and occipital condyles with associated platybasia (►**Fig. 2**). There was also a mild subluxation of the right atlantoaxial joint with a hypoplastic odontoid process that was curved with the tip posteriorly causing central rotatory subluxation and basilar invagination. The C2 to C3 disc space was reduced.

Two-dimensional echocardiography showed a 14 mm ASD with mild pulmonary stenosis with a pressure of 32 mm Hg across the valve and normal biventricular function.

Endovascular coiling of the aneurysm was planned. Routine preoperative investigations were unremarkable including the coagulation profile. Tablet nimodipine 60 mg 4 hourly was started as per standard guidelines.

Standard monitors were applied to the patient in the digital subtraction angiography suite. An invasive blood pressure monitoring was started before the induction of anesthesia. Fentanyl (120 µg) and etomidate (18 mg) were given to induce anesthesia. Atracurium was used for neuromuscular blockade. Intubation was performed using HugeMed anesthesia videolaryngoscope (Shenzhen HugeMed Medical Technical Development Co. Ltd., Guangdong province, China) blade 4 with simultaneous application of manual in-line stabilization (MILS) and the trachea was intubated using an 8mm endotracheal tube. Anesthesia was maintained with oxygen in air and sevoflurane. Central venous pressure monitoring was started. Baseline arterial blood gas analysis revealed normal oxygenation, ventilation, blood pH, and electrolytes. Baseline activated clotting time (ACT) was 90 seconds.

During endovascular coiling, nimodipine is routinely added to the heparinized saline flush solution in our institute as a prophylactic measure against postprocedure vasospasm. Heparin boluses were given intermittently to keep ACT two to three times the baseline. Nimodipine flushing resulted in hypotension necessitating noradrenaline infusion that was tapered and stopped at the end of the procedure. The procedure lasted for 4 hours. The total intravenous fluid used was 500 and 1,500 ml of flush was used by the neuroradiologist. The total urine output was 800 mL. The trachea was extubated after the reversal of the neuromuscular blockade. His stay in the neurosurgical intensive care unit was uneventful. After 7 days, the patient was discharged with a modified Rankin score of 1.

Discussion

This is only the fifth reported case of intracranial aneurysm in NS, although arteriovenous malformations and moyamoya have been reported earlier.[2,3] Our patient had a solitary aneurysm in the anterior communicating artery. This could be a chance association or due to an underlying connective tissue disorder due to a genetic defect linked with a mutation

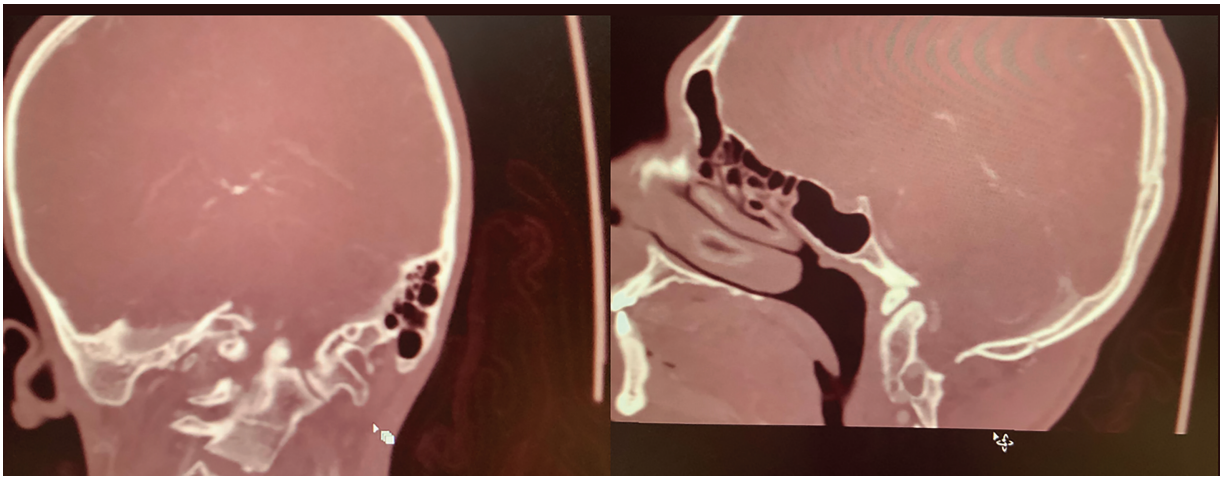

Fig. 2 Head computed tomography showing complex craniovertebral junction anomaly.

in the PTPN-11 gene resulting in defective vascular development and aneurysm formation.[3] Patients with NS present with multiple congenital anomalies having a diverse clinical presentation and a genetically heterogeneous makeover. It is now regarded as a disorder of unregulated RAS-MAPK signaling pathway also termed "RASopathy."[1]

Cardiovascular malformations are seen in 70 to 80% of the patients with NS. The most common malformation is pulmonary valve stenosis (50–60% of patients). Hypertrophic obstructive cardiomyopathy is present in 20% of the cases. Other lesions include ASD, ventricular septal defect, and atrioventricular canal defects. Mitral and aortic stenosis, tetralogy of Fallot, and patent ductus arteriosus are rarely encountered.[1] Our patient had undergone balloon valvuloplasty for pulmonary stenosis and had residual pulmonary stenosis and an uncorrected ASD. Hence, air bubble precautions were taken by both the anesthesiologist and the neuroradiologist while administering fluids to prevent paradoxical air embolism. Hypoxia, hypercapnia, acidosis, and hypothermia were prevented to minimize the increase in pulmonary vascular resistance. Goal-directed fluid therapy to avoid fluid overload was performed by monitoring the systolic and pulse pressure variation.

Craniovertebral junction anomalies like Chiari I malformation have been reported in NS.[4] Our patient had a complex craniovertebral junction anomaly diagnosed by CT. Musculoskeletal abnormalities such as pectus deformity and scoliosis are common in NS.[1] Webbing of the neck with torticollis, prominent trapezius, contractures, high arched palate, and malocclusion of the teeth are common and may cause difficulty in airway management. A flat chest and mild kyphoscoliosis were seen in our patient, in addition to a webbed neck, torticollis, and a high-arched palate.

We used video-laryngoscopy to secure the airway while employing MILS to avoid cervical joint manipulations. This has been seen to offer a similar advantage to fiberoptic intubation under general anesthesia in terms of spinal kinematics in craniovertebral junction anomalies/ instability.[5]

Hemostatic abnormalities including bleeding diatheses, factor deficiencies, low platelet count, and platelet function defects have been reported in NS.[1] Endovascular procedures do not involve significant blood loss, but one must be wary of hematoma formation at arterial puncture sites or retroperitoneal hematoma. Appropriate factor or plasma should be transfused either prior to the procedure or kept ready in the event of hemorrhage during the procedure.

Conclusion

The management of patients with NS is a complex endeavor owing to the presence of multiple congenital anomalies. Careful evaluation of the patient and a multidisciplinary approach were used in this rare presentation.

Previous Presentation
Case report has been presented in Indian Society of Neuroanesthesiology and Critical care Conference on 22 January 2021.

Authors' Contributions
SM was involved in writing up of the first draft of the paper and final editing. VN was involved in editing of the draft, data collection, and initial draft preparation. AD was involved in data collection.

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Conflict of Interest
None declared.

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