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ePoster Presentation

Growth hormone deficiency in patient with de novo mutation in SHOC2 causing Noonan Syndrome-like disorder with Loose Anagen Hair, and Castleman syndrome

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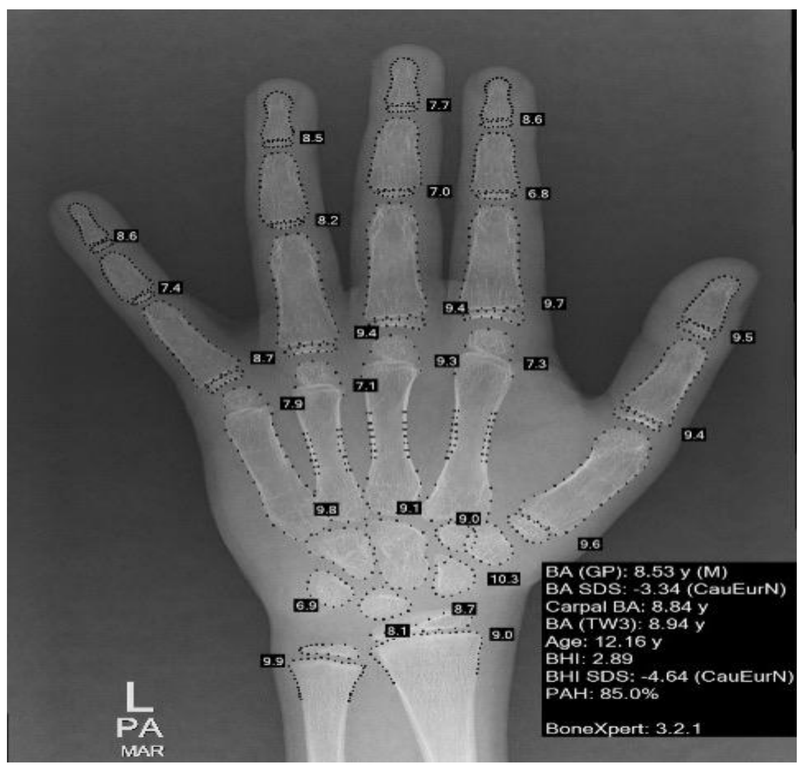
INTRODUCTION

Clinical manifestations of Noonan syndrome (NS) include short stature, distinctive facial features, webbed/wide neck, cryptorchidism, and congenital heart disease, notably pulmonic stenosis. NS is also recognised to predispose to malignancy – particularly hematological disease. Almost half of all NS cases are due to PTPN11 mutation. Other common mutations include SOS1 and RAF. Several rare mutations and NS subtypes are recognised. All of the known genes encode proteins within the RAS-Mitogen Activated Protein Kinase pathway. Herein, we report an 11-year-old presenting with growth failure, dysmorphic features (proptosis, short neck, peculiar deep voice, and very sparse hair), learning difficulties and developmental delay who was found to have a de novo mutation in SHOC2.

Case presentation

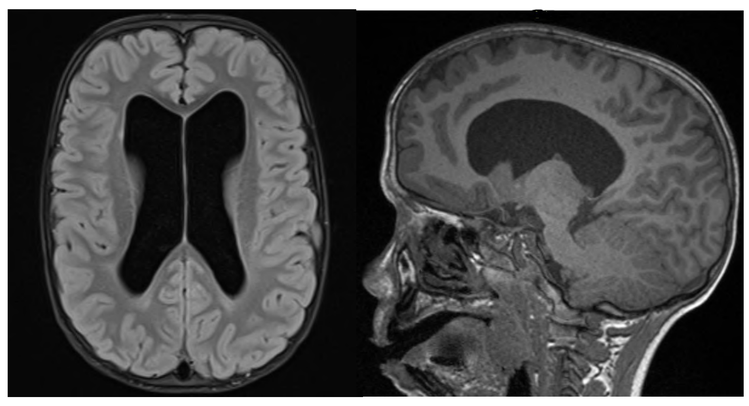
An 11-year-old boy of Arabic descent presented to the endocrinology clinic with severe short stature. He also had poor hair growth, developmental delay and learning difficulties. His past medical history is significant for meningitis and pneumonia on day 5 of life with delayed recognition and treatment. He developed hydrocephalus (but did not require a shunt). He also developed focal seizures, those were attributed to hypocalcemia which responded to IV calcium and magnesium. He had a small PFO and PDA which subsequently closed spontaneously. Investigations included microarray and FISH looking Di George Syndrome and both were normal.
His bone age was 2 years delayed with extremely poor growth. Growth hormone (GH) deficiency was suspected, and he underwent an Arginine GH stimulation test which showed severe GH deficiency (peak GH 2.7µg/L), while his IGF 1 was -1.07 SDS and IGFBP-3, -1.93 SDS, which supported the diagnosis of GH deficiency. He commenced GH replacement therapy, but after a few months he developed suspicious lymphadenopathy in the neck and abdomen. A biopsy was reported as showing Castleman's disease, hence GH was stopped, since there appeared to be a temporal replacement. Subsequently he restarted GH but once again had development of suspicious lymphadenopathy.
It was clear that likely had an underlying genetic disorder accounting for his complex problems and ultimately underwent a Whole Exome Trio which confirmed a de novo pathogenic mutation in SHOC2, the cause of NS with loose anagen hair (OMIM 607721).
All patients with SHOC2 NS have short stature, with GH deficiency found in 70% of patients. This form of NS is associated with loose anagen hair, which he had. He also had a very distinctive deep voice which is a recognised feature of this condition.

Bone age



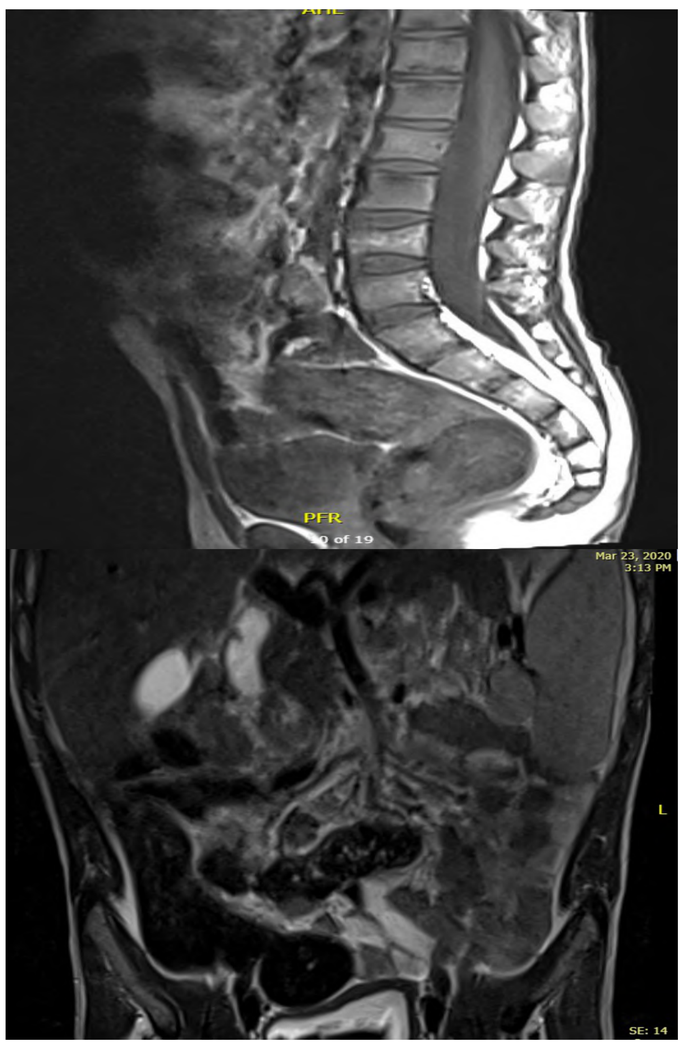
The child's chronological age is 12.16 years (12 years 2 months).
The bone age according to the GP atlas assessed by bone age assessment software is 8.53 years (8 years 6 months).

MRI Brain



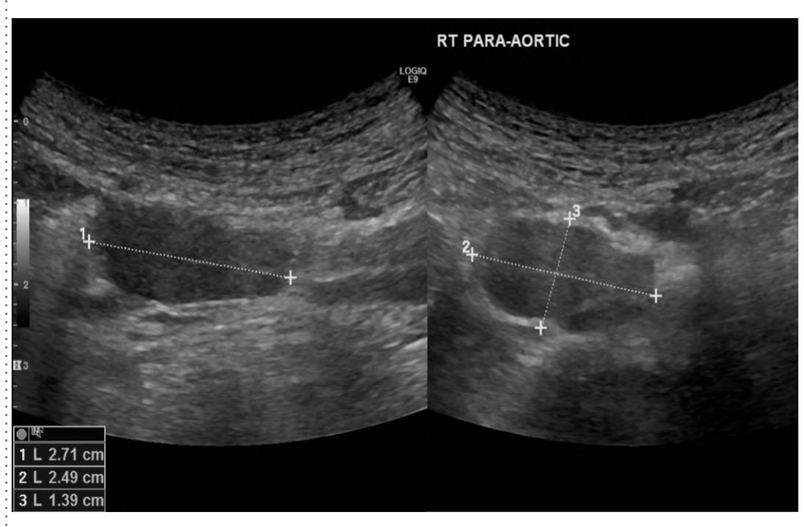
There is mild enlargement of the head more on the frontal aspect. All ventricles are dialated including the temporal horns with disproportionate widening of the frontal horns. There are no MRI features to suggest periventricular/ transependymal seepage of CSF. The cerebral aqueduct is patent.

MRI Spine & Abdomen



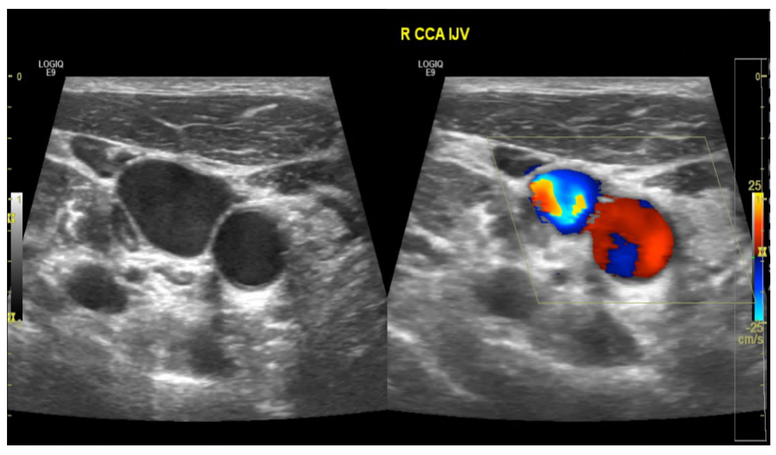
A large conglomerate nodal mass in the right retroperitoneal region. It is starting from the aortic bifurcation and extending down along the right common iliac vessels. It measures 11.4 mm in short axis and extends for a length of 44 mm. A few prominent lymph nodes are present in the para aortic region.
There is reduced vertical height with anterior wedging of L4 vertebral body.
There are Schmorl's nodes present involving the lower end plate of T11, and upper end plates of the T12, L1, and L3 vertebral bodies. These are surrounded by marrow oedema, which shows low signal on T1, high signal on T2 weighted images and shows enhancement on postcontrast studies, this represents type I Modic changes.

US Abdomen



Multiple para aortic and lymph nodes can be seen, the largest two measure 2.77 x 0.77 cm and 2.7x 1.39 cm. The latter is globular in shape with no clear hilum could be seen.

US Neck



Bilateral jugulodigastric lymph nodes are the largest nodes seen in the neck measuring 1.83 X 0.70 cm on the right side and 1.5 X 0.75 cm on the left side. Bilateral submandibular triangles show lymph nodes with the largest measuring 0.8 cm in short axis. No features of lymph nodes in the posterior triangle or in the supra clavicular location.
The lymph nodes do not show abnormal vascularity, cystic changes, calcifications or peri nodal inflammatory changes

CONCLUSIONS

We present a case of NS with loose anagen hair, who developed multicentric Castleman's syndrome temporally related to GH therapy. NS is associated with higher rates of malignant disease, especially hematological malignancies, but Castleman's disease has not, to our knowledge, been reported with NS.

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