

Case Reports

Asymptomatic ganglioneuromas in a 13 year old girl with Noonan syndrome

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Introduction

Ganglioneuromas are rare, benign tumours occurring in adolescence and early adulthood¹. They arise from neural crest tissue, including sympathetic ganglia and adrenal medulla².

Case report

A thirteen year old girl with congenital hypothyroidism and Noonan Syndrome was found to have bilateral suprarenal masses when a routine ultrasound scan of abdomen was done for screening of renal anomalies. She had features of Noonan syndrome such as high arched palate, webbed neck, low hair line, low set ears, wide carrying angle and partial ptosis. However, she was of average build and her height was on the 10th centile. She did not have goitre, sweating, palpitations, dizziness, loss of weight, headache visual disturbances, pigmentation or virilisation. Her pulse rate was regular, 84 beats per minutes and her blood pressure was 90/60mm

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mercury. She was on an appropriate dose of thyroxine and was clinically and biochemically euthyroid.

She had age appropriate skeletal maturity, normal parathyroid hormone level, bone profile and 24 hour urinary vanillyl mandelic acid (VMA). Magnetic resonance imaging (MRI) of abdomen, chest and neck revealed two extra-renal large ganglioneuromas, one extending towards the thoracic cavity (Figure 1). The right sided suprarenal mass was 73mm x 50mm x 54mm and was compressing the right kidney. The second lesion was a left para-spinal mass 92mm x 32mm x 42mm extending from the left renal hilum superiorly. The thyroid gland appeared atrophic, and there was no evidence of medullary carcinoma of the thyroid.

She underwent surgical excision of the right sided suprarenal mass; however, excision of left sided paraspinal lesion was withheld due to intra-thoracic extension that may lead to higher postoperative morbidity in comparison to continuing with an asymptomatic benign lesion. Histology of the excised lesion revealed a well circumscribed tumour with ganglions and mature nerve cells in the periphery, with few scattered lymphocytes within the tumour, confirming the expected diagnosis of ganglioneuroma. Blast cells, atypical cells, mitosis or necrosis were not seen in this tissue. Follow up with regular imaging was recommended due to the extremely rare possibility of recurrences.



Figure 1: MRI abdomen & chest of patient with 2 extra-renal large ganglioneuromas, right sided suprarenal mass and left para-spinal mass extending from left renal hilum superiorly

Discussion

Ganglioneuromas are commoner among females than males, 60% occurring before 20 years of age^{1,2}. Ganglioneuromas may occur anywhere along the para vertebral sympathetic plexus, commonly in retroperitoneum (32-52%) and posterior mediastinum (39-43%) and less commonly in cervical ganglia (8-9%), adrenal medulla, large bowel, heart and skin². When considering this patient, it is a rare occurrence to have two lesions together involving adrenal gland and retroperitoneal paraspinal ganglions which extended to the posterior mediastinum at presentation.

Ganglioneuromas are usually asymptomatic but may cause pressure effects on surrounding organs². Usually they are identified incidentally with the imaging done for other unrelated symptoms. Rarely there can be hormonally active tumours, which secrete catecholamines, vasoactive intestinal polypeptides, or androgenic hormones, that can be detected biochemically, although rarely capable of manifesting as hypertension, diarrhoea or virilization^{1,2}. The most important differential diagnoses for ganglioneuromas are neuroblastomas and adrenal carcinomas^{1,2}. In contrast to ganglioneuromas, these two conditions are hormonally active and can be identified clinically and biochemically by assessing urinary catecholamines, dopamine and VMA. However imaging is the most important tool in differentiating these two categories^{1,2}. In computed tomography (CT) or MRI scans, ganglioneuromas are homogeneous, well defined, oval, crescentic or lobulated mass lesions, most of the time surrounded by major blood vessels, with minimum compromise

of the lumen. There may be discrete and punctate calcifications in these tumors, while the calcifications are amorphous and coarse in neuroblastomas¹.

Noonan syndrome is an autosomal dominant disease, 70% of inheritance is due to mutations in *PTPN11*, *SOS1*, *RAF1*, *KRAS*, *BRAF* and *MEK1* (*MAP2K1*) genes^{3,4}. Even though genetic confirmation was not done in this patient, her features were clinically suggestive of Noonan syndrome. These gene mutations are associated with haematological malignancies, neuroblastomas, rhabdomyosarcoma, pheochromocytoma, Wilms tumour, liver, breast, colon, ovarian, thyroid malignancies and melanomas but definite association with ganglioneuromas are not identified^{4,5}. However there is one documented case with Noonan syndrome having ganglioneuroma⁶ and another patient with mild cutaneous neurofibromatosis type 1, ganglioneuroma and Noonan phenotype⁷.

Prognosis of ganglioneuromas is excellent following complete surgical or laparoscopic excision of the tumour. Recurrence is extremely rare. Histopathologic examination is the mainstay of confirmation of the diagnosis and excluding rare possibility of malignancy⁸. As there are few cases of recurrences, follow up of these patients with imaging, is recommended⁹.

Ganglioneuromas of the adrenal are very rare, benign tumors, usually hormonally inactive, as well as asymptomatic. There is no known association with Noonan Syndrome. To the best of our

knowledge this is the only documented case of ganglioneuroma in a patient with Noonan syndrome in Sri Lanka. We do not have facilities to confirm Noonan syndrome genetically.

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