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Ganglioneuroma in Children: A Diagnostic Dilemma

KEYWORDS: Ganglioneuroma, Diagnosis, MRI, Histopathology, Immunohistochemistry.

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ABSTRACT *The relatively low incidence of Ganglioneuroma often makes the diagnosis in dilemma. Usually, they are clinically silent; regardless of their size they should be included in the differential diagnosis of any retroperitoneal mass.[1-3]*

A four year old girl presented to us with complaints of vague abdominal pain on & off since last 6 months. On clinical examination, a globular mass with firm in consistency was felt over the right lumbar and umbilical region. Laboratory examinations were normal and imaging studies & FNAC revealed a benign mass. The mass was excised almost completely except from the base, where it was adherent to the IVC and Aorta. Post operative outcome was uneventful. Histopathology and Immunochemistry confirmed the diagnosis of Ganglioneuroma.

Introduction:
Ganglioneuroma is rare tumour that occurs in approximately 1 in 100,000 children; occurs slightly more often in girls than boys, with a female-to-male ratio of about 1.5:1.

Ganglioneuroma are tumours of adolescents and young adults (40-60%), but individuals of all ages can be affected with mean age of occurrence is 7 years. They have a pseudocapsule, are firm to the touch and have a light colour ranging from white to yellow. Internally, the tumour may have a whorled appearance with trabeculae.

Ganglioneuroma are usually benign differentiated tumours of the sympathetic nervous system. They originate from embryonic undifferentiated cells of the neural crest and are part of the wider spectrum of neuroblastic tumours, which also includes neuroblastoma and ganglioneuroblastoma.[1] These tumours can grow at any site of the sympathetic nervous tissue but they usually occur in the abdomen. Fifty-two percent of ganglioneuromas are located in paraspinal retroperitoneum (sympathetic ganglia), 39% in posterior mediastinum, and 9% are located in the pelvis or neck.[2,3] Of the abdominal ganglioneuromas, 49% originate in the adrenal gland and 51% are extra-adrenal.[3] In some cases, ganglioneuromas are the final stage of maturation of neoplasms such as neuroblastoma or ganglioneuroblastoma. Nevertheless, these tumours can arise de novo based on age at diagnosis and anatomic location.[3]

They may also develop within a neuroblastoma treated with chemotherapy.

The histological difference between ganglioneuroma, ganglioneuroblastoma and neuroblastoma is their stage of neuroblast maturation. (Shimada, 1999).[8] A tumour composed primarily of neuroblasts is referred to as neuroblastoma, a tumour composed entirely of mature ganglion cells and other mature tissue is a ganglioneuroma and a tumour with both immature and mature cell types is a ganglioneuroblastoma. Therefore, ganglioneuroma is considered as a benign tumour.

Case History:
A four year old girl presented with complaints of vague abdominal pain on & off since last 6 months. On clinical examination, a globular mass was felt in the right lumbar and umbilical region which was firm in consistency.

Laboratory examination was normal including Haemogram and Biochemistry.

CECT abdomen revealed a large heterogeneously enhancing soft tissue density retroperitoneal mass lesion measuring 7.3 cm x 5.8 cm x 8 cm on right side extending from L1 to L3, compressing the IVC and pushing right ureter laterally with few discrete specks of calcifications.

MRI of abdomen was performed for localization & characterization of the mass (Fig 1: showing T1 weighted image), revealing a large mass in abdominal cavity on right side, extending in midline, measuring 101mm x 82 mm x 62 mm, showing moderate enhancement on contrast. The lesion was compressing the IVC and Aorta. Both the kidneys and adrenal glands were identified separately

FNAC of the mass showed benign spindle cells, having spindle shaped nuclei suggestive of differential diagnosis of shwannoma or smooth muscle neoplasm.

Based on above findings, the differential diagnosis of a retroperitoneal benign mass was made and operative exploration was planned.

The girl was operated through right supraumbilical incision. A round mass with smooth surface, firm in consisten-

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cy; adherent to its base was seen. Complete excision was done except from the base, where it was adherent to the IVC and Aorta. Post operative outcome was uneventful

Histopathology sections (Fig 2: showing microscopic slide view), on gross examination of mass, it was light yellow coloured & firm to touch. Microscopic examination showed, benign neoplasm with interrupted thin fibrous capsule, consisting of nerve fibre bundle of Schwann cells along with numerous ganglion cells, was seen. These ganglion cells were mono to binucleated; there was no evidence of any atypia, overall findings, confirmed the diagnosis of Ganglioneuroma.[9]

Immunohistochemistry is positive for Synaptophysin (SMP88) & S100 [3] (Polyclonal) of tumour cells.

Discussion:

The relatively low incidence of ganglioneuromas often makes their diagnosis difficult. Usually, they are clinically silent. Regardless of their size, they should be included in the differential diagnosis of any retroperitoneal mass. Similarly, clinical signs and symptoms of hormone excess are usually absent, although ganglioneuromas are hormonally active, producing a wide range of neuropeptides. Patients may rarely present with vague abdominal pain or neurological symptoms due to mass effect.[1-3]

Ganglioneuromas are rare, benign, fully differentiated tumours that contain mature Schwann cells, ganglion cells, fibrous tissue and nerve fibers. These tumours have no immature elements (such as neuroblasts), atypia, mitotic figures, intermediate cells or necrosis. The presence of any these tissue characteristics excludes the diagnosis of ganglioneuroma.

It is more difficult to differentiate ganglioneuromas from schwannomas or neurofibromas, as seen in our case with findings of FNAC. In general, schwannomas and neurofibromas are round and can cause bone erosion and destruction. Most ganglioneuromas are flat and elongated and they normally do not affect bone. Schwannomas may demonstrate cystic degeneration that does not occur in ganglioneuromas. Neurofibromas do not have a capsule; while the presence of the capsule would point to ganglioneuroma as a diagnosis.

Ganglioneuromas are typically discovered during routine imaging studies. On computed tomography scan.[4] they appear well delineated and they tend to grow around major blood vessels without narrowing them , as was seen in our case. On magnetic resonance, ganglioneuromas appear homogeneous and have relatively low signal intensity on T1-weighted images. On T2-weighted images, the signal intensity is proportional to the ratio of myxoid stroma to cellularity as well as to the amount of collagen present at the tumour site.[5] Although, iodine-tagged metaiodobenzylguanidine uptake can be increased in patients with ganglioneuromas it does not discriminate the exact type of the catecholamine-producing tumour. Diagnosis can be established after a CT-guided biopsy.[3]

Their management involves total surgical excision when feasible because it allows for good tissue sampling and a thorough pathology examination of the specimen to ensure correct diagnosis of Ganglioneuroma, however, in some instances; it can be challenging and demanding because of their tendency to engage neighbouring vital anatomical structures. The prognosis is excellent for ganglioneuroma after surgical removal.[2,3,6,7] After being completely excised, they do not usually recur, although malignant transformation into peripheral nerve sheath has been described.[6]

Metastases in these tumours are exceedingly rare and are thought to be the end result of matured ganglioneuroblastoma or neuroblastoma metastases rather then true ganglioneuroma metastases. After tumour excision, immunoperoxidase staining test of the tumour ganglion cell can also add to diagnosis, showing a strong S-100 protein positivity, as positive in our case, for neuron-specific enolase and spindle-cell component.[3] The slow-growing pattern of the tumour necessitates long term follow-up of operated patients, including repeated imaging along with careful physical examination for local recurrence or new symptomatology.

Conclusions

A child with asymptomatic retroperitoneal abdominal mass, correct diagnosis is a challenge for management. Ganglioneuroma should be included in the differential diagnosis of any retroperitoneal mass. Their management involves total surgical excision including meticulous operative dissection which is directly correlated with an improved patient's post-operative outcome and excellent prognosis. However, in some instances; it can be challenging and demanding because of their tendency to engage great vessels and neighbouring vital structures.

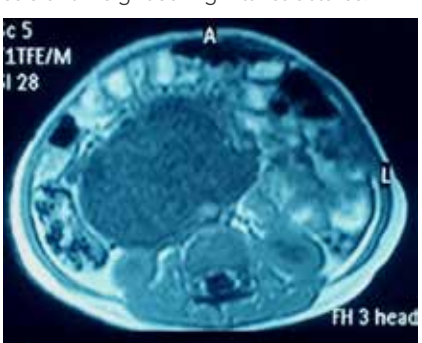

Fig 1: MRI images of ganglioneuroma (T1 weighted) en casing the aorta

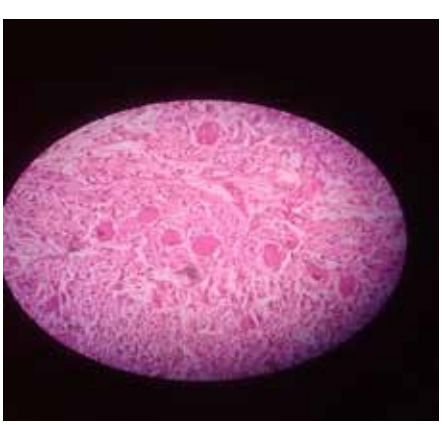

Fig 2: Microscopic slide view of Ganglioneuroma

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