GANGLIONEUROMA

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Abstract

Ganglioneuroma is a tumor of the peripheral nervous system. Along with neuroblastomas, ganglioneuromas and ganglioneuroblastomas are collectively known as neuroblastic tumors. They originate from neural crest sympathogonia, which are completely undifferentiated cells of the sympathetic nervous system.

These tumors can grow wherever sympathetic nervous tissue is found, but they most frequently occur in the abdomen. Common location includes the adrenal gland, paraspinal retroperitoneum (sympathetic ganglia), posterior mediastinum, head and neck. Location such as the urinary bladder, bowel wall, abdominal wall and gallbladder are considered unusual.

Key words: ganglioneuroma, ganglioneuroblastoma, neuroblastoma

Pathophysiology

The histologic difference between ganglioneuroma, ganglioneuroblastoma and neuroblastoma is their stage of neuroblast maturation. (Shimada, 1999). A tumor composed primarily of neuroblasts is referred to as neuroblastoma (NB), a tumor composed entirely of mature ganglion cells and other mature tissue is a ganglioneuroma (GN) and a tumor with both immature and mature cell types is a ganglioneuroblastoma (GNB). Therefore, ganglioneuroma is considered as a benign tumor. In rare cases, von Recklinghausen disease, Hirschprung disease, central failure of ventilation and DiGeorge syndrome are associated with ganglioneuroma and ganglioneuroblastoma. (Lonergan, 2002). Ganglioneuromas are rare, benign, fully differentiated tumors that contain mature Schwann cells, ganglion cells, fibrous tissue and nerve fibers. These tumors 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.

These tumors can arise de novo and result from the maturation of a ganglioneuroblastoma or neuroblastoma into a ganglioneuroma. They may also develop within a neuroblastoma treated with chemotherapy. Metastases in these tumors are exceedingly rare and are thought to be the end result of matured ganglioneuroblastoma or neuroblastoma metastases rather then true ganglioneuroma metastases. As many as 37% of ganglioneuromas secrete cathecolamines.

Frequency: ganglioneuroma are rare tumors than occur in approximately 1 in 100,000 children. In the US about 30-50% of ganglioneuromas are retroperitoneal and approximately 40% occur in the posterior mediastinum. Roughly 20% of these tumors occur in the adrenal medulla and cervical lesions constitute only 10% of these cases. Uncommon locations such as heart, bone and intestine also have been described. Central nervous system location is rare.

Sex: ganglioneuroma occur slightly more often in girls than boys, with a female-to-male ratio of about 1,5:1.

Age: ganglioneuromas are tumors of adolescents and young adults (40-60%), but individuals of all ages can be affected. The mean age of occurrence is 7 years.

Gross anatomic features:

Ganglioneuroma are considered to be mature tumors and do not have immature elements. Ganglioneuroma average 8cm in size and have a pseudocapsule. They are firm to the touch and have a light color ranging from white to yellow. Internally, the tumor may have a whorled appearance with trabeculae.

Risk groups: two histologic classification systems are commonly used in the United States to stratify neuroblastic tumors into risk groups: the Shimada classification and the Pediatric Oncology Group (POG) classification. Both systems assess histologic features such as cellular differentiation, to arrive at a prognostic classification.

The POG system is based on the degree of differentiation of the different histologic elements.GN shows completely differentiated stromal and cellular components. NB contains less than 50% differentiated elements and GNB is intermediate. NB may be further subclassified as undifferentiated (the most immature NB), poorly differentiated or differentiating(the most mature NB).The Shimada classification combines histologic features and patient age at diagnosis. The histologic features consist of stroma, grade and architecture of

The age groups of the Shimada classification system are less than 1,5 years, 1,5-5 years and more than 5 years age. Children with favorable histologic characteristics are either less than 1,5 years of age with a low or intermediate MKI and differentiating or partially differentiating tumor or 1,5-5 years old with a low MKI and differentiating tumor. All other combinations are considered unfavorable histologic characteristics.

Staging -In 1986, an international consensus group devised the International Neuroblastoma Staging System (INSS) , based on clinical, radiologic and surgical feature.

Histopathology Age-linked Grading System of Shimada:

Type	Favorable Histologic Characteristics	Unfavorable Histologic Characteristics
Stroma-rich	Well differentiated intermixed	Nodular
Stroma-poor		
Age <18 mo	MKI <200/5,000	MKI >200/ 5,000
Age 18–60 mo	MKI <100/5,000 and differentiat- ing	MKI >100/ 5,000 or undiffer- entiated
Age >5 y	None	All

Stage	Description
1	Localized tumor confined to the area of origin; complete gross excision, with or without microscopic residual disease; identifiable ipsilateral and contralateral lymph nodes negative microscopically
2A	Unilateral tumor with incomplete gross excision; identifiable ipsilateral nonadherent lymph nodes negative microscopically
2B	Unilateral tumor with complete or incomplete gross excision; positive ipsilateral nonadherent lymph nodes; identifiable contralateral lymph nodes negative microscopically
3	Tumor infiltrating across the midline (vertebral column) with or without regional lymph node involvement; or unilateral tumor with contralateral regional lymph node involvement; or midline tumor with bilateral regional lymph node involvement or extension by infiltration
4	Dissemination of tumor to distant lymph nodes, bone, bone marrow, liver, or other organs (except as defined in stage 4S)
4S	Localized primary tumor as defined for stage 1 or 2 with dissemination limited to liver, skin and/or bone marrow (<10% tumor) in infants younger than 1 y

Biologic behavior

In rare cases, GN secretes sufficient quantities of VMA (vanillylmandelic acid) or HVA (homovanillic acid). Cathecolamine production by GN was previously believed to be unusual, because it was theorized that more mature tumors have more mature biologic behavior. However, in the largest series of GNs to date (49cases), 37% of the patients has elevated VMA or HVA levels.

Clinic

Ganglioneuromas are usually asymptomatic regardless of their size, and they are typically discovered on a routine radiograph. If the tumor is in the mediastinum, it may cause chest pain, cough, difficulty breathing or compression of the trachea.

If the tumor is in the retroperitoneal space, it may result in abdominal pain and distension. If the tumor is in near the spinal cord, it may cause spine deformity and possible compression of the spinal cord.

These tumors may be hormonally active and hypertension, diarrhea, flushing and virilization may occur as a result the secretion of cathecolamine, vasoactive intestinal polypeptide, or androgenic hormone.

Differential diagnosis

-Adrenal adenoma
-Adrenal carcinoma
-Neuroblastoma, ganglioneuroblastoma
-Pheochromocytoma

Radiography

Altough GN tends to be relatively homogeneous, the imaging characteristics of GN are similar to those of GNB and NB; hence, they cannot be discriminated at imaging evaluation save for the presence of metastases, which are quite rare in GN. Plain radiographs show a posterior mediastinal mass, which may cause rib spreading and foraminal erosion. A mass may also be noted in the retroperitoneumpelvis or neck.

CT- Scanning is the imaging modality that is commonly used to evaluate neuroblastic tumors. It is the superior imaging technique when it comes to identifying tumor size,organ of origin, tissue invasion, adenopathy and calcification. Newly diagnosed cases are evaluated with standard chest, abdominal and pelvic CT.

Retroperitoneal and adrenal GNs appear well defined. Their shape ranges from round to lobulated, they

show discrete and punctate calcification in 42-60% of cases, and they tend to grow around major blood vessels, which are not compressed by the tumor.

MRI creates images with better tissue discrimination than CT. Ganglioneuromas appear homogeneous on MRI and have relatively low signal intensity on T1-weighted images. On T2-weighted MRIs, the signal intensity is proportional to the ratio of myxoid stroma to cellularity and also to amount of collagen present in the tumor. Tumors with intermediate to high signal intensity on T2-weighted images have a higher degree of cellularity and more collagen. Markedly high T2 intensity signifies a high myxoid stroma component and low cellularity and collagen amount (Rha, 2003).

Ultrasound of GN shows a homogeneous, hypoechoic, well circumscribed mass.

Scintigraphy - Iodine-tagged medaiodobenzylguanidine (MIBG), a cathecolamine analog, is used to identify cathecolamine-producing tumors. MIBG has 88% sensitivity and 99% specificity for tumors containing sympathetic tissue such as GNB, GN, NB, pheochromocytomas and carcinoids. The disadvantage is that there is no way to discriminate the type of tumor in which the uptake occurs.

Treatment

GN are staged by using the INSS. Treatment is usually in the form of surgical excision, if the tumors are localized. Complete surgical resection is important because it allows for good tissue sampling and a thorough pathology examination of the specimen to ensure correct diagnosis of ganglioneuroma. In rare cases, these tumors recur, so periodic radiologic surveillance is performed after resection.

Prognosis is usually good, because this tumor is generally benign. Rarely, a GN may become malignant and metastasize or recur.

Complications – may occur as a result of surgery. If the tumor has been present for a long time and is causing symptoms (such as spinal cord compression), removal of the tumor may not necessarily reverse the deficit.

CASE REPORT

We present a case of an 11 year-old boy was diagnosed with hepatic hidatic cyst, 4 months ago. Now, he was admitted in our clinic with abdominal pain and failure to thrive. On physical examination, his vital signs were normal. He looked pallor. Chest was clinically clear. Bowel sounds were existing and normal. On investigation, hemoglobin was 13.3, other blood parameters were within normal limit. Liver function tests and renal function tests were normal. Chest X-ray revealed nothing.

Ultrasound has shows a round, homogeneous, mixed(hypo-, iso- and hiperechoic), well circumscribed mass, situated in the right hepatic lobe, near to upper right renal pole.

The abdominal CT-scan has showed a 6,5/5,7/4 cm solid, heterogeneous mass, with microcalcification, situated at the right suprarenal gland. It was located between the diaphragm superior, the right renal artery inferior and the inferior vena cava medially. The right kidney was displaced caudal and posterior. Other abdominal viscera looked normal. This tumoral mass was thought to be a neuroblastoma.

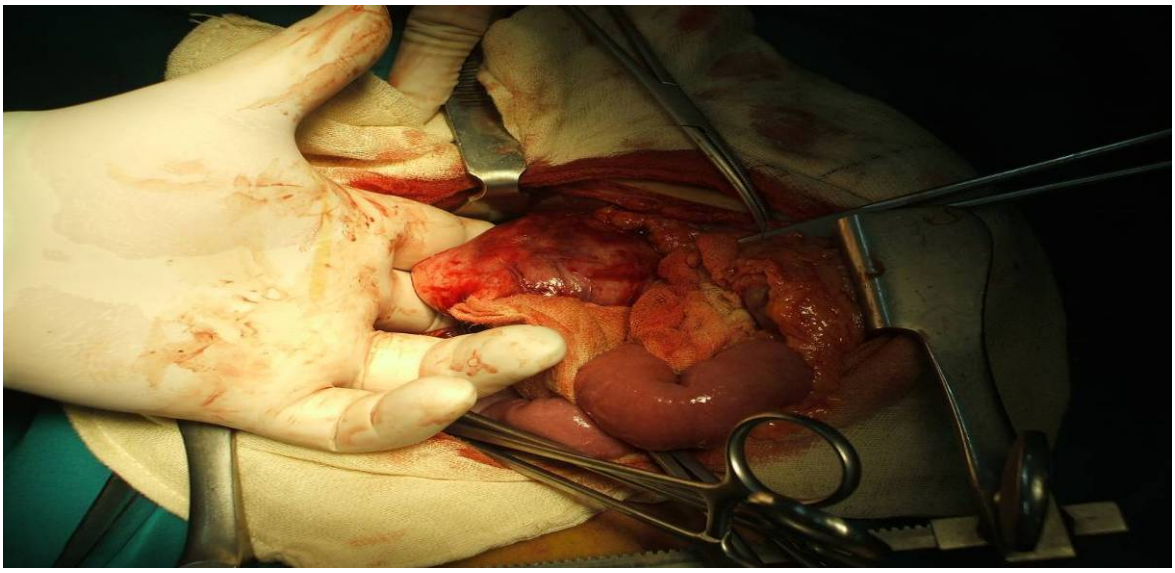

Fig.1. Intraoperative aspect. The tumor is in contact with upper pole of the right adrenal gland.

Based on above examination, after a previously preoperative prepare, laparotomy was done for exploration: the lateral attachment of the superior ascending colon and hepatic flexure are divided and the colon retracted medially and inferiorly. The division of the peritoneum is extended up to the right of the duodenum which is then mobilized

after the fashion of Kocher. This allows access to the upper kidney, part of the adrenal. Perinephric fascia (Gerota) is divided over the kidney and it revealed a 7/5/4 cm, firm, solid, mass, who was arising from retroperitoneum, in contact with upper pole of the right adrenal gland. Grossly, the tumor appeared as a grayish, white, solid mass, slightly lobulated, with a pseudocapsule. The plane of cleavage between the tumor and the adjacent structures was established and the tumor was completely excised. No peritoneal seedling of tumor was there. No intraoperative bleeding occurred. A drain tube was left in the tumor site.

Postoperative period was uneventful, except a hemorrhage from the tumoral layer, during the first day, who was treated conservatively. Patient was discharged on 11th postoperative day. He had a uneventful recovery and is maintaining good health at 3 month after surgery at this moment.

Microscopic, the tumor containing mature ganglion cells, supported by a connective tissue network containing Schwann cells; perivascular calcification, focal necrosis and thrombosis. The diagnosis of ganglioneuroma was made.

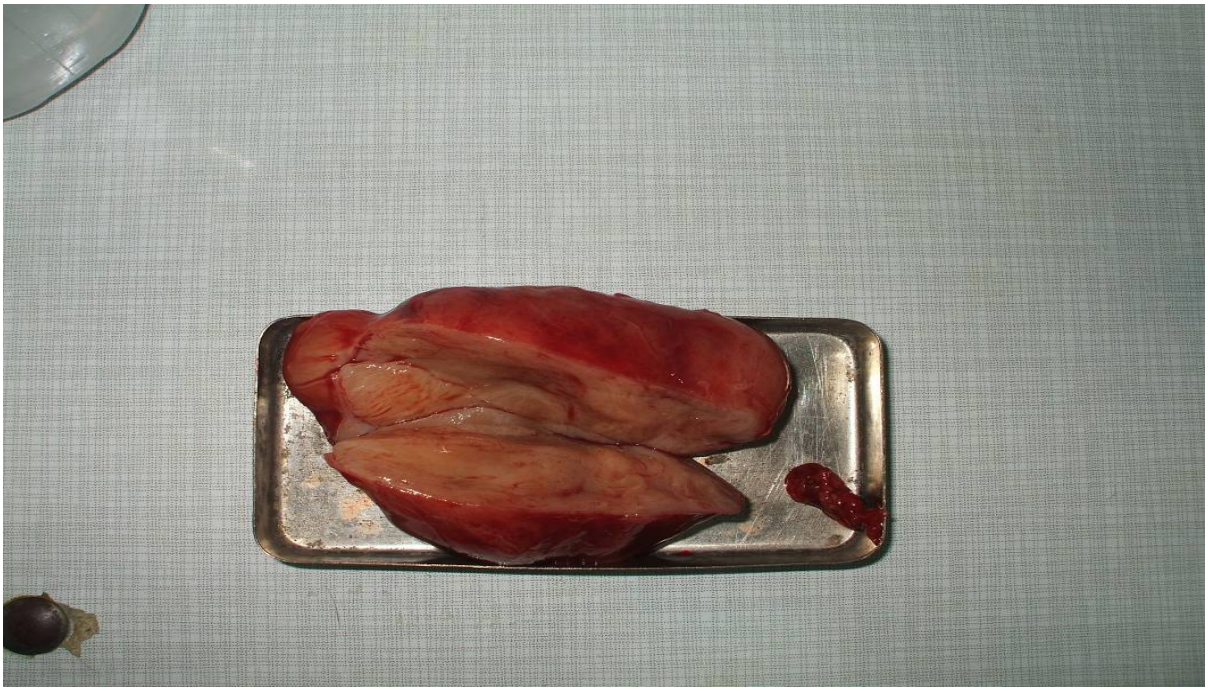

Fig. 2. The tumor after resection appeared as a grayish, white, solid mass, slightly lobulated, with a pseudocapsule.

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