

Case Report

Ganglioneuroblastoma: Unusual presentation as a pleural mass mimicking mesothelioma

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ABSTRACT

Ganglioneuroblastoma (GNB) is a rare peripheral neuroblastic tumor that is derived from developing neuronal cells of the sympathetic nervous system, and usually occurs in young children. We present a case of GNB occurring as pleural mass in a 2-year-old boy, which led to diagnostic confusion. On fine-needle aspiration cytology (FNAC), it was misinterpreted as mesothelioma. He underwent thoracotomy with excision of the mass. Histopathological findings showed features of a biphasic tumor suggestive of mesothelioma. Immunohistochemistry (IHC) performed for mesothelioma markers were inconclusive. On review of the histology slides, GNB was considered, which was subsequently proven by IHC. The rarity of this tumor, along with its nearly restricted occurrence at a young age, necessitates a strong suspicion in patients presenting with a symptomatic intrathoracic mass.

KEY WORDS: Ganglioneuroblastoma, immunohistochemistry, mesothelioma, pleura

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INTRODUCTION

Ganglioneuroblastoma (GNB) is a rare variety of peripheral neuroblastic tumor that can arise anywhere along the sympathetic nervous system. It occurs almost exclusively in the pediatric population, with some reported cases in the adult population.^[1]

This rare tumor occurs in less than 5 out of every 1,000,000 children each year.^[2]

CASE REPORT

A 2-year-old boy presented with complaints of fever with respiratory distress.

Chest X-ray [Figure 1] showed a soft tissue density mass at the right retrocardiac region with bilateral hilar congestion. To evaluate the mass further, a computed tomography (CT) of the thorax was performed, which

showed a partial collapse of the right lower lobe and a large, solid, homogenous, pleural-based noncalcified space-occupying lesion (SOL) with heterogeneous enhancement [Figure 2]. No communication was seen with the spinal canal.

CT-guided fine-needle aspiration cytology (FNAC) of the mass was performed under general anesthesia.

Cytology of the aspirated material showed dual population of cells comprising of round cells with hyperchromatic pleomorphic nuclei, prominent nucleoli, abundant eccentric basophilic cytoplasm, and a few spindle-shaped cell clusters [Figure 3a]. The cytological diagnosis offered was a neoplastic process of mesothelial cell origin, possibly mesothelioma.

The mass was excised and the specimen was sent for histopathological examination.

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On gross examination of the specimen, it appeared as a nodular circumscribed mass measuring 8 × 6 × 5 cm in size with attached pleura of 3 × 2 cm. The cut section was solid and grayish white in appearance.

Microscopically, the sections showed histology of a neoplastic lesion composed of a background of spindle cells with abundant fibrillary component, along with large polygonal cells having vesicular nuclei and plentiful eosinophilic, foamy cytoplasm. Mitotic figures were inconspicuous. The margins appeared to have been encroached upon by the tumor [Figure 3b]. Histological diagnosis was given as malignant mesothelioma of biphasic type.

Immunohistochemistry (IHC) was suggested for confirmation. Subsequently, the case was referred to us for IHC for mesothelioma markers. IHC was performed for calretinin, cytokeratin (CK), epithelial membrane antigen (EMA), Wilms' tumor 1 (WT1), and vimentin, which turned out to be inconclusive of mesothelioma. The hematoxylin and eosin (HE)-stained tissue sections were reevaluated. On review of the slides, GNB was suspected. IHC was repeated with markers chromogranin and S100. IHC revealed results of chromogranin positivity in ganglion cells [Figure 3c] and diffuse S100 positivity in spindle cells in the background [Figure 3d].

Overall, the histopathological features and IHC findings led to the final diagnosis of GNB intermixed (Schwannian stroma-rich). On follow-up, urinary catecholamine levels were estimated, which were within normal limits. Three months postoperative follow-up CT showed ill-defined thickening in the posterior parietal pleura near the initial tumor bed. Whole body skeletal scintigraphy performed with technetium-99m (Tc-99m) and bone marrow examination findings were unremarkable. The patient was clinically in good health on 6 months follow-up.

DISCUSSION

GNB is a primary malignant tumor of the sympathetic nervous system. This tumor can arise in various locations: in the cervical, mediastinal, adrenal, and retroperitoneal locations in the ascending order of frequency.^[3] GNB has rarely been described in the lung with the existence of only a few well-documented cases.^[4] There is no literature of this tumor presenting as a pleural mass, as was seen in our case.

GNB is graded into four distinct categories by the International Neuroblastoma Pathology Classification, which include neuroblastomas (Schwannian stroma-poor), GNB intermixed (Schwannian stroma-rich), ganglioneuroma (Schwannian stroma-dominant), and GNB nodular (composite Schwannian stroma-rich/stroma-dominant and stroma-poor).^[5]

GNB has intermediate malignant potential, between that of neuroblastomas and ganglioneuroma. Histologically,



Figure 1: Chest X-ray PA view

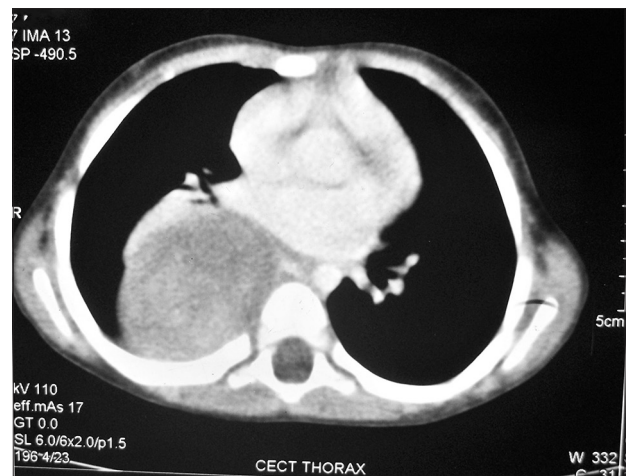


Figure 2: CECT of the thorax reveals a large, right lower, lobar, pleural-based homogenous solid noncalcified space occupying lesion

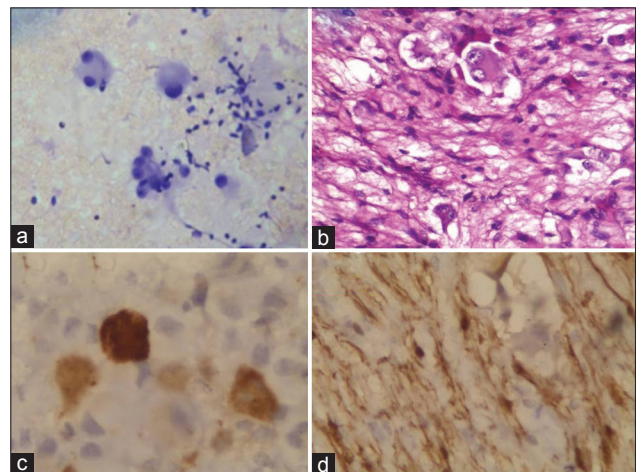


Figure 3: (a) Cytology showing large cells with central to eccentric nuclei and prominent nucleoli and clusters of small and spindly cells. (MGG ×100) (b) Histopathology of the same case (H and E ×200) (c) Immunohistochemistry with chromogranin showing positivity in ganglion cells. (×400) (d) Immunohistochemistry performed with S100 reveals positive background spindle cell stroma. (×400)

GNB is considered malignant because it contains primitive neuroblasts, along with mature ganglion cells.^[6]

Patients with GNB often present clinically with pain caused by either the primary tumor or by metastatic disease. Patients with mediastinal tumors can present with stridor and shortness of breath secondary to tracheal deviation or narrowing. Large thoracic tumors can cause mechanical obstruction resulting in superior vena cava syndrome. Nerve or nerve root compression by the mass can result in peripheral neurological signs. Patients with cervical masses can present with Horner's syndrome.^[7]

However, in our patient the only complaint was shortness of breath with fever. Metastases were ruled out by thorough investigations.

A CT scan is the imaging modality of choice to evaluate neuroblastic tumors. It is superior both in terms of determining tumor size and other characteristics including the organ of origin, tissue invasion, vascular encasement, lymphadenopathy, and calcifications.^[8] In our case, contrast-enhanced computed tomography (CECT) of the thorax showed a large, right lower, lobar, pleural-based solid homogenous noncalcified SOL with heterogeneous enhancement. No communication was seen with the spinal canal.

A cytologist may encounter GNB at uncommon locations and also in various age groups.^[9] Nevertheless, here cytology was misinterpreted owing to the atypical presentation of the mass.

Closest differential diagnosis of GNB intermixed is ganglioneuroma maturing. In GNB, intermixed, scattered "residual" microscopic neuroblastomatous foci are present as pockets of neuropil containing varying numbers of neuroblastic cells with various stages of maturation including differentiating neuroblasts and/or ganglion cells. The proportion of the ganglioneuromatous component to "residual" neuroblastomatous foci should exceed 50% of the total field(s) from representative section(s) of the tumor. Meanwhile, ganglioneuroma maturing is composed predominantly of ganglioneuromatous stroma with a minor component of individually scattered, evenly or unevenly distributed differentiating neuroblasts and/or maturing ganglion cells in addition to fully mature ganglion cells. Fully mature ganglion cells are always covered with satellite

cells.^[10] Immunohistochemical stains with antibodies such as neurofilament, synaptophysin, chromogranin, and S100 are generally positive in both ganglioneuroma and GNB.^[9]

CONCLUSION

The rarity of GNB warrants a great deal of suspicion when a younger patient presents with a symptomatic mass. Given the rare atypical presentation and wide variety of clinical symptoms the tumor can present with, it is essential that GNB remains one of the important differential diagnoses in pediatric patients presenting with intrathoracic mass.

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Conflicts of interest

There are no conflicts of interest.

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