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abstract

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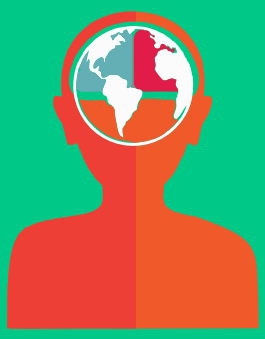

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abstract

A Rare Case of Pediatric Cervical Ganglioneuroblastoma: Diagnostic Challenges and Surgical Management

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Introduction: Ganglioneuroblastomas are commonly found in the extracranial region but in the head and neck region it is very rare disease. For patient evaluation diagnostic modalities like CT scan with contrast, MRI and fine-needle aspiration biopsy (FNAB) can help but the accuracy for definitive diagnosis is very limited. In this report we present the case of a 4-year-old male who presented with a neck mass which was slow-growing, along with multiple enlarged cervical lymph nodes. His workup raised a suspicion for ganglioneuroblastoma, which was later confirmed histopathologically. The patient was treated surgically which included resection of neck mass and cervical lymphnode dissection. No recurrence was observed at 6 months and 1-year follow-up. This report aims to contribute to existing literature by discussing diagnostic challenges, imaging findings, and surgical management of this rare tumor, providing insights into optimal clinical approaches.

The International Neuroblastoma Pathology Classification divides the peripheral neuroblastic tumors into neuroblastomas, ganglioneuromas, and ganglioneuroblastomas. Among the neuroblastic tumors, approximately 20% are represented by ganglioneuroblastomas. There is a range of cellular differentiation exhibited by them, from immature neuroblasts to mature ganglion cells, and this spectrum of differentiation bridges the gap between neuroblastomas and ganglioneuromas. Both mature ganglion cells and immature neuroblasts make up these tumors, and there is a higher incidence that is noted among males and the individuals of Caucasian descent.

Among the extracranial tumors in children, peripheral neuroblastic tumors are the most common presentation. These tumors rank third among the most frequently diagnosed pediatric malignancies, following leukemias and central nervous system cancers. The origin of these tumors

is from neural crest cells and they can develop anywhere along the sympathetic nervous chain. Approximately 8-10% of all childhood neoplasms, which affect children between the ages of 0 to 4 years, are represented by neuroblastic tumors. These include cervical, thoracic, and pelvic tumors. These tumors most frequently present in the adrenal gland as a mass in approximately 35% of the cases. These tumors also occur as a retroperitoneal mass in 30% of the cases. Among the retroperitoneal mass presentation, 20% appear in the posterior mediastinum and around 2-3% appear in the pelvic region.

The typical presentation is of a neck mass which is sometimes detected incidentally during radiological investigations. However, the early detection can be challenging due to these lesions' indolent and slow-growing nature. These cervical masses can be evaluated by imaging techniques, which provide insights into their size, location, composition, and their relationship with the surrounding structures. However, these modalities cannot reliably distinguish ganglioneuroblastomas from other neurogenic tumors. Valuable diagnostic information is offered by fine-needle aspiration biopsy, but it does not always yield a definitive histopathologic diagnosis. In order to make a conclusive diagnosis of ganglioneuroblastoma, surgical resection, followed by a comprehensive histopathological examination, is warranted.

In the literature, especially from low and middle income countries, the reported cases of ganglioneuroblastomas are infrequent and rare. In this case report, the presentation of a 4-year-old male with a neck mass to a tertiary care hospital in Pakistan is discussed. This neck mass was later diagnosed as a rare subtype of ganglioneuroblastoma, nodular ganglioneuroblastoma, which was located in the cervical region, which is an even rarer site of presentation. The aim of this report is to explore the presentation of this uncommon case of ganglioneuroblastoma, along with its' clinical features, and the surgical outcomes.

Case report: A 4-year-old male presented to the general pediatric clinic with progressively enlarging multiple neck masses on the right side over the past two years. He had no known comorbidities, and the mass was not associated with any constitutional symptoms. There were no pressure symptoms such as dyspnea or dysphagia at the time of presentation.

On examination, multiple enlarged cervical lymph nodes were palpable on the right side. The nodes were firm, with the largest measuring approximately 4 × 4 cm, while the others ranged from subcentimeter to 1.5 cm in size. None were adherent to the overlying skin. The patient had previously undergone an incisional biopsy of the neck mass at another hospital, which was reported as benign reactive lymphadenopathy.

Contrast enhanced CT and MRI imaging of the neck revealed a large well-defined isodense area seen in the posterior right neck, measuring 57 × 35 × 30 mm, showing heterogenous contrast enhancement. The lesion contained foci of calcification and demonstrated increased vascularity, with imaging features highly suggestive of a paraganglioma (Figure 1). Multiple enlarged but benign-appearing lymph nodes were also noted at levels II and III on the right side. The lesion caused splaying of the external and internal branches of the right common carotid artery and compression of the internal jugular vein (IJV). It exhibited an isointense signal on T1- and T2-weighted sequences with homogeneous intense enhancement on post-contrast sequences.

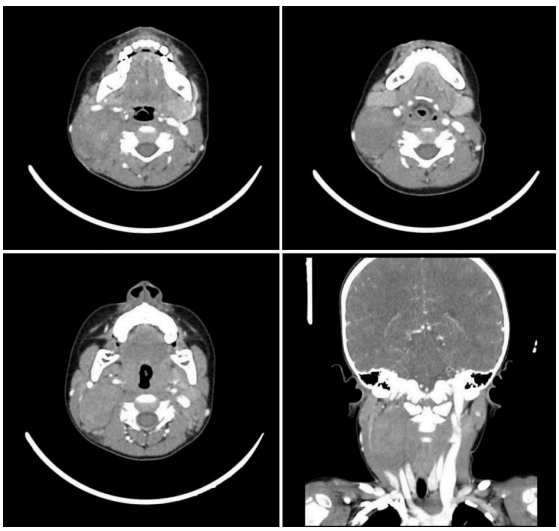


Figure 1: CT Scan Imaging

Upon request, the previously biopsied lymph node tissue blocks were re-evaluated, revealing a small focus of ganglion-like cells and Schwannian stroma, raising suspicion of metastatic ganglioneuroblastoma. A contrast-enhanced CT scan of the chest, abdomen and pelvis ruled out metastatic deposits.

Surgical excision of the tumor was carried out (Figure 2). The mass was located inside the carotid sheath, displacing the carotid artery medially and the internal jugular vein (IJV) laterally, with the mass arising from a nerve. Multiple enlarged lymph nodes were also present and excised during the procedure.

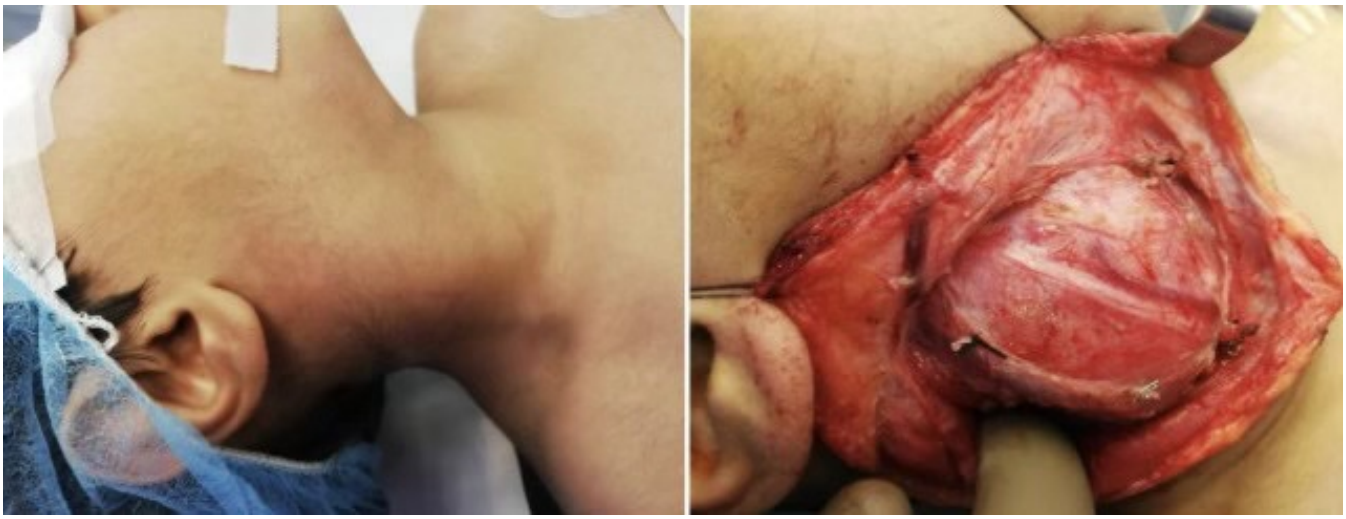
No immediate or delayed post-operative complications, including nerve weakness, were observed. Histopathological analysis confirmed the diagnosis of GNB, intermixed type. A total of 11 lymph nodes were excised, 4 of which tested positive for metastasis. The tumor resection was performed with an intact capsule, and the case was classified as having favorable histology according to the International Neuroblastoma Pathology Classification. A fluorescence in situ hybridization (FISH) study for N-MYC gene amplification was negative. The patient was followed closely during follow-up visits. Upon 18-month follow-up, the patient did not show any signs or symptoms of recurrence.

Conclusion: Ganglioneuroblastoma are classified as malignant tumors due to the presence of primitive neuroblast interspersed among mature ganglion cells. They are generally considered less aggressive compared to neuroblastomas. Reports of ganglioneuroblastoma are limited. Most patients, around 90%, are diagnosed with ganglioneuroblastoma before the age of 5, with the average age of diagnosis being about 4 years old. Rarely, patients may be diagnosed over the age of 10.

Preoperative clinical symptoms are essential in assessing patients. Peripheral GNBs of cervical origin often present with respiratory symptoms due to airway compression. These symptoms can range from mild snoring to severe respiratory distress.

Additional symptoms include dysphagia or nerve palsies, caused by the tumor's compressive effects. Specific presentations, such as Horner's syndrome or iridocyclitis, can also be diagnostic.

In the pediatric population, isolated cervical masses are a rare presentation of neuroblastic tumors. When they do occur, these masses are typically benign, with common examples being fibromas, lipomas, or hemangiomas. Malignant cervical masses are more likely to be lymphomas or leukemias. Occasionally, the malignancy may be metastatic, as seen in cases of GNB or other neural



tumors. GNBs arise along the sympathetic chain due to a developmental deficiency of neuronal cells.

While they are usually sporadic, a family history of neuroblastic tumors is significant in 1-2% of cases, with inheritance involving autosomal dominant alleles.

Daneshbod et al. reported a case in which fine-needle aspiration cytology (FNAC) successfully identified ganglioneuroblastoma, while a case series by Manjlay et al. found FNAC to be non-diagnostic. Zeng et al. recommends that for an accurate diagnosis of GNB, a core needle biopsy or immunohistochemistry should be performed prior to undergoing surgery. ERBB3 has recently emerged as a clear-cut marker of GNB in gene expression and IHC studies.Another study that focused on IHC findings revealed that positive anaplastic lymphoma kinase (ALK) mutations indicated poor prognosis in patients with GNB. Without these modalities, diagnosis remains a challenge especially due to a lack of established guidelines for these tumors. However, clinical presentation in conjunction with advanced imaging modalities can play a helpful role in guiding the diagnostic process. Among imaging techniques, CT scans are particularly valuable, offering detailed insights into the tumor's size, primary origin, extent of invasion, lymphadenopathy, and the presence of calcifications.

After the primary diagnosis is established, staging investigations such as serum catecholamines and urinary levels of homovanillic acid (HVA) and vanillylmandelic acid (VMA) can serve as biochemical markers, detecting ganglioneuroblastoma in approximately 60% of cases. For disease surveillance catecholamine levels can act as a useful indicator as they are elevated in case of recurrence.
MRI is preferred modality of investigation over CT scan for its superior diagnostic precision, offering enhanced tissue contrast and detailed visualization of tumor characteristics in the parapharyngeal space.

Managing patients with ganglioneuroblastoma necessitates a multidisciplinary approach, which includes surgical excision, chemoradiotherapy, and/or biological therapies. Several key factors influences the management option, including the patient's age, tumor stage, and spread of tumor in the neck. Surgical resection remains the cornerstone of treatment, with meticulous attention to preserving vital structures. In cases where complete excision is not achievable, chemotherapy is often employed as an adjunctive measure to mitigate residual disease. Neck lymph node dissection, particularly selective dissection, is recommended even in the absence of metastasis on imaging or clinical examination.

Chemotherapeutic regimens, including agents such as doxorubicin, cyclophosphamide, vincristine, platinum-based compounds, and etoposide, have demonstrated efficacy in treating neuroblastic tumors. Emerging therapies, including the use of immunomodulators and retinoids, offer promising potential for advancing the future treatment landscape of ganglioneuroblastoma.

In a child presenting with neck mass, ganglioneuroblastoma should be included in the differential diagnosis after ruling out common pathologies, especially in younger patients with a lesion in the parapharyngeal space. In these cases, a biopsy is the gold standard investigation to ensure an accurate diagnosis.

Informed Consent: The patient's parents consented for publication of this case report.

Conflict of Interest: None

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