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Case Report

Adult-onset ganglioneuroblastoma of the posterior mediastinum with osseous metastasis [☆]

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ABSTRACT

Ganglioneuroblastomas are a member of the neuroblastic family of tumors most commonly seen in children but they may also occur in adults. Ganglioneuroblastomas have metastatic potential and, like other neuroblastic tumors, osseous metastasis is possible. Imaging features of ganglioneuroblastomas tend to be variable. We describe a case of an adult female who developed a ganglioneuroblastoma of the posterior mediastinum that metastasized to the thoracolumbar spine, highlighting rarely documented osseous metastasis.

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Introduction

Neuroblastic tumors are predominantly pediatric burdened neural crest tumors that are rarely seen in the adult population. Neuroblastoma, a subtype of neuroblastic tumor, accounts for 7% of pediatric malignancies but is responsible for an incidence of only 1 in 10 million adults per year [1]. Ganglioneuroblastoma is a histologically different entity that demonstrates less malignant potential than neuroblastoma but part of the greater family of neuroblastic tumors [2]. Although the chest (posterior mediastinum) is the 3rd

most common site for neuroblastic tumors as a whole, irrespective of age, following the adrenal medulla and extra-adrenal retroperitoneal sympathetic ganglia, only a few cases of adult-onset ganglioneuroblastoma that were isolated to the chest have been previously reported in the literature [3–6]. Our case is a unique presentation of adult-onset ganglioneuroblastoma of the posterior mediastinum with osseous metastasis. In addition to discussing the significance and unique features of our case, this case review aims to highlight the presentation, pathophysiology and treatment of a mediastinal adult ganglioneuroblastoma found in recent literature.

[☆] Conflicts of Interest: None.

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Fig. 1 – Axial (a), coronal (b), and sagittal (c) T2 weighted MRI sequences of the posterior chest and thoracic spine demonstrate a large heterogenous right paravertebral soft tissue mass that was biopsy proven ganglioneuroblastoma.

Case Report

A 23-year-old previously healthy female presented to an outside hospital with sudden-onset of right-sided chest pain and difficulty breathing. The initial chest radiograph was remarkable for a mass in the right chest cavity. Follow-up diagnostic evaluation demonstrated a right-sided chest mass with extension to the paraspinal region without invasion of the spine. Fine needle aspiration of the mass revealed an initial diagnosis of neurofibroma. Two months later, the patient underwent partial resection of the paraspinal portion of the mass followed by a thoracotomy with near complete mass resection 5 months post-initial presentation. Residual gross tumor was reportedly left within the right chest cavity due to its proximity to vital structures and resection margins were positive for tumor. The patient was eventually discharged following a short uncomplicated hospital course.

The patient was referred to our institution's Pediatrics Hematology and Oncology Clinic for further management. Further workup at our institution included the following: whole body bone scan, metaiodobenzylguanidine scintigraphy (MIBG), Positron emission tomography- Computed tomography (PET/CT), contrast-enhanced CT of the chest, abdomen

and pelvis, contrast-enhanced MRI of the thoracic and lumbar spine, and review of the resected mass by the Pathology Department. Although the bone scan was negative for metastatic disease, MRI demonstrated an enhancing posterior thoracic mass with extension across the adjacent T7-L1 anterior vertebral bodies and into their respective neural foramina, concerning for metastatic disease versus postsurgical granulation tissue. She was started on an intense chemotherapy regimen with radiation therapy. Review of the tissue samples from the out-side hospital confirmed a diagnosis of poorly differentiating ganglioneuroblastoma, nodular subtype with low mitotic karyorrhectic index and an unfavorable histopathology by the International Neuroblastoma Pathology Classification grading system. The patient underwent a PET/CT which showed uptake within the left femur which was concerning for malignancy. At this point, the patient was lost to follow-up and was not seen until 8 years later when she presented to our Emergency Department for burning chest pain. A lytic lesion was found in the left femur, and she subsequently underwent bone biopsy and was treated with internal fixation. The bone biopsy of the lesion in the left femur was consistent with a granular cell tumor compatible with a Schwannian tumor that has un-

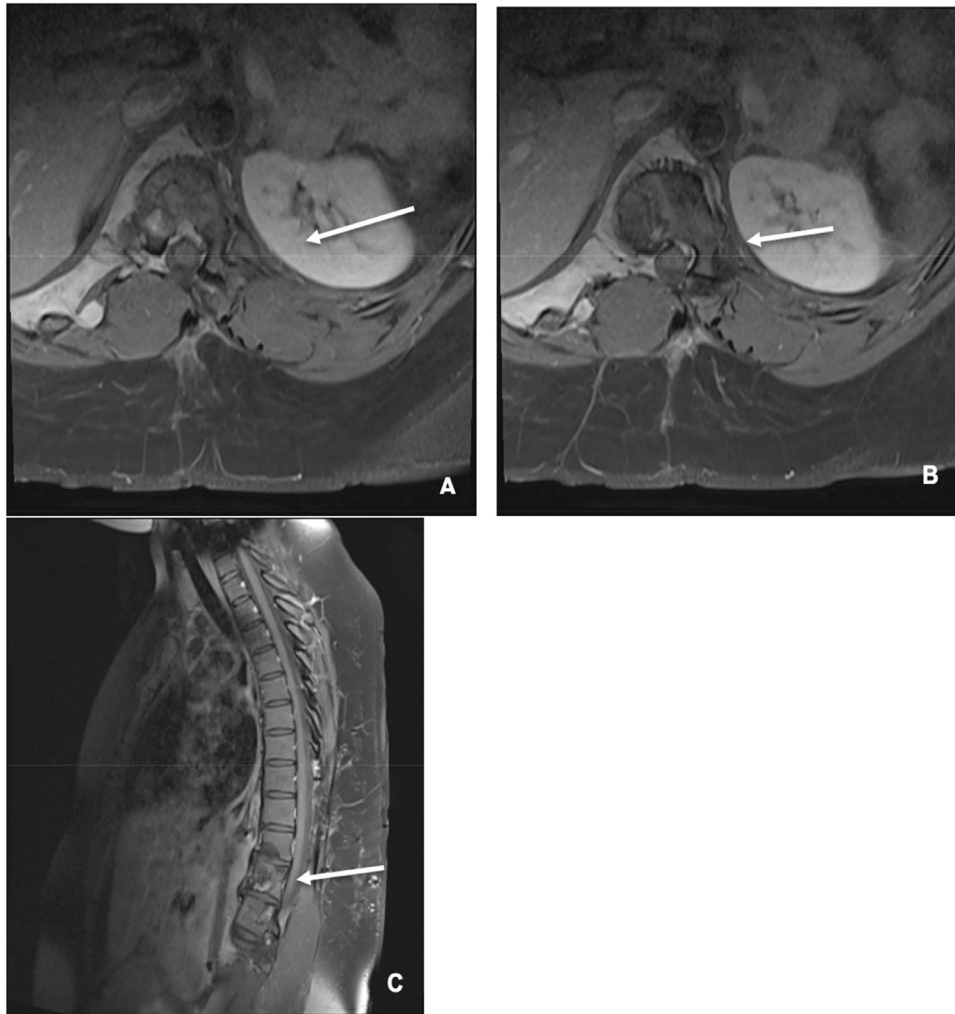


Fig. 2 – Axial (a & b) and sagittal (c) contrast enhanced fat suppressed T1 weighted MRI sequences of the posterior chest and thoracic spine demonstrate surgical changes of multilevel laminectomies with new abnormal heterogeneity of the T11 and T12 vertebral bodies, consistent with metastatic disease.

dergone degeneration and thought to be a degenerative form of Schwannian and other neural tumors.

Subsequent diagnostic evaluation demonstrated disease progression. Noncontrast and contrast-enhanced MRI of the spine revealed a right paraspinal enhancing mass displacing the diaphragmatic crus inferiorly and extending from the T8-T9 disc space to the L1-L2 disc space (Fig. 1). Postsurgical changes of laminectomy involving the T8-L1 levels were observed, with heterogenous destructive lesions of the T11 and T12 vertebral bodies that were consistent with metastatic disease (Fig. 2). Additionally, a PET/CT demonstrated multiple FDG-avid foci, most pronounced at the T11 and T12 vertebral bodies, left lesser trochanter/proximal femur (corresponding radiograph Fig. 3), and right iliac bone (Fig. 4). Finally, an MIBG examination demonstrated no suspicious focus of radiotracer uptake (Fig. 5).

Review of the pathology specimen of the posterior mediastinal mass excision revealed ganglioneuroblastoma, nodular subtype, poorly differentiating, with low mitotic-

karyorrhectic index (MKI: <100 per 5000 cells :<2%), with unfavorable histopathology (Figs. 6-9).

Discussion

Ganglioneuroblastoma differs histopathologically from neuroblastoma in that it contains an increased proportion of Schwannian stroma/spindle cells (>50% of the tumor area) and neuropil, along with microscopic foci or collections of neuroblasts with recognizable ganglion cells or their immediate precursors [2,3]. It is characteristically a stage I/II benign tumor in children, however, in adults it is more likely stage III/IV due to its indolent course resulting in delayed diagnosis. Other neurogenic tumors of the thorax include ganglioneuroma. Neuroblastoma and ganglioneuroma are on the malignant and benign spectrums of malignant potential, respectively. Ganglioneuroblastoma is thought to represent the inter-



Fig. 3 – Radiograph of the left femur demonstrating an expansile intramedullary lucent lesions within the proximal diaphysis.

mediate malignant potential. Typical presenting symptoms of ganglioneuroblastoma are dependent on the region of origin, including prevascular, middle mediastinal, or paraspinal location. Considering the anterior origin with posterior/paraspinal extension of our patient's mass, symptomatology included chest pain and shortness of breath, however, other presenting symptoms may also include associated Horner's Syndrome (ptosis, myosis, anhidrosis), stridor, or other secondary mass effect [7].

Diagnostic imaging findings of an adult pulmonary GNB are variable [8]. However, contrast-enhanced CT imaging will demonstrate a heterogeneous mass within the anterior and/or posterior mediastinum. Special attention should be paid to adjacent vital structures to evaluate for sequelae of mass effect—close inspection of the heart, aorta, trachea, and spine should be performed. CT may also reveal an irregular, cystic, poorly margined, locally invasive mass with presence of metastatic disease [9].

Contrast-enhanced MRI imaging also demonstrates a heterogeneously enhancing soft tissue mass, with similar distribution as previously described [10]. Apparent diffusion coefficient has been shown to be a useful sequence in differentiating neuroblastoma from ganglioneuroblastoma, suggest-

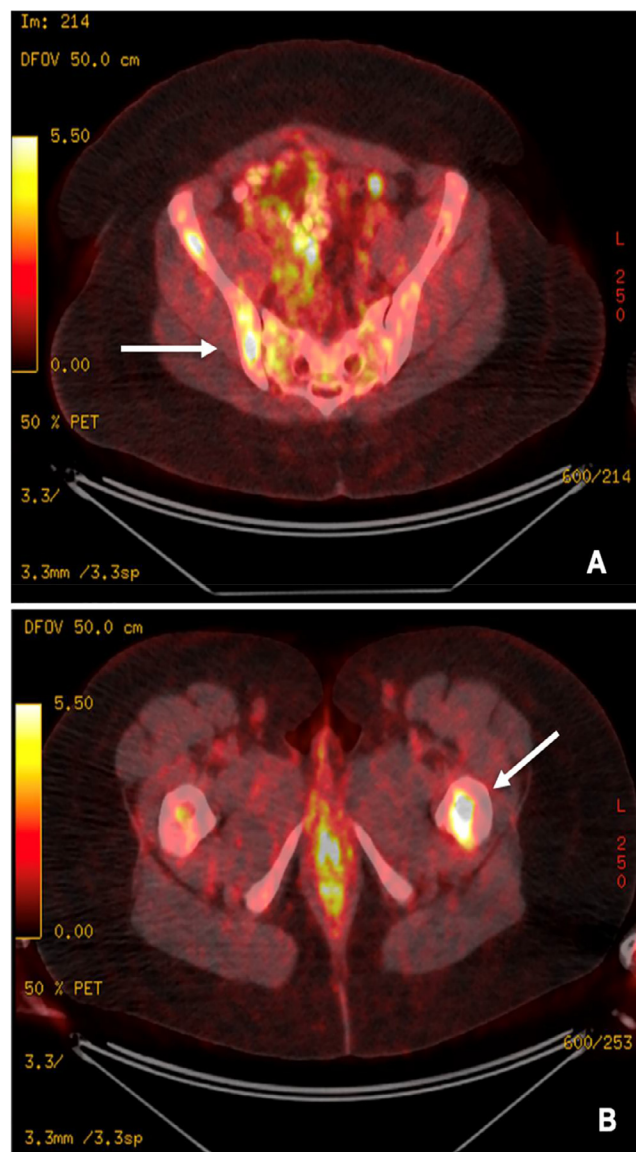


Fig. 4 – Fused PET/CT axial images of pelvis at the levels of the sacroiliac (a) and proximal femur (b) demonstrate FDG-avidity at the left lesser trochanter and bilateral iliac bones, consistent with metastatic disease.

ing that an apparent diffusion coefficient value greater than $1.1 \times 10^{-3} \text{ mm}^2/\text{s}$ favors a diagnosis of ganglioneuroblastoma/ganglioneuroma [11].

Nuclear medicine studies are also useful diagnostic tools. Given MIBG's role as a precursor of norepinephrine, an MIBG scan is incredibly useful and can aid in diagnosing metastatic lesions to the skeletal structures. PET/CT is an additional tool that can aid in diagnosing distant metastasis.

Treatment varies with tumor involvement and histopathology but typically includes a combination of surgical debulking, chemotherapy, and radiation.

Neuroblastoma is typically considered to demonstrate the most metastatic potential in the neuroblastic tumors and bone is the most common site of metastasis [3]. Neuroblas-

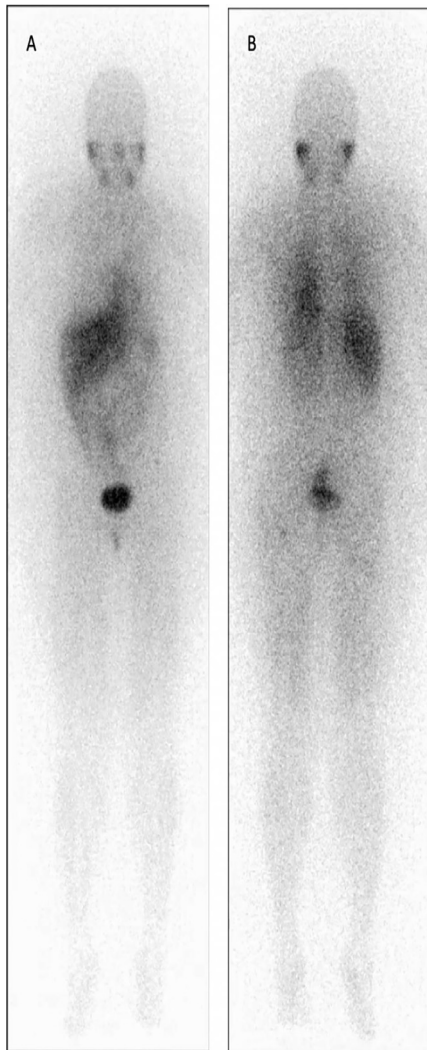


Fig. 5 – Metaiodobenzylguanidine scintigraphy of the whole body, anterior (a) and posterior (b). Images demonstrate no suspicious focus of radiotracer activity. Indeterminant uptake noted within the liver, thought to be false positive. Pathology Slides:

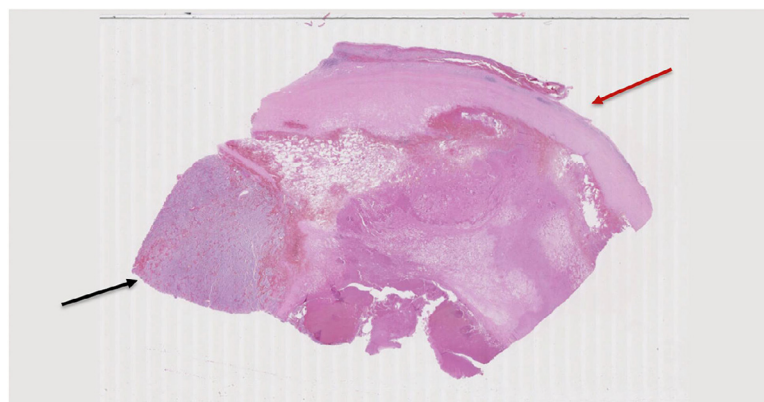


Fig. 6 – H & E stain, low power view (3x): Posterior mediastinal mass, excision, with immature component (neuroblastoma) (black arrow), with mature component (red arrow).

tomas and ganglioneuroblastomas are both viewed to have metastatic potential but neuroblastoma greater than ganglioneuroblastoma [3]. Ganglioneuroblastomas are viewed to be the most mature of the 3 neuroblastic tumors and viewed to be benign [3]. A case report found bone metastasis in an adult with adrenal ganglioneuroblastoma [12]. Another case reports lytic and sclerotic bone metastasis of ganglioneuroblastoma in a child [13]. We did not find parallel cases in the literature of adult pulmonary ganglioneuroblastoma that show evidence of metastasis [4–6]. Our case illustrates the rare occurrence of distant osseous metastasis in ganglioneuroblastoma. Attention to the bony structures should be emphasized, particularly with high-grade unfavorable histopathology.

Conclusion

Ganglioneuroblastomas are malignancies in the neuroblastic family of tumors that are typically seen in the pediatric population. Ganglioneuroblastomas are considered to have an intermediate metastatic potential between neuroblastoma and ganglioneuroma from greatest to least on the spectrum of metastatic potential, respectively. We present here a unique case of an adult pulmonary ganglioneuroblastoma that demonstrates skeletal metastasis. To the best of our knowledge no previously reported cases in the literature have shown skeletal metastasis from an adult pulmonary ganglioneuroblastoma. Clinicians should be aware of the possibility of ganglioneuroblastoma development in adult populations and its malignant potential.

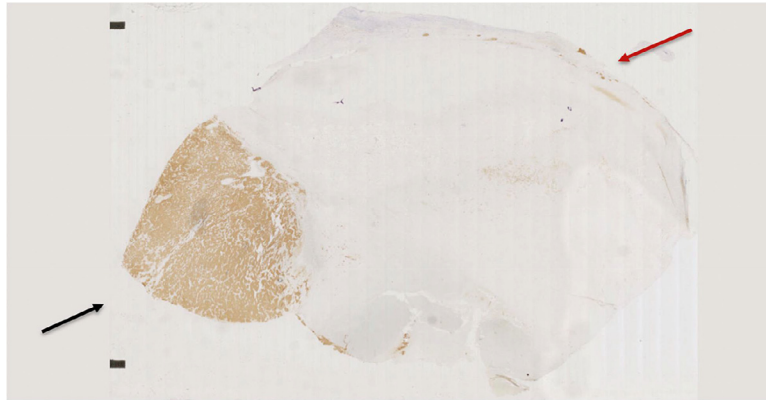


Fig. 7 – NSE stain, low power view (3.5x): Posterior mediastinal mass, excision, with immature component (neuroblastoma) (black arrow) and mature component (red arrow).

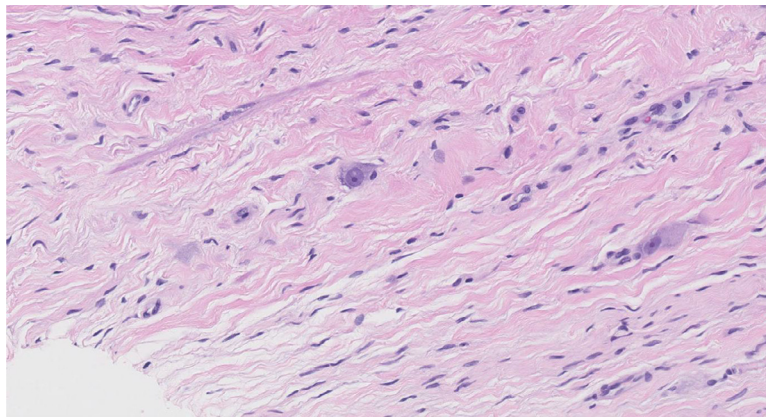


Fig. 8 – H & E stain, low power view (200x): Paraspinal pleural space, core needle biopsy, showing Schwannian stroma rich lesion with rare ganglion cells.

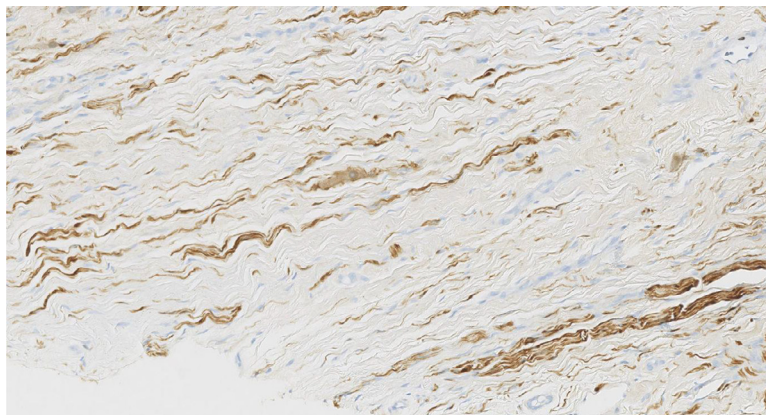


Fig. 9 – S-100 stain, low power view (140x): Paraspinal pleural space, core needle biopsy, showing Schwannian stroma rich lesion with rare ganglion cells.

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