Case Report

A Rare Case of Giant Mediastinal Ganglioneuroma in A 3-year-old

Harry Galuh Nugraha, MD, Riza Putri Aulia Hernowo, MD*

Department of Radiology, Faculty of Medicine Universitas Padjadjaran, Jl. Pasteur No. 38, Pasteur, Kec. Sukajadi, Kota Bandung, Bandung, Indonesia, 40161

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ABSTRACT

Ganglioneuroma is a rare, differentiated, and benign neurogenic tumor that could grow into a huge size with minimal or no symptoms at all. Ganglioneuroma is typically found in older children or adults and is commonly detected within the posterior mediastinum (other than retroperitoneal). Here, we present a case of a 3-year-old patient with shortness of breath, and radiological examination showed a giant mediastinal tumor which proved to be a ganglioneuroma after histopathological examination. This study highlights the possibility of ganglioneuroma occurring in younger children and the role of imaging in assessing ganglioneuroma as a posterior mediastinal tumor.

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Introduction

Ganglioneuroma is a rare tumor and belongs to the neurogenic tumors, which are the most common tumors occupying posterior mediastinal masses in children [1]. Ganglioneuroma commonly arises from sympathetic ganglion cells and it is a differentiated and slow-growing type [2]. It is usually discovered incidentally in older pediatric patients or adults as it is typically asymptomatic; however, it can grow into a massive size and cause compression symptoms [3]. Radiological examination is essential to localize and characterize the tumor and the surrounding structures. In this report, we present a young child with a giant posterior mediastinal ganglioneuroma who presented with dyspnea; together with the radiological and pathological findings.

Case presentation

A 3-year-old girl presented to our emergency room with shortness of breath. The patient had been relatively well before and only developed dyspnea within the last few months. The patient had no fever, night sweats, loss of appetite, weight loss, vomiting, flushing, hypertension, nor abdominal pain. The clinical examinations showed no abnormality except for low oxygen saturation. Routine laboratory examinations were

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* Corresponding author.
E-mail address: rizahernowo2@yahoo.com (R.P.A. Hernowo).

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performed and the results were within normal limits. Frontal chest x-ray revealed an opaque right hemithorax and scoliosis (Fig. 1), which prompted further investigation with Computed Tomography (CT) scan. CT scanning with intravenous contrast revealed a well-circumscribed solid mass occupying the right posterior mediastinum, with measurement of 10.21 (W) x 9.19 (L) x 11.75 (H) cm, extending from first thoracic vertebrae until low cardiac level (Fig. 2). The mass appeared hypodense and mildly heterogeneous with punctate calcifications. The mass had no connection with the trachea and bronchi. The mass appeared to be pushing mediastinal organs and trachea to the left side, with no evidence of invasion into lung parenchyma, mediastinal organs, or chest wall. (Fig. 3) With contrast material, the mass demonstrated mild heterogeneous contrast enhancement and showed no vascular involvement. CT scanning showed no spinal destruction; however, nerve involvement could not be assessed as Magnetic Resonance Imaging (MRI) examination was not performed.

Given the size of the mass and the symptoms due to the mass compression, surgical resection was recommended. The patient was placed in the left lateral decubitus position and a right-sided posterolateral thoracotomy was performed under general anesthesia (Fig. 4). A huge mass was found to be occupying almost the whole right hemithorax, pushing the lungs to the inferior, and was capsulated by the pleura with no invasion to the adjacent structures. Gross examination revealed a solid capsulated mass with whitish color on the cut surface (Fig. 5) weighing 499 cm. microscopic evaluation showed mature, well-differentiated ganglion cells; uniform spindle cells, and Schwannian stroma (Fig. 6). There was no feature of malignancy and no mitotic nor apoptotic activity was observed. After the operation, the patient showed stable condition and chest radiograph revealed expansion of most of the right lung (Fig. 7). The patient was then discharged home with no complications.

Discussion

Ganglioneuroma belongs to the family of neurogenic tumors and it arises from neural crest cells, specifically the sympathetic ganglion cells [2]. Ganglioneuroma shares a common histogenic lineage with neuroblastoma and ganglioneuroblastoma; and these tumors represent a continuum of maturation and differentiation, with ganglioneuroma at the most benign and differentiated end of the spectrum [1,2,4]. Because neuroblastoma and ganglioneuroblastoma can mature into ganglioneuroma, ganglioneuroma may arise de novo or from differentiating neuroblastoma or ganglioneuroblastoma [3,5,6].
Ganglioneuroma consists of mature ganglion cells, Schwann cells, nerve fibers, and mucous matrix [7]. The microscopic feature of ganglioneuroma is the presence of mature ganglion cells, which can be detected by the abundant and granular eosinophilic cytoplasm, large nuclei, and prominent nucleoli [2,7,8]. The Schwannian stroma is identified by its elongated uniform nuclei and ill-defined cytoplasm [8]. Ganglioneuroma has no immature elements (neuroblasts), atypia, mitotic figures, intermediate cells, or necrosis; and the presence of these features precludes ganglioneuroma [6,7,9,11].

Ganglioneuroma can arise anywhere in the place of peripheral autonomic ganglion cells. However, it most commonly occurs within the posterior mediastinum and retroperitoneum, arising from the sympathetic ganglia running parallel to the vertebral column [2,10]. Other less common locations include visceral ganglia, parapharyngeal region, cranial nerve ganglia, retropharyngeal region, or adrenal medulla [2,4,5]. Involvement of the central nervous system has been reported but it is rare [9,11]. Ganglioneuroma is often seen in older children or adults, however, it can occur in all age groups with no difference in distribution between males and females [3,7,9]. The median age of patients with ganglioneuroma varies between studies, ranges from seven to ten years old [5,6,12]. This age predilection may help to differentiate ganglioneuroma from neuroblastoma, which is more often seen during the first few years of life [13].

Ganglioneuroma typically extends to three to five vertebrae but due to its slow growth and benign nature, ganglioneuroma may develop into a massive size [3,14,15,16]. Ganglioneu-
Ganglioneuroma is usually asymptomatic until it grows bigger and causes pressure effects on the adjacent structures; resulting in shortness of breath, cough, globus sensation, and Horner syndrome [3,5,8]. Some cases of mediastinal ganglioneuroma can extend into the spinal canal resulting in neurologic symptoms and painless spinal deformity [17]. Ganglioneuroma may also expand to the nerve root thus destroying the lateral and anterior vertebral elements, which results in scoliosis, as well as displacing the adjacent skeletal structures [15,17].

Ganglioneuroma may also secrete a sufficient amount of catecholamines that manifests with several symptoms of catecholamine excess, such as labile hypertension and flushing [3,4]. Supposedly, ganglioneuroma has very little or no metabolic activity as it was hypothesized that more mature tumors have more mature biologic behavior, and should any catecholamine be secreted, it will be metabolized in the tumor [3,5,6]. However, studies show that some patients with ganglioneuroma have elevated catecholamine levels, such as VMA (vanillylmandelic acid) or HVA (homovanillic acid), which is presumed to be associated with the increased size of the tumor [3]. The use of Scintigraphy-Iodine-tagged mediadobenzylguanidine (MBG), a catecholamine analog, may not be useful in diagnosing ganglioneuroma. Even though MBG has high sensitivity and specificity for tumors containing sympathetic tissue, it has no capability in differentiating the type of tumor in which the uptake occurs [6].

Radiological examinations help to determine the tumor location and characteristics; however, most neurogenic tumors have similar imaging features thus histological examination is still the only way to confirm the diagnosis. Radiographically, intrathoracic ganglioneuroma will be identified as a well-defined mass located in the posterior mediastinum, and as it follows the direction of the sympathetic chain, it will be located anterior and lateral to the vertebral column, revealing a craniocaudal length to major axis (CC/M) ratio greater than 1 [2,10,12,18]. Complications such as rib spreading and foraminal erosion may be seen on plain radiographs [5]. By ultrasonography, ganglioneuroma is identified as a homogeneous, hypoechoic, well-circumscribed mass [6].

More advanced examinations including CT and MRI are usually performed to assist in evaluating the extent of disease, establishing a differential diagnosis list, and judging the treatment response [1]. On unenhanced CT, ganglioneuroma may be homogeneous or heterogeneous and has low internal attenuation relative to muscle due to the abundant myxoid matrix, but may also appear slightly hyperattenuating if it is dominated by ganglion cells [12,19]. Approximately 20% of ganglioneuromas have calcifications; and to distinguish it with neuroblastoma or ganglioneuroblastoma which has coarse calcifications, fine punctate calcifications are more often seen in ganglioneuromas [7,12,15,20,21].

In MRI, the appearance of ganglioneuroma may be less specific than CT [20]; however, MRI is more superior in evaluating chest wall involvement and identifying intraspinal extension, which is quite rare [1,10,15]. This makes MRI more helpful in assessing treatment response and for surgical considerations [1]. In MRI, ganglioneuroma shows as a homogenous mass with intermediate signal intensity on mostly all sequences. However, in T2-weighted images, ganglioneuroma occasionally shows heterogeneous intermediate to high signal intensity, depending on the proportion of myxoid stroma, cellular components, and collagen fibers within the tumor [2,12,15,22]. Intermediate to high signal intensity represents areas with high cellularity and more collagen, while markedly high intensity indicates higher myxoid stroma components and low cellularity and collagen amount [23]. Ganglioneuroma may also show a “whorled appearance”, which is due to curvilinear bands of low signal intensity representing the interlacing bundles of Schwann cells and collagen fibers within the mass [15,24,25].

Following contrast administration, ganglioneuroma shows mild to moderate enhancement on CT scanning; and this is different with neuroblastoma which demonstrates strong uptake of contrast [7,20,21]. In MRI, there is a poor early enhancement on dynamic MRI and higher accumulated contrast medium in non-dynamic MRI due to a high proportion of myxoid matrix and enlarged extracellular space [20]. Delay enhancement may occur due to blocked perfusion of contrast agents by mucus [19].

The presence of fat inside the tumors has been reported in earlier studies. One mechanism postulated is that the tumor had presented before and some of it is replaced by fat after being degenerated, and another mechanism is that the tumor involves the surrounding fat component, especially in the paravertebral region [25]. Ganglioneuroma with fat will appear as an area with high signal intensity on both TI-T2 and low signal intensity on the fat-suppressed post-contrast images [2,7]. This presence of fat helps differentiate ganglioneuroma from other tumors in posterior mediastinum, especially if the mass clearly enters the spinal canal [2].

Ganglioneuroma requires complete surgical resection when possible due to the possibility of this tumor growing aggressively and invades the adjacent structures [4]. Despite being benign, surgery is suggested in patients who have symptoms, encroachment on the vertebral foramina, and increased catecholamine release, as well as in patients with significant size of tumor. Laminecetomy is indicated if there is intraspinal involvement [26]. No medical treatment is indicated in ganglioneuroma. Prognosis is usually good as ganglioneuroma rarely becomes malignant or metastasize. Local recurrence is rare but radiologic surveillance after resection is still recommended [4]. Complications may only occur as a result of the surgery; however neurogenic symptoms, such as due to spinal cord compression, may not be reversed after the removal of the tumor [6].

In this report, the patient came to the emergency room with shortness of breath. The result of the chest radiograph and CT scanning suggested that there was a large mass occupying the posterior mediastinal region that it compressed the adjacent structures. In pediatric patients, neurogenic tumors are the most common and other possible diagnoses include bronchogenic cyst, enteric cyst, or meningocele [27]. Among other neurogenic tumors, ganglioneuroma is more often seen in older children but is not limited to any age group, thus the patient's demographic data has little value in narrowing down the differential diagnoses.

Plain radiograph in this patient shows a huge opacity in the left hemithorax with the heart pushed to the right and scoliosis, indicating a massive mediastinal mass. Further examination using CT scanning revealed the presence of a true...
A posterior mediastinal mass which is heterogeneous and low-attenuating with a speck of calcifications and mild contrast enhancement. These characteristics support the diagnosis of neurogenic tumors, especially ganglioneuroma by judging the size of calcifications. MRI should be done to further assess the nerve involvement and the true etiology of scoliosis; however, it was not done due to the urgency of the symptoms and the patient's condition.

Despite the imaging examinations, the true diagnosis of ganglioneuroma is made by histopathological examination that revealed mature well-differentiated ganglion cells. The finding of mature ganglion cells directly precludes other neurogenic tumors. This diagnosis is in accordance with the lack of symptoms, that the patient only complained of shortness of breath as the mass had grown into a massive size and compressed the adjacent structures.

**Conclusion**

Ganglioneuroma is one of the rare neurogenic tumors occurring in the posterior mediastinum, which may be a diagnostic challenge both clinically and imaging. This report demonstrated a mediastinal ganglioneuroma in a patient presenting with shortness of breath. The tumor in our patient was unusual as it occurred in a young pediatric patient and the size was massive. Even though the confirmed diagnosis was made by histopathological examination, preoperative imaging examinations help to determine the location, assess the mass characteristics, and choose the appropriate treatment options.

**Patient Consent Statement**

Patient consent received for this case report.

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