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Case report

Primary lung and pleural malignancies in children: Imaging of a case series

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Early diagnosis of primary lung and pleural malignancies is a challenge because it is extremely rare in children. The patient often presents with metastatic disease and non-neoplastic lesions. Clinical detection and imaging studies are nonspecific findings and may be indistinguishable from other lung malformations, resulting in a delay in diagnosis and treatment and an increase in tumor morbidity and mortality. We present four cases of children whose clinical presentation and initial imaging had suspicious abnormalities and were eventually revealed to be primary lung and pleural malignancies. The literature on primary lung and pleural malignancies is also briefly reviewed.

Keywords: Children, malignant mesothelioma, lung cancer, lung tumor, pediatric, pleural malignancy.

Primary lung and pleural malignancies are rare in children. The patient often presented with an inflammatory lesion/congenital lung neoplasm or metastasis disease. The ratio of primary lung malignancy to metastasis to inflammatory or congenital premalignant tumors is reported to be 1:5:60. [1 - 4] Additionally, primary lung and pleural malignancies may be nonspecific clinical symptoms and imaging findings that are undistinguished from more common congenital malformations, leading to delay in diagnosis. Therefore, imaging findings correlated with histopathological features are more helpful to characterize diseases and guide clinical management.

Despite the rarity of primary lung and pleural malignancies in children, early diagnosis is important to improve prognosis and prevent life-threatening complications. Most of the children in this collective series with primary lung and pleural malignancies have been seen at our institute for more than five years. The significant clinical, radiographic, and histopathological abnormalities are discussed.

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Case presentation

Case one

A 10-year-old boy with no known underlying disease, who presented fever, dry cough, and weight loss for 1.5 months, was admitted due to shortness of breath and hemoptysis. Physical examination revealed a decrease in breath sound in the right lung. His chest radiography showed mass-like opacity in the upper and middle right hemithorax with evidence of right lung volume loss and narrowing of the right bronchus intermedius **(Figure 1A).** Then he underwent computed tomography (CT) of the chest and entire abdomen. The study revealed a heterogeneous enhancing large lobulated mass with internal calcification involving the anterior and middle mediastinum, as well as right upper and middle lobes **(Figure 1B).** This mass also obliterated the upper lung and invaded the middle lobar bronchi, and the SVC and right pulmonary artery directly **(Figure 1C-E)**. At the same time, the presence of an enlarged subcarinal node and metastatic nodules in the liver was noted **(Figure 1F).**

The core needle biopsy showed a malignant small round cell tumor, and the immunohistochemical study revealed Ki 67 positive in almost tumor cells. The diagnosis was concluded as neuroendocrine carcinoma, most likely small cell carcinoma, and differential diagnosis in atypical carcinoid tumor.

He was treated with chemoradiation (carboplatin and etoposide); unfortunately, he developed brain metastasis eight months later. With palliative treatment, he passed away a few months after that.

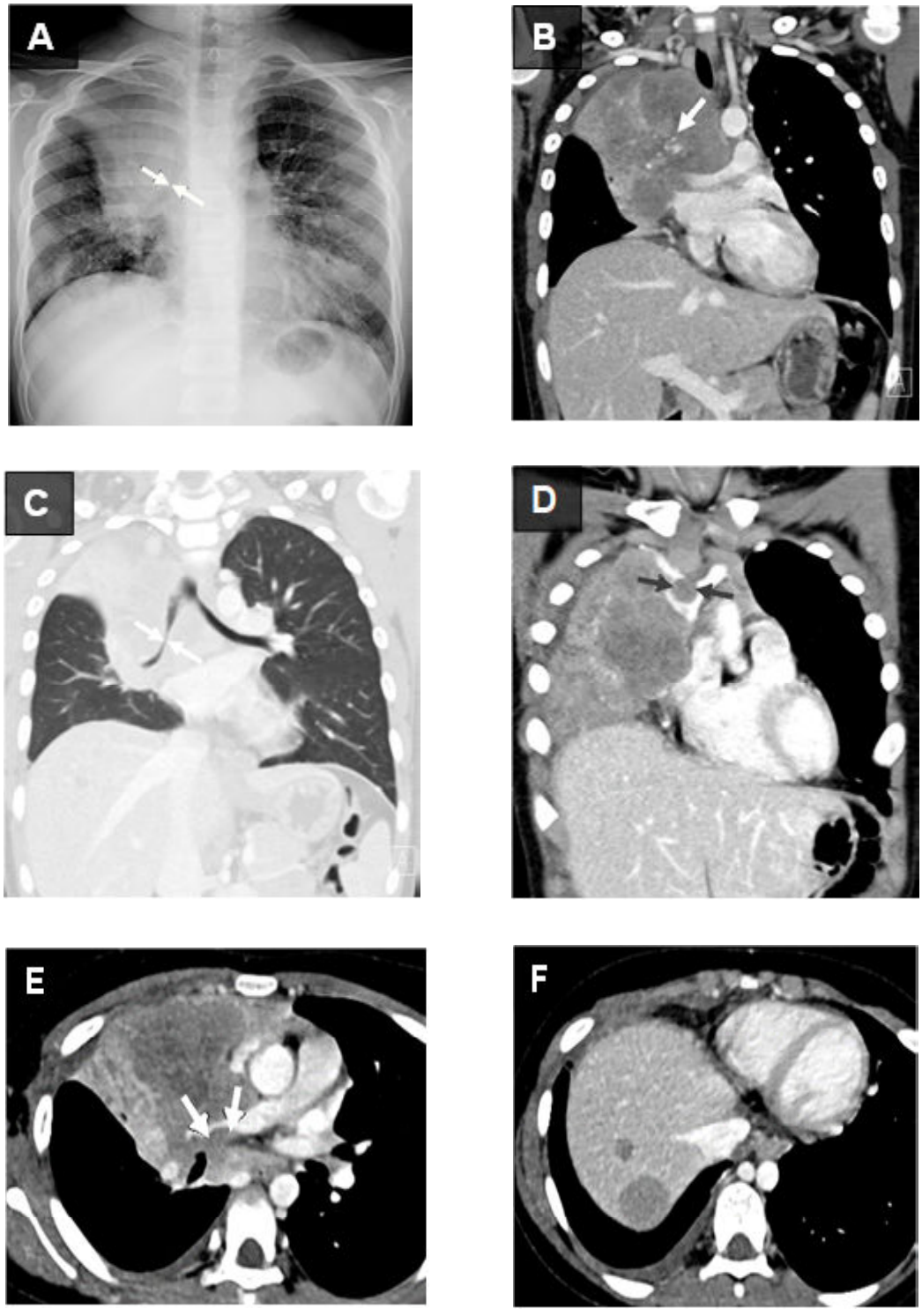

Figure 1. A 10-year-old boy with shortness of breath and hemoptysis. **(A)** Chest radiography showed mass-like opacity in the upper and middle right hemithorax with narrowing of the right bronchus intermedius (arrow) and evidence of loss of volume in the right lung. Subsequent chest CT revealed a heterogeneous enhancing large lobulated mass with internal calcification (arrow) involving the anterior to middle mediastinum, as well as right upper and middle lobes; **(B)** This mass obliterated the right upper and middle lobar bronchi; **(C)** and invaded directly the SVC (arrows in **D**) and the right pulmonary artery (arrows in **E**). Presence of subcarinal nodal metastases **(E)** and liver metastases **(F)**.

Case two

A 14-year-old girl presented with chronic cough and weight loss for 2 months that did not respond to oral antibiotic therapy. Physical examination revealed a decrease in the breath sound of the left lung. The chest radiograph showed near-total opacity of the left hemithorax without mediastinal shift **(Figure 2A).** Chest CT demonstrated the heterogeneous enhancing soft tissue mass that occupies the entire left upper lung (LUL) with left main bronchus obliteration, as well as left pulmonary artery and left superior pulmonary vein invasion **(Figure 2B)**. Bronchoscopy demonstrated an external compression obstructive LUL bronchus and an irregular nodular surface of the endobronchial mucosa that suspected endobronchial metastasis, which was biopsied with bronchial wash. The girl also underwent chest magnetic resonance imaging (MRI) **(Figure 2C-E),** which revealed a large intrapulmonary mass in LUL, showing an intermediate signal intensity on the T1-weighted image and hypersignal intensity on the T2-weighted image. After administration of the gadolinium-based contrast agent, there was a heterogeneous enhancement of the mass. Invasion of the left bronchus, left pulmonary artery, and left superior pulmonary vein was observed. The bone scan and brain MRI showed no evidence of metastasis. The pathological report of the biopsy sample revealed a malignant small round cell tumor. Post-adjuvant therapy consisted of radiation and chemotherapy with a regimen of cisplatin and etoposide. She was lost to follow-up after seven months of the last chemotherapy.

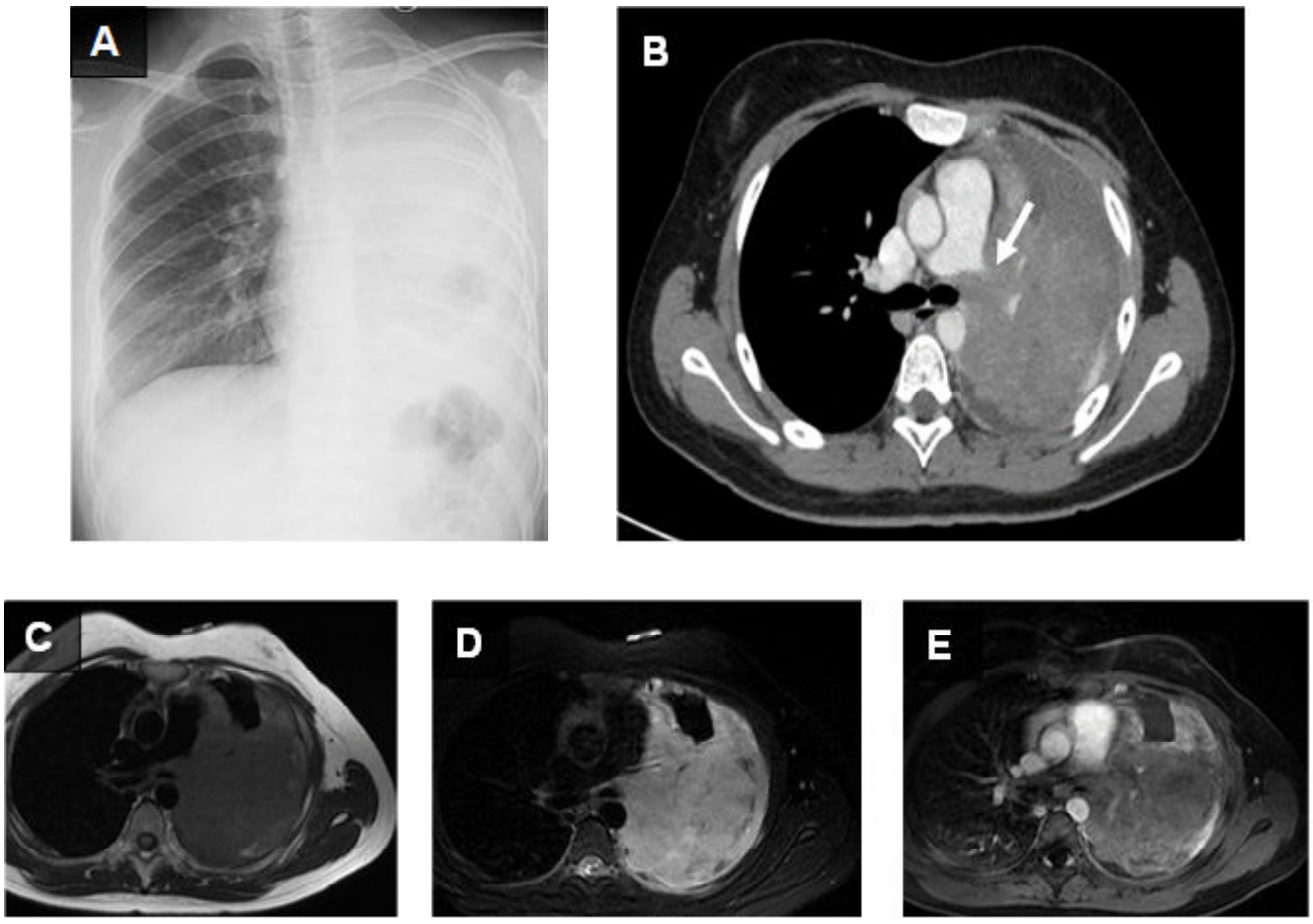

Figure 2. A 14-year-old girl presented with chronic cough and weight loss. **(A)** The chest radiograph showed a near-total opacity of the left hemithorax without mediastinal shift. **(B)** Chest CT demonstrated the heterogeneous enhancement of the soft tissue mass that occupies the entire LUL and obliterates the left pulmonary artery (Arrow). MRI of the chest revealed a large intrapulmonary mass in LUL, showing intermediate signal intensity on the T1-weighted image **(C)** and hypersignal intensity on the T2-weighted image **(D)**. After administration of the gadolinium-based contrast agent, there is a heterogeneous enhancement of the mass **(E)**. Note a small left pleural effusion.

Case three

A 14-year-old boy was evaluated for complaints of prolonged fever, cough, weight loss, and bilateral cervical lymphadenopathy. The initial chest radiograph revealed diffuse reticulonodular opacities in both lungs and bilateral thickenings of paratracheal soft tissue **(Figure 3A)**. The boy underwent chest CT **(Figure 3B-C),** which revealed enhancing matted mediastinal nodes with extensive acute thrombosis of the SVC and bilateral brachiocephalic and subclavian veins. There were diffuse irregular thickenings of the interlobular septa, thickening of the peribronchial wall, and multiple focal nodules and masses in both lungs, indicating pulmonary lymphangitic carcinomatosis. There was no malignant lesion in other parts of the body during initial staging. A biopsy sample of the supraclavicular mass showed an atypical epithelioid cell neoplasm, especially carcinoma, and the pathological review indicated adenocarcinoma. Systemic chemotherapy, the regimen for primary lung adenocarcinoma, was initiated. He did not respond well to treatment and finally developed progression of the disease **(Figure 3D)** and died within two months after diagnosis.

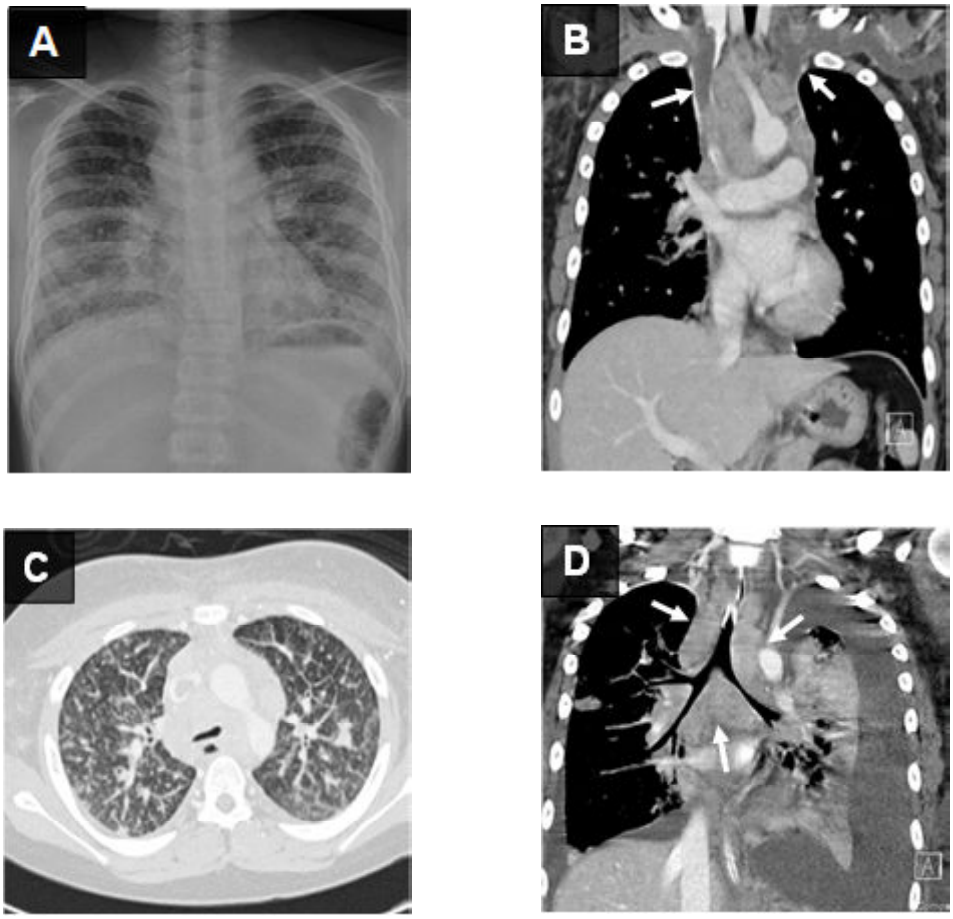

Figure 3. A 14-year-old boy presented with prolonged fever, cough, weight loss, and bilateral cervical lymphadenopathy. **(A)** The initial chest radiograph revealed diffuse reticulonodular opacities in both the lungs and the bilateral paratracheal soft tissue. Coronal chest CT; **(B)** revealed enhanced matted mediastinal nodes with extensive acute thrombosis of the SVC and bilateral brachiocephalic and subclavian veins **(arrows).** Axial lung window CT; **(C)** found diffuse irregular interlobular septal thickenings, peribronchial wall thickening, and multiple focal nodules and mass in both lungs, indicating pulmonary lymphangitic carcinomatosis. After two months from diagnosis; **(D)**, the progression of the disease was documented as an increase in the size of the matted mediastinal nodes **(arrows),** total atelectasis of the left lung, and the development of a bilateral pleural effusion (malignant pleural effusion).

Case four

A 12-year-old boy presented with chronic cough, progressive dyspnea, and chest pain. The patient underwent a chest CT outside the institution that found a multiloculated hydropneumothorax with multiple septations and multiple necrotic lymph nodes in the left supraclavicular and mediastinal nodes. The patient was referred to King Chulalongkorn Memorial Hospital and his initial radiograph revealed moderate left pneumothorax and minimal left pleural fluid after placement of the left intercostal drainage **(Figure 4A)**. He was sent to perform an ultrasound of the left lower neck and showed a heterogeneous mixed solid and cystic mass, predominantly solid, in the anterior mediastinum and the left side neck **(Figure 4B)**. The next day, a chest MRI was performed showing the lobulated infiltrative mass in the left apical hemithorax and the left lower neck. This lesion had slightly hypersignal intensity on the T1-weighted image, bright signal intensity on the T2-weighted image, and intense enhancement after injection of a gadolinium-based contrast agent **(Figure 4C-E)**. These findings were diagnosed with a venolymphatic malformation. Then Tc-99m dextran (lymphatic) was performed and focal radiotracer accumulation was found in the left supraclavicular region, consistent with the provisional diagnosis of lymphatic malformation.

The patient had wedge resection of the left upper lobe, mediastinal cyst resection with parietal pleurectomy in the left upper hemithorax. Pathological review indicated malignant neoplasm, most likely mesothelioma with invasion of the lung parenchyma and lymph node. Immunohistochemistry was compatible with mesothelioma. Left pleuro-pneumonectomy surgical treatment followed by adjuvant chemoradiation therapy was done with good control. Five years later, he developed hoarseness and dysphagia. The mass of the left neck increased in size and was diagnosed as a recurrent disease. He passed away eight months after the last treatment.

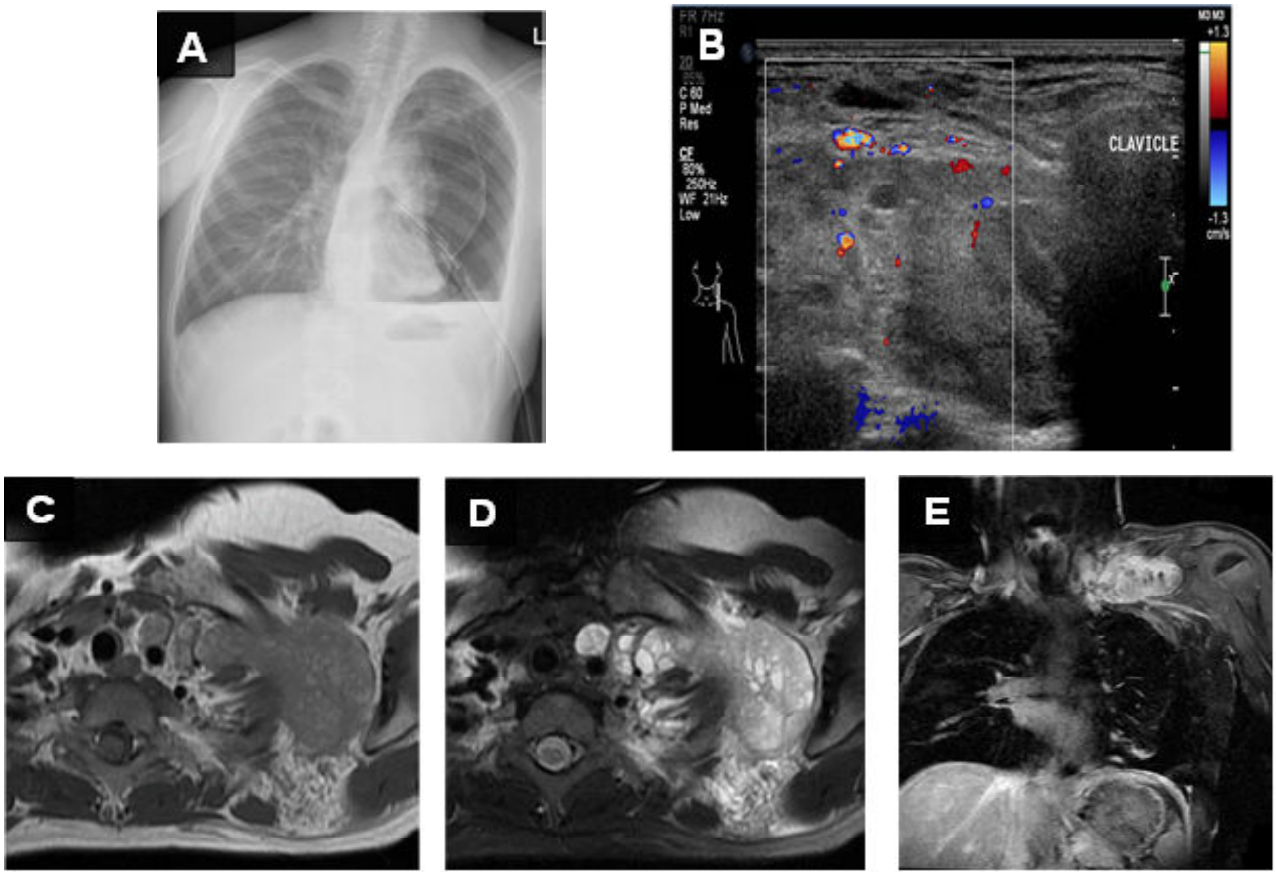

Figure 4. A 12-year-old boy had chronic cough, progressive dyspnea, and chest pain. **(A)** The initial radiograph revealed moderate left pneumothorax and minimal left pleural fluid after placement of the left intercostal drainage. **(B)** Subsequent ultrasound found heterogeneous echogenic solid and cystic mass, predominantly solid, in the anterior mediastinum and the left side of the neck. Chest MRI showed the lobulated infiltrative mass in the left apical hemithorax and left lower neck, which had a slight hypersignal intensity on the T1-weighted image **(C)**, a bright signal intensity on the T2-weighted image **(D)**, and intense enhancement after injection of a gadolinium-based contrast agent **(E)**.

Discussion

Primary lung malignancies are rare in children and adolescent, and only few population-based studies are found in the literature [1, 5 - 6], so incidence data on primary lung and pleural malignancies in children are limited and difficult to interpret the disease. However, the incidence of primary lung cancer is estimated to be approximately 0.2% of all children's malignancies and the mortality rate for primary malignant tumors is approximately 30.0% in general. [2] Adenocarcinoma is the most prevalent pediatric bronchogenic carcinoma.[3] However, the most common primary lung malignancy in newborns and infants is pleuropulmonary blastoma, which represents 0.3% to 0.5% of all primary lung malignancies.[1, 7] The ratio of primary tumors to metastatic tumors to inflammatory/congenital tumors is reported to be 1:5:60. [2 - 4]

The symptoms of lung and pleural malignancies are nonspecific and usually similar to infection or congenital lesions, resulting in a delay in diagnosis and treatment. [1] Nonspecific presenting symptoms, such as chronic cough, are generally treated with antibiotics before the diagnosis of pediatric lung cancer. Other common presentations include weight loss, chest pain, and hemoptysis due to metastatic disease. Consequently, clinicians often rely on image interpretation to aid in further investigation or to make a diagnosis.

Primary lung adenocarcinoma has a poor prognosis in children, reporting a 5-year survival rate of 26.0%. [3] Adenocarcinoma usually manifests itself as a solid nodule, but it can also be subsolid and is only occasionally seen as a ground glass nodule and can result in consolidation of the lobe or 'whiteout' of the lung, with or without pleural effusion. [2]

Small cell lung carcinoma accounts for up to 18.0% of all lung cancers in adults and is associated with smoking. It is very rare and is not associated with smoking in children. [4] Dishop MK. and Kuruvilla S. [2] found that patients with small cell lung carcinoma had a central lung mass with advanced disease, including local spread and mediastinal disease, and their prognosis was poor. The most common manifestation of small cell lung cancer is a large mass centrally located within the lung parenchyma or a mediastinal mass involving at least one hilum. [8]

Of the four pediatric patients in our case series, two had small cell carcinoma, one had lung adenocarcinoma, and the other had malignant pleural mesothelioma. All of our patients have advanced disease and subsequently deteriorate after diagnosis and treatment.

Our first and second cases presented with a lung mass with advanced adjacent structural invasion and mediastinal involvement, similar to the characteristic features of small cell lung cancer located within the central aspect of the chest and the mediastinal manifestation that mentioned in previous observation.[8]

Our third case presented with prolonged fever and cervical lymphadenopathy and had metastatic disease at diagnosis. Chest CT findings represent multiple focal nodules and masses in both lungs, diffuse bilateral pulmonary lymphangitic carcinomatosis, acute vascular thrombosis, and multiple intrathoracic nodal metastases that are similar manifestations to the review article by Lichtenberger III JP, *et al.* in 2018. [7] They mentioned that the spectrum of adenocarcinoma is variable according to the characteristics and associated findings such as local invasion of the pleura, chest wall, or diaphragm. Furthermore, the pulmonary lesion is not different from adult lung adenocarcinoma.

Pleural malignancy is also rare in children, especially malignant pleural mesothelioma. Less than 5.0% of cases are in children and less than 300 cases of this have been published in the literature.[9] It is not associated with asbestos or radiation exposure, which is a different entity in adults. The histopathological classification has been defined from the WHO histological classification of tumors of the pleura: 1) mesothelial tumor; 2) lymphoproliferative disorders; and 3) mesenchymal tumors. For the radiologist and pathologist, it can be very challenging and often impossible to distinguish among the different histological subtypes of pleural tumors. CT is used for the evaluation and staging of mesothelioma. It appears as a nodular mass along the pleural surfaces that may be calcified. MRI is a better assessment of tumor spread than CT, with respect to invasion of the diaphragm and endothoracic fascia. [10]

Our fourth case presented us with chronic cough and chest pain and was found to have left hydropneumothorax and a chest mass on subsequent imaging. lnitially, the image showed as a lymphoproliferative disorder which was different from the case in the literature [9] that presented with a chest mass originating from the right upper lobe. This case confirms that the diagnosis of pleural tumor is very difficult.

However, we have only four cases of primary lung and pleural malignancies in children, Therefore it is a great opportunity to collect more cases in the future and may include the other malignancies of the thorax region.

Conclusions

Primary lung and pleural malignancies in children are rare in nature and are not specific to the presenting symptoms. The histopathological and imaging spectrum of primary lung tumors in children shows little overlap with the types of lung tumors seen in adults and will be used to characterize the lesion and guide the treatment. Although rare in the pediatric population, the tumor is a life-threatening condition. Therefore, primary lung and pleural malignancies must be considered in the evaluation of childhood lung masses.

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Conflict of interest statement
Each of the authors has completed an ICMJE disclosure form. None of the authors declare any potential or actual relationship, activity, or interest related to the content of this article.

Data sharing statement
The data sets generated or analyzed during the present study are available from the corresponding author on reasonable request.

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