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Case Report

A rare case of pleuropulmonary blastoma detected in fetus ^{☆,☆☆}

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ABSTRACT

Pleuropulmonary blastoma (PPB) is among the rarest malignant tumors diagnosed in children. PPBs can be histopathologically classified into 3 types: cystic tumor (type I), mixed cystic and solid tumor (type II), and pure solid tumor (type III). We describe a case of type III PPB that was detected in a prenatal fetus, confirmed using histopathological methods. To the best of our knowledge, this is the first case describing a type III PPB detected in a fetus. Prenatal ultrasonography is an excellent tool for detecting pulmonary lesions during the diagnostic phase, and the possibility of PPB should be considered when solid tumors are detected. Early detection can allow for the performance of full resection, leading to a better prognosis for this cancerous tumor.

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Introduction

Lung tumors in children are rare, representing only 0.5%-1% of all malignant lung tumors. Pulmonary blastoma, fetal adenocarcinoma, and pleuropulmonary blastoma (PPB) are the 3 most commonly encountered lung cancers in children [1,2]. PPB is an exceedingly rare malignant tumor, typically diag-

nosed in children, with a tendency to progressively invade adjacent organs. PPB can be classified into 3 types according to histopathological features: cystic tumor (type I), mixed cystic and solid tumor (type II), and pure solid tumor (type III) [3]. The histological features of PPB include primitive blastoma and a malignant mesenchymal stroma with multidirectional differentiation. Despite the introduction of multimodal treatment approaches, individuals with PPB typically have a poor prog-

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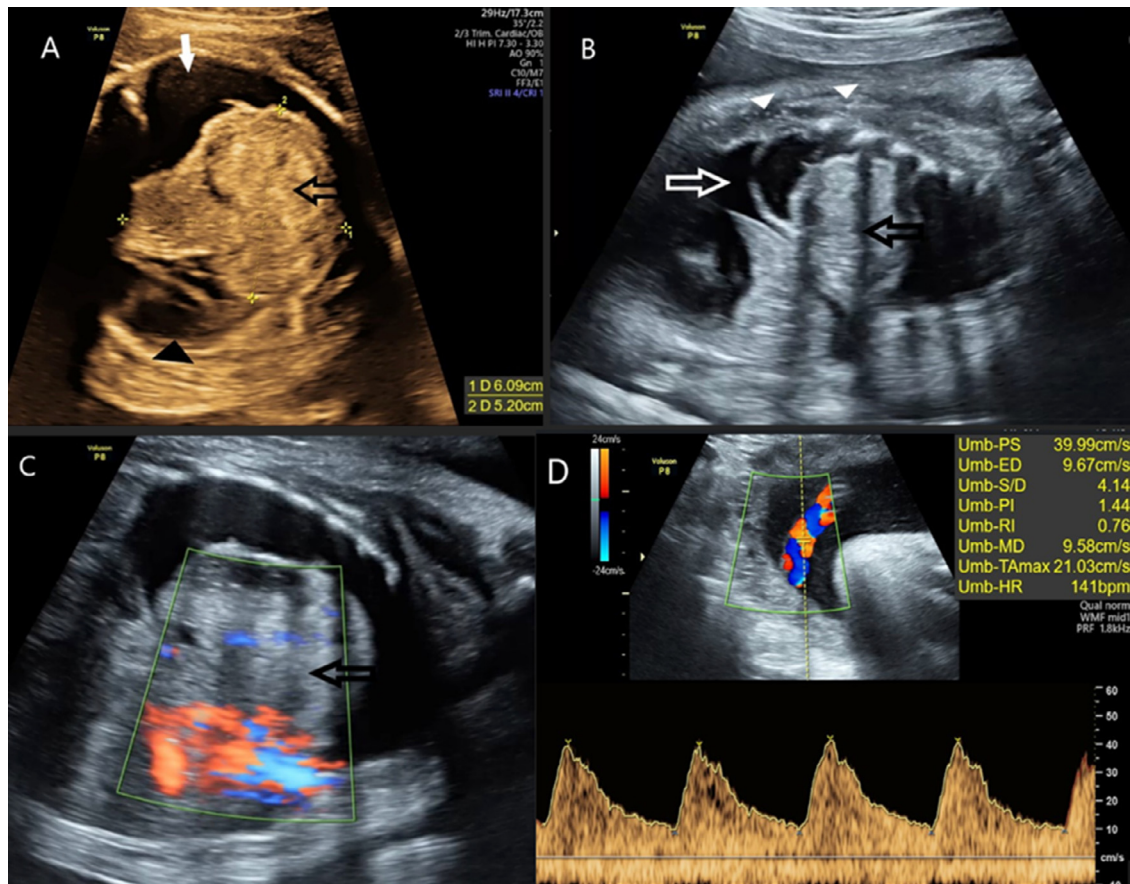


Fig. 1 – Prenatal ultrasound: The axial plane reveals a heterogeneous tumor that shifts the mediastinum and causes pleural effusion (A). The parasagittal plane reveals an inverted diaphragm with ascites and skin edema (B). The tumor shows minimal vascularization (C). Umbilical Doppler showing an elevated vascular impedance (D). Open arrow: tumor, black arrowhead: heart, white arrow: pleural effusion, open white arrow: ascites, white arrowhead: skin edema.

nosis. To date, only 4 cases of PPB have been reported in the literature, all of which have been classified as types I and II. We describe a case of type III PPB that was detected prenatally and successfully and completely resected when the child was 2 months old.

Case report

A 21-year-old primigravida woman at 36 weeks of gestation was referred to our maternity hospital (Hung Vuong Hospital) due to uterine contractions and vaginal bleeding. Owing to coronavirus disease 2019 (COVID-19) quarantine procedures and isolation policies, this patient had undergone few prenatal assessments, and limited information was available beyond an ultrasound examination performed at 7 weeks of gestation. Her medical history was unremarkable. A fetal sonography examination revealed a large, heterogeneous, solid mass with some small cystic components on the free wall of the left ventricle of the fetus, shifting the mediastinum to the right. The mass measured 61 × 52 × 60 mm without calcification. Bilateral pleural effusion was also noted, domi-

nating the left side, in addition to severe skin edema, ascites, and polyhydramnios (maximum vertical pocket = 88 mm). No other structural abnormalities were observed. On Doppler ultrasound, the tumor displayed minimal vascularization. The umbilical artery pulsatility index (PI) was 1.44 (100th percentile; Fig. 1), and the ductus venosus PI was 1 (100th percentile). These findings indicated a diagnosis of mediastinal tumor combined with hydrops fetalis. Pleural tumor was considered a differential diagnosis due to the anatomic location of the tumor. The mother was admitted to the hospital for fetal conditioning follow-up. She underwent an emergency cesarean section one day after admission (on October 28, 2021) due to abnormal cardiotocography. At term, the male infant weighed 3300 grams, with Apgar scores at 1 and 5 minutes of 5 and 6, respectively. The infant presented with severe skin edema and acute respiratory distress and was admitted to the neonatal intensive care unit (NICU) before being transferred to another pediatric center for further assessment. Computed tomography (CT) revealed a left mediastinal tumor, measuring 57 × 66 × 57 mm, which shifted the mediastinum to the right and inverted the diaphragm. The solid tumor regions showed heterogeneous enhancement and presented with some low-attenuation structures suggesting cystic components (Fig. 2).



Fig. 2 – Post-term CT scanning: Mixed solid and cystic tumor located in the left thorax shows low attenuation and shifts the mediastinum toward the right. Open arrow: tumor, solid arrow: shifted heart, arrowhead: remaining left lung.

At 2-month-old, the patient underwent exploratory surgery of the left hemithorax through a thoracotomy. During the operation, there was no lymph node metastasis observed and a pleural mass adjacent to the left diaphragm was completely excised (Fig. 3). Histopathology confirmed a diagnosis of type III PPB characterized by the proliferation of solid compact spindle cell clusters, a hypervascular stroma, a regular mitotic index, and cystic degenerative components. Immunohistochemistry staining (Fig. 4) showed the following outcomes: cytokeratin (–), desmin (–), S100 (–), myogenin (–), terminal deoxynucleotidyl transferase, myeloperoxidase (–), CD15 (–), CD68 (–), CD4 (–), CD34 (–), CD31 (+; focal), Ki-67(+, < 10%), and vimentin (+). Adjuvant chemotherapy was administered, and the infant was discharged at 3 months of age (January 31, 2022).

Discussion

PPB was first described in 1988 as a malignant tumor arising from the pulmonary mesenchyma in children [4]. Fewer than 500 cases have been reported in the literature, and PPB has an estimated frequency of 1:250,000 live births [5].

The microscopic features of PPB in children resemble those of PPB in adults, including the combination of blastoma and mesenchymal components, although PPB does not include malignant epithelial tissue. Priest et al [3] histopathologically classified 50 PPB cases into 3 types: cystic tumor (type I), mixed

cystic and solid tumor (type II), and pure solid tumor (type III). The median ages for types I, II, and III are 10, 34, and 44 months, respectively. In the absence of metastatic lesions, type I PPB has a lower recurrence rate than types II and III. The 5-year survival rate for type I was reported as 83%, compared with 42% for the other 2 types. These findings suggest that cystic PPB may be more likely to be detected earlier, resulting in a better outcome than solid PPB. The transition from type I PPB to type III PPB had also been reported. In these cases, although the biopsy displayed features consistent with type I, the final histopathological diagnosis is type II or III. Other cases show recurrent tumors characterized as type III, despite a type I primary lesion. These findings suggest the progressive nature of PPB, which may explain the worse outcomes associated with changes in the histopathological features from type I to type II or III [6,7].

Prenatal diagnosis is exceedingly rare, and to date, only 4 cases of PPB have been reported *in utero* (Table 1) [8–11]. The median gestational age of these cases was 33.4 weeks (range: 21–40 weeks). Three of these 5 cases were symptomatic at term, and 2 required invasive airway intubation (IAI) due to severe respiratory distress (RD). On prenatal diagnostic imaging, 3 of the 5 cases presented with multicystic features in the right thorax, whereas the remaining 2 cases presented with mixed cystic and solid lesions. Our case was the only example of a predominantly solid mass. Due to overlapping features with congenital pulmonary airway malformation (CPAM) [5], the diagnosis of PPB in these cases was most often made by histology. Though a solid mass (type III PPB)



Fig. 3 – Gross macroscopy of the tumor after resection.

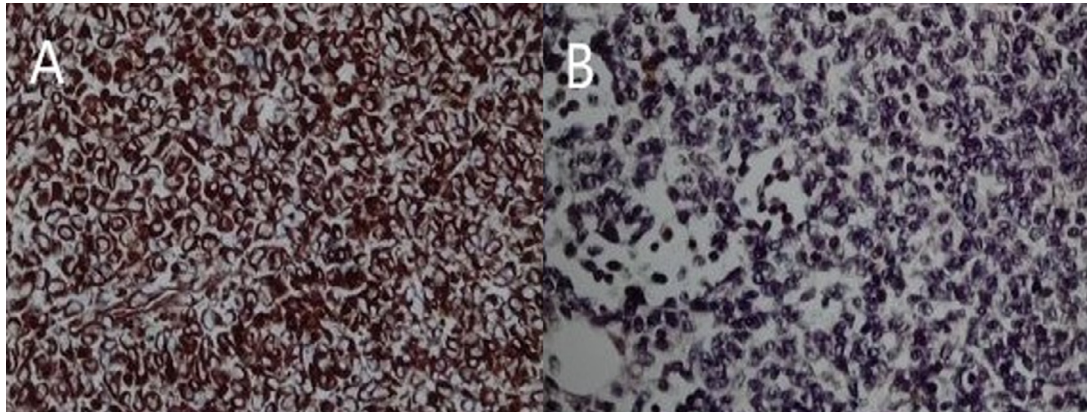


Fig. 4 – Immunohistochemistry: vimentin (+) (A), terminal deoxynucleotidyl transferase (–) (B).

in our case is more pathognomonic and can be differentiated sonographically with multicystic, hyperechoic appearance of CPAMs. Findings that are common between CPAM and PPB include mediastinal shifting, pleural effusion, and hydrops fetalis, which were observed in our case. Upon histopathological examination, 2 of the 5 cases were assessed as type I PPB, 2 were type II, and our case appears to be the very first report of type III PPB identified during the prenatal period [3]. The predominantly solid components observed on ultrasonic examination are consistent with the type III classification, whereas the remaining cases were characterized by cystic features [8].

Distant metastasis is another feature of PPB only associated with types II and III, and PPB has a tendency to metas-

tasize to the brain, medullary spinal cord, and bone. In previous reports, as well as our case, no evidence of distant metastases was identified at the time of diagnosis. The pregnancy outcomes of the reported cases were all favorable, the tumors were fully excised, and only one recurrent case was detected at 2 months of age [9].

PPB is an aggressive early childhood tumor, and no suitable therapy for patients with PPB has been established, to our knowledge. Even in individuals with microscopic residual illness, the major objective of therapy after diagnosis should be aggressive surgery. Because chemotherapy has a low response rate, chemotherapy should be combined with local radiation in the majority of patients with PPB [12].

Table 1 – Characteristics of PPB cases diagnosed during the prenatal period.

Study	GA (weeks)	Location	Features	Size (cm)	CDTS	Associated findings	Symptoms	Type
Miniati (2006) [9]	21	Right	Cystic-solid	2.5	CPAM	None	None	II
Miniati (2006) [9]	40	Right	Multicystic	NA	NA	Minor shift	RD	I
Mechoulan (2007) [10]	32	Right	Multicystic	2 × 1.5 × 0.3	CPAM	None	None	I
Higashidate (2004) [11]	37	Left	Cystic-solid	6 × 6 × 3	CPAM	Minor shift	RD, IAI	II
Our case	36	Left	Predominant solid	6 × 5 × 6	Mediastinal tumor	Mediastinal shift, pleural effusion, ascites, skin edema	RD, IAI	III

CPAM, congenital pulmonary airway malformation; GA, gestational age; IAI, invasive airway intubation; RD, respiratory distress.

Conclusion

We describe a case of type III PPB detected prenatally. During the diagnostic process, prenatal ultrasound can identify pulmonary lesions well, and PPB should be considered, particularly in cases featuring solid tumors. Early diagnosis can enable complete resection, leading to better outcomes for this malignant tumor.

Ethical approval

Hung Vuong Hospital does not require ethical approval for reporting individual cases or case series.

Availability of data and material

The datasets generated and/or analyzed during the current study are not publicly available due to privacy concerns but are available from the corresponding author on reasonable request.

Author contributions

Nguyen Dinh Vu and Nguyen Minh Duc contributed equally to this article therefore considered as first authorship. Nguyen Dinh Vu and Nguyen Minh Duc prepared, drafted, and revised the manuscript critically, for important intellectual content. Nguyen Dinh Vu and Nguyen Minh Duc contributed substantially to the acquisition, analysis, and interpretation of data. Each author gave final approval to the version of the manuscript submitted for publication and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Patient consent

Informed consent was obtained from the legal guardian of patient included in the study.

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