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Case report

Type II pleuropulmonary blastoma in a 3-years-old female with dyspnea: a case report and review of literature ☆

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ABSTRACT

Pleuropulmonary blastoma (PPB) is a rare but aggressive pediatric tumor originates from either lung or pleura. It was recently linked to the DICER I mutation as a part of predisposition syndrome for different type of tumor. It is characterized histologically by a primitive, variably mixed blastomatous and sarcomatous tissue. PPB is classified into four subtypes: cystic (type I and type Ir); cystic and solid (type II); solid (type III).

PPB has no characteristic imaging findings. Integrated imaging can help to make a differential diagnosis and to recognize the subtypes in order to set up therapy. An early recognition and differentiation from congenital airway malformations and other benign cysts are very important.

The treatment consists in a multimodal therapy including surgery and chemoterapy.

We report a case of 3 years old female admitted at our hospital with fever, non productive cough and dyspnea, who was diagnosed with type II PPB.

Background

Pleuropulmonary blastoma (PPB) is a rare, highly aggressive and malignant pediatric tumor with a familiar predisposition [1]. PPB is the most common primary pulmonary malignancy in children (˜25%) [2] aged less 5 or 6 years. About 500 cases have been reported to date [3]. PPB consisting of type I, Ir, II and

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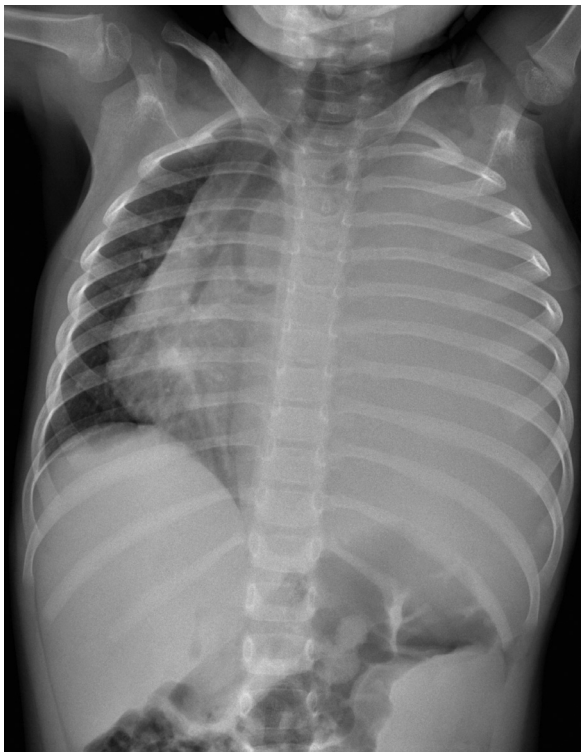

Fig. 1 – Chest X-ray showed a complete opacification of the left hemithorax with contralateral midline shift.

III and was considered as an unique clinicopathologic entity with typical clinical and histopathological manifestations.

It has been linked to the mutation of DICER1 as part of a predisposition syndrome for different types of tumors [4] including Wilms tumor (WT). We described a case of type II PPB treated in our hospital with a short review of literature focusing on the differential diagnosis and on integrated imaging.

Case report

A 3 years old female was admitted at Emergency Department of our hospital with fever, non productive cough and dyspnea. Physical examination was significant for absence of breath sounds on the left. Laboratory tests were normal. There were no reported anomalies in the antenatal ultrasound (US). Her previous medical and family history was unremarkable.

Chest X-ray was immediately performed and showed a complete opacification of her left hemithorax with contralateral midline shift (Fig. 1). The patient underwent Computed Tomography (CT) of chest and abdomen. Chest CT showed heterogenous large solid-cystic mass lesion (approximately 15,7 × 10,9 × 9,6 cm) with inhomogeneous enhancement filling almost the entire left hemithorax with significant mass effect and displacing the mediastinum to the right side.

The mass extended upon the left hemidiaphragm displacing the spleen and the left kidney inferiorly.

Partial lateral left chest wall invasion was documented.

The internal lobulated nodular solid portion was localized mainly along the postero-superior profile of the lesion and the cystic spaces were fluid-filled without air-fluid levels. Residual left lung was completely atelectatic. Massive left pleural effusion was also seen. The same exam did not show any systemic arterial supply to the mass, excluding sequestration (Fig. 2).

To better study the characteristics of the pleural effusion, a thoracic US was performed. The pleural effusion presented densely corpuscular ecostructure and appeared partially organized with evidence of septa with varying thickness (Fig. 3). Abdominal US revealed no abnormality. Brain MRI was also performed to rule out the presence of brain metastases. A trucut US-guided biopsy was performed..

The patient received five cycles of chemotherapy. Adjuvant chemotherapy was performed according to the TREP (Tumori Rari Età Pediatrica) protocol. The recommended regimen includes Ifosfamide, Vincristine, Cyclophosphamide, Actinomycin-D and Doxorubicin

Her follow-up CT at 1 months showed a volume reduction of solid component of about 54%. After two weeks, the patient underwent left thoracotomy and segmentectomy of left lower lobe.

Intraoperatively, a large multilobulated solid/cystic lesion was found occupying almost the whole left hemithorax. The solid component of the lesion was yellowish/white in color with multiple areas of hemorrhage (Fig. 4). Residual left lung was normal and totally compressed; it expanded well after resection of the lesion. Histological diagnosis of the tumor was type II PPB because it contained both solid and cystic components (Fig. 5).

The patient is almost 2 month in follow-up and under closer surveillance (Fig. 6). She is currently disease free. Genetic analysis showed that our patient had not a positive germline mutation particularly in the DICER1 gene. Radiotherapy was not administered to the patient.

Discussion

Pleuropulomonary blastoma is a very rare and aggressive embryonal tumor that aries from the lung or, less often, from the pleura and accounting for less than 1% of all primary malignant lung tumors in the pediatric population [5].

PPB is the most common primary pediatric pulmonary neoplasm and in most cases it occurs before 4 years of age [6]. It has a rare occurrence beyond the first decade of life and only a few isolated cases of PPB have been reported in literature in adult population [7,8,9]. There is no gender predilection [10].

For unknown reasons, the tumor has a predilection for the right lung. Localization on the left, as in our patient, is more rare. PPB can contain blastematous and sarcomatous elements; differently from the adult type of pulmonary blastoma which presents malignant epithelial and mesenchymal tissues [3].

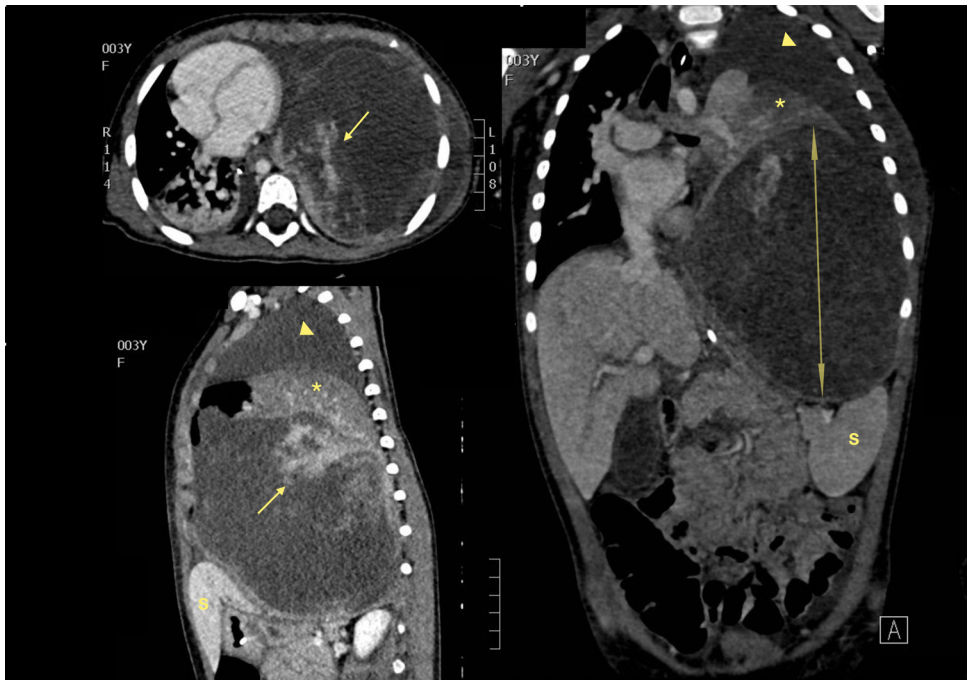

Fig. 2 – Chest CT showed a solid-cystic mass lesion with inhomogeneous enhancement filling almost the entire left hemithorax and displacing the mediastinum to the right side (double arrow). The mass extended upon the left hemidiaphragm displacing the spleen (S) and the left kidney inferiorly. Solid portion was localized mainly along the postero-superior profile of the lesion (arrow). Cystic spaces were fluid-filled without with air-fluid levels. Residual left lung was normal and totally compressed (*). Massive left pleural effusion was also seen (head of arrow)

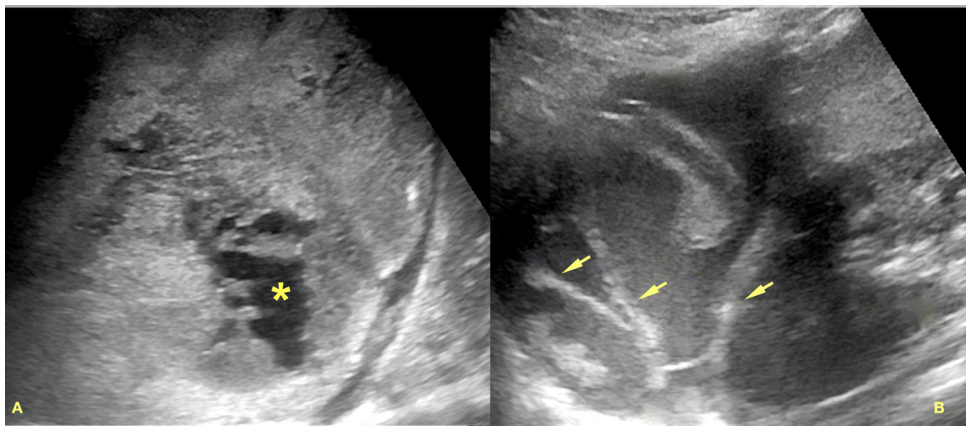

Fig. 3 – Thoracic US showed the voluminous inhomogeneous solid mass with anechoic fluid areas (*) in its context (A). A massive pleural effusion was also seen; it presented densely corpuscular ecostructure and appeared organized with evidence of septa with varying thickness (B).

PPB is associated with hereditary tumor predisposition syndrome caused by pathogenic gremlin variants in DICER I, an essential component of the microRNA processing pathway. Wilms tumor, cystic nephroma, Sertoli Leyding cells tumor are some of the neoplasm reported among DICER 1 pathogenic variant carriers. The association of DICER 1 mutation and PPB is reported in approximatively 66% of recorded cases [4]. Approximately 25% of affected pediatric patients have features in keeping with a familial cancer syndrome [11].

PPB is classified into four type on the basis of the morphological and histological features: types I, Ir (I regressed that was added in 2006), II and III. The progression over time from type I to type III tumor is well documented. Natural biological progression explains the correlation of the pathological type with age at the diagnosis and patient outcome [12].

Type I PPB is rare and presents as benign appearing air-filled lung cysts - cannot be differentiated from other benign cystic lung lesions on imaging studies. The differen-

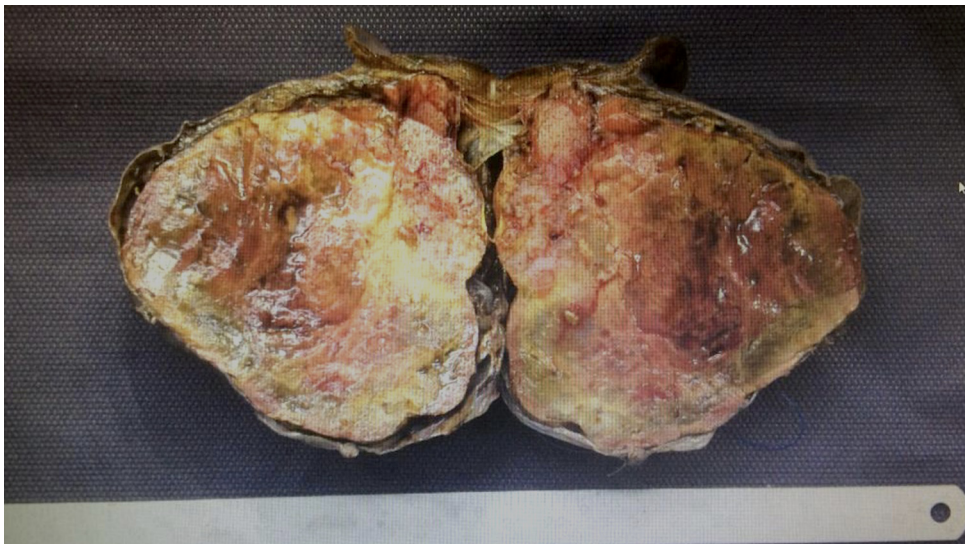

Fig. 4 – Operative sample. A large multilobulated solid/cystic lesion was excised. The solid component of the lesion was yellowish/white in color with multiple areas of hemorrhage.

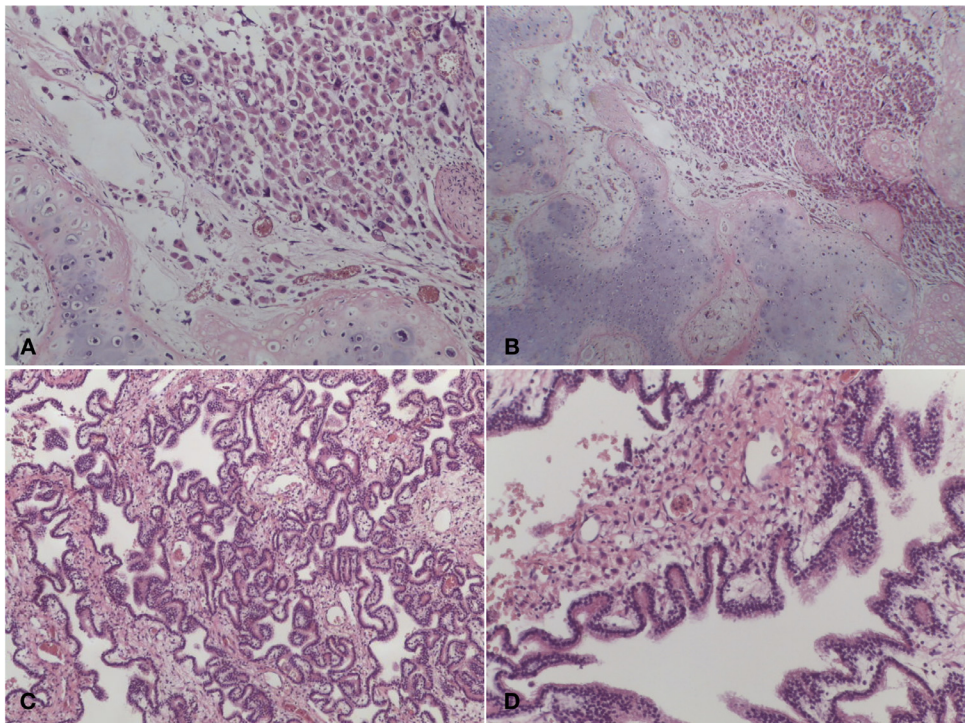

Fig. 5 – A) Tumoral lesion composed of solid yellowish-colored areas with peripherals cystic space B) Nodules of malignant cartilage and areas of rhabdomyosarcoma EE x 200 C) Cystic spaces are lined by multilayed of tall colomnar epitelial cells with papillary projections. EE x 200 D) Rhabdomyoblastic cells within the stroma beneath the lining epithelium EE x 400.

tial diagnosis for type I includes congenital pulmonary airway malformation (CPAM) and fetal lung interstitial tumor (FLIT), pulmonary interstitial emphysema or pneumatocele [13].

However, a predictive feature for CPAM is prenatal diagnosis during the second trimester, whereas PPB is generally discovered postnatally [14]. In addition, type I PPB is more likely to be multifocal than other congenital cysts [15]. Furthermore a cystic lesion is more likely to be PPB if there is a family history of PPB or associated tumor, bilateral or multisegment involvement, the presence of a complex cyst, the finding of pneumothorax and a mutation in the DICER1 gene.

Type Ir is a purely cystic tumor and have not a primitive cells component. Not all cystic type I PPB are destined to progress to the more malignant types. Type Ir might represent a “regressed” or an “abortive” form of type I

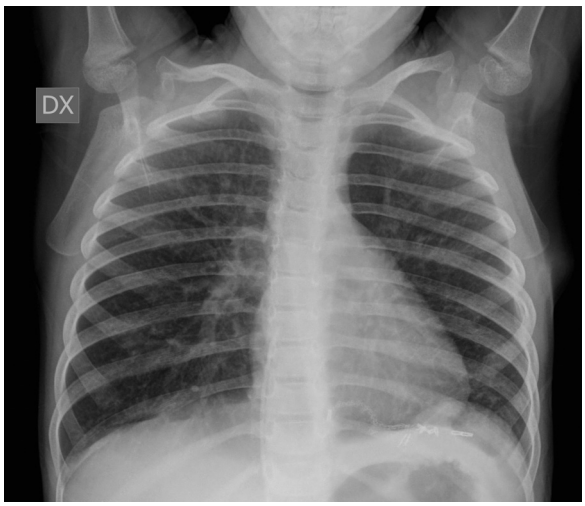

Fig. 6 – Chest X-ray 1 month after surgery.

tumor. Differential diagnosis is the same as for type I PPB [3].

Type II tumor have cystic and solid components; it is similar to Wilms tumor morphologically and therefore, it is sometimes incorrectly called "extra-renal Wilms tumor ".

Type III are purely solid lesions without epithelial-lined cystic spaces [16] usually presenting as large, well-circumscribed masses.

Type II and III usually present as a large masses partly filling the hemithorax which invade mediastinum, vessels and diaphragm. Pleural effusion is a frequent complication while lymph nodes are rarely involved. The tumor may be friable due to hemorrhages and necrosis.

Differential diagnosis for types II and III, particularly when they are locally aggressive, includes tumors such as neuroblastomas. Although chest wall invasion has been reported with PPB as in our case, the presence of chest wall involvement favors diagnosis of these other malignancies over PPB [14, 17].

Type I account for 15%-20% of all PPB and has the most favorable prognosis; the survival rate is 94% compared to 71% for type II and 53% for type III, which instead behave aggressively and together account for 80%-85% of all PPB. All reported deaths with type I occurred with progression to type II or III [10].

Type I occurs in infant with median age at diagnosis of 8-10 months Median age at diagnosis for type II and type III is later, respectively 35 and 41 months [2].

Clinically, the patient may present with chest or upper abdominal pain, dry cough, fever, dyspnea, tachipnea, fatigue, respiratory distress with or without an associated pneumothorax, hemoptysis, anorexia, malaise, or neurological symptoms resulting from brains metastasis. The brain and bones are the most frequent site of metastases [18]. Type II and III PPB tumors can also metastasize to liver.

PPB is difficult to diagnose because the tumor has no characteristic imaging findings. It may appear as a cystic lung lesion and it should be considered in the differential diagnosis of other benign cystic lung lesions on imaging. An early recognition and differentiation from congenital airway malformations and other benign cysts are very important.

On chest X-ray, large solid lesions can result in complete opacification of the hemithorax with mediastinal deviation to the contralateral side with or without pleural effusion and pneumothorax [19]. On CT, type I PPB appears as a single or a multicystic lung lesions (typically from 2 to 9 cm in diameter) that have mass effect on adjacent structures, sometimes with contralateral mediastinal shift. Type II lesions show solid components together air- or fluid-filled cavities with possible air-fluid levels [14]. Intralesional hemorrhage or infection can occupy the cysts and result in a more solid appearance. Large lesions can be accompanied by pleural effusion and contralateral mediastinal shift. Type III PPB are solid lesions that show low attenuation at CT and heterogeneous enhancement after administration of intravenous contrast medium with or without pleural effusion, atelectasis, and mediastinal shift.The MRI imaging appearance depends on the type and on the mixture of cystic and solid components. In type III, masses are typically large and heterogenous on T1- and T2-weighted images. Regions of necrosis which do not enhance on contrast-enhanced images are often present.

Type III PPB shows increased fluorodeoxyglucose (FDG) uptake at FDG PET/CT [17].

Multiple needle core biopsies are more accurate to keep in view all the different morphological characteristics of the tumor; however, tumor resection and histological examination should be performed to reach a confident definitive diagnosis on which the appropriate therapy will be based [1, 5].

Treatment of PPB depends on the tumor type and including surgery, chemotherapy and radiation therapy [20]. The main goal of therapy should be radical surgery, followed by adjuvant chemotherapy. A close follow up after type I PPB diagnosis might detect early recurrence if the parents do not favor adjuvant chemotherapy.

In type II and III, systemic chemotherapy is recommended together with aggressive surgery. The recommended chemotherapeutic agents are ifosfamide, vincristine, actinomycin D, and doxorubicin (IVADo regimen). Because the response to chemotherapy is poor, some authors suggest that chemotherapy should be given with local radiotherapy in the majority of the patients. Resection followed by multimodal neoadjuvant chemotherapy and radiotherapy is the treatment of choice in more extensive disease with dissemination [21].

Conclusion

PPBs are primitive dysodontogenic or embryonic neoplasms of infancy and early childhood. Very few cases have been reported in patients over 10 years of age. PPB is divided into subtypes correlates to the age of diagnosis and patient prognosis. The patients are at a risk of developing primitive childhood tumors. There are no specific radiological features on imaging. Combining imaging and histopathological examinations and clinical data should help in determining the diagnosis of PPB. Prompt recognition and differentiation from other benign congenital malformations or cystic lesions or other tumors are necessary to intiate an early treatment. The radical resection

of the mass and the absence of metastasis are favorable prognostic factors. PPB should be included in the differential diagnosis of cystic/solid nonhomogeneous thoracic large masses, compressing the mediastinal and chest wall structures.

Patient consent

According to guidelines of the Radiology Case Reports Journal, "formal consents are not required for the use of entirely anonymised images from which the individual cannot be identified for example, xrays, ultrasound images, pathology slides or laparoscopic images, provided that these do not contain any identifying marks and are not accompanied by text that might identify the individual concerned".

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2021.06.022.

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