

# PLEUROPULMONARY BLASTOMA: A CASE REPORT

Blastoma pleuropulmonar: Presentación de un caso



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## Palabras clave (DeCS)

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## Summary

Pleuropulmonary blastoma is a rare mesenchymal neoplasm that should always be considered in the setting of a solid or cystic lung mass in children under 5 years old. It is usually located in the periphery of the lung. However extra pulmonary involvement of the mediastinum, diaphragm, and pleura can exist. It is classified according to its histological and imaging pattern in three types: cystic, mixed (solid-cystic) and solid. Radical surgery is the treatment of choice and the only one that has demonstrated a decrease in the rate of recurrence. The use of neoadjuvant chemotherapy and radiotherapy are defined according to the histological type and presence of tumor-free margins. We present the case of a 3-year-old female patient with findings on conventional radiography and thoracic tomography of a solid mass with histopathological diagnosis of pleuropulmonary blastoma.

## Resumen

El blastoma pleuropulmonar es una neoplasia mesenquimal rara que se debe considerar siempre en el escenario de una masa pulmonar sólida o quística en niños menores de 5 años. Se localiza usualmente en la periferia del pulmón; sin embargo, puede existir compromiso extrapulmonar de mediastino, diafragma y pleura. Se clasifica según su patrón histológico e imagenológico en tres tipos: quístico, mixto (sólido-quístico) y sólido. La cirugía radical es el tratamiento de elección y la única que ha demostrado disminución en la tasa de recurrencia. Se indica el uso de la quimioterapia neoadyuvante y la radioterapia según el tipo histológico y las márgenes libres de tumor. Se estudia el caso de una niña de 3 años con hallazgos, en radiografía convencional y tomografía de tórax, de masa sólida con diagnóstico histopatológico de blastoma pleuropulmonar.

## Introduction

Pleuropulmonary blastoma (PPB) is a rare neoplasm that originates in the pleuropulmonary mes-

enchyma in children aged 5 to 6 years. Classified by Dehner in three types: cystic (type I), mixed with solid and cystic component (type II) and purely solid (type

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III), of which types II and III are of aggressive behaviour with higher rates of recurrence (1). The treatment of choice, especially for types II and III, is radical surgical management to reduce the recurrence rate without modifying the survival of these patients. The use of neoadjuvant chemotherapy and radiotherapy is under debate.

Congenital pulmonary malformations of the airway should be considered as differential diagnoses, which should be resected, since, in imaging studies, they are indistinguishable from pleuropulmonary blastoma type I. In children with persistent pneumonias, which do not improve after adequate antibiotic management, pleuropulmonary blastoma type III as well as pulmonary sequestration should be considered.

## Case description

A 3 year old girl with no history of importance, consulted for a clinical picture of 6 days of evolution of cough and fever. She presented fever and tachycardia on physical examination. The paraclinics were normal, with no findings suggesting tumor lysis. Serum markers, such as alpha-fetoprotein and beta-gonadotrophin chorionic, were negative.

In the initial radiography, a solid mass was visualized that involved almost the entire upper left lobe, diverting the mediastinum and trachea to the right, without costal bone erosion or extension to soft tissues of the thoracic wall (Figure 1). Contrasted chest tomography confirmed the finding of a solid mass with density of soft tissues without calcifications, with heterogeneous enhancement after administration of the contrast medium, without invasion of the chest wall or rib cage and with effect of mass on the left source bronchus and bronchus, which displaced it in the caudal sense without complete occlusion of its light

(Figures 2 and 3). Due to the large size of the lesion and location in contact with mediastinum, pulmonary parenchyma and pleura, it was difficult to establish its mediastinal or pulmonary origin; however, due to the age of the patient and the frequency of the symptoms, a germinal tumor of mediastinal origin was considered as the first diagnostic possibility. Surgery was performed in which, by means of left posterolateral thoracotomy, a lung mass firmly adhered to the apical parietal pleura was released and extracted. It was not possible to differentiate an adequate cleavage plane between the mass and the lung, so a lobectomy was performed. During this procedure there was tumor rupture, so a thorough washing of the pleural cavity and the extraction site was performed. No metastases were seen or felt in the lower lobe, nor nodes of pathological aspect.

Macroscopically, a mass with nodular characteristics was found, yellowish, soft, with necrotic and haemorrhagic areas of  $11 \times 10 \times 8$  cm, well circumscribed, not encapsulated, with an area of continuity solution of  $4.5 \times 2.5$  cm (Figure 4). Histologically, predominantly solid primitive malignant mesenchymal tumor slices with hemorrhagic cystic areas were visualized. With fusocellular-looking neoplastic cells, aggressive sarcomatous with primitive blastematous zones. Hilum and edges free of lesion. Complement of immunohistochemistry with CD 34 (-), CKAE1/AE3 (-), S100 (-), MyoD1 positive focal nuclear. Histopathology concluded pleuropulmonary blastoma type III.

The histological diagnosis of pleuropulmonary blastoma type III in the left lung without metastatic compromise was confirmed, and management was initiated with chemotherapy scheme IVADO (ifosfamide + vincristine + actinomycin D + doxorubicin). A CT scan was performed at 4 months without evidence of tumor relapse (Figure 5).

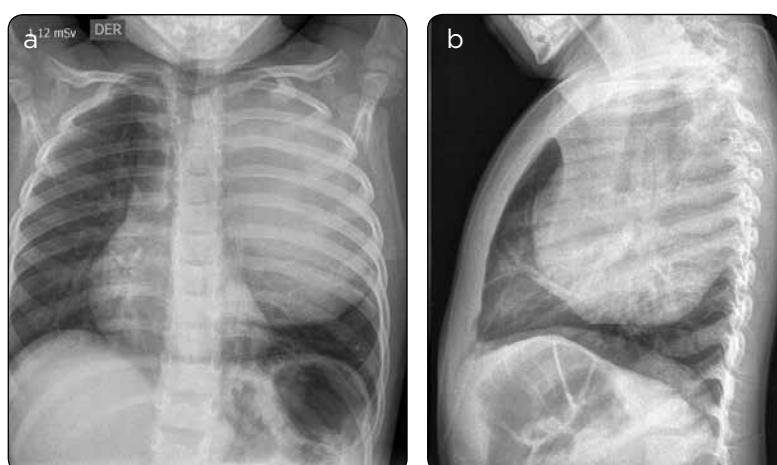


Figure 1. a and b) Posteroanterior and lateral chest radiograph: solid mass is visualized occupying the upper two thirds of the left hemithorax forming acute angles with the thoracic wall, which suggests intrapulmonary origin; however, contact with the middle mediastinum does not rule out mediastinal etiology. It diverts the cardiomedastinum to the contralateral side, and displaces the left source bronchus towards the caudal without compressing it completely. No intralesional calcifications or extension to thoracic wall or osseous compromise are visualized.

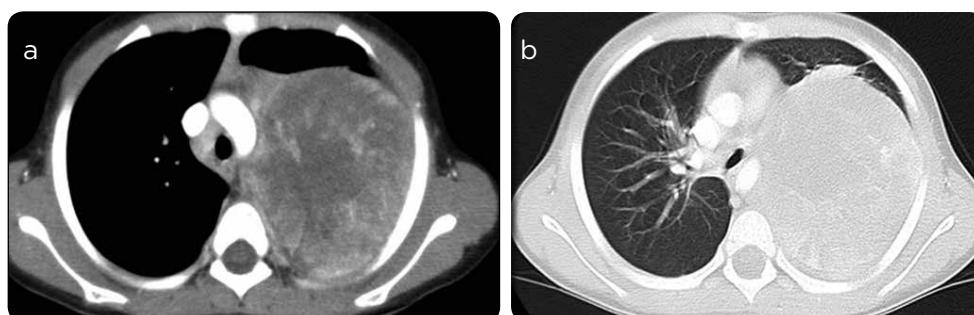


Figure 2. a and b) Axial CT cuts of thorax with contrast medium: solid intrapulmonary mass is confirmed with heterogeneous enhancement, without calcifications. In close contact with the mediastinum and pleura. No extension to the thoracic wall is visualized.

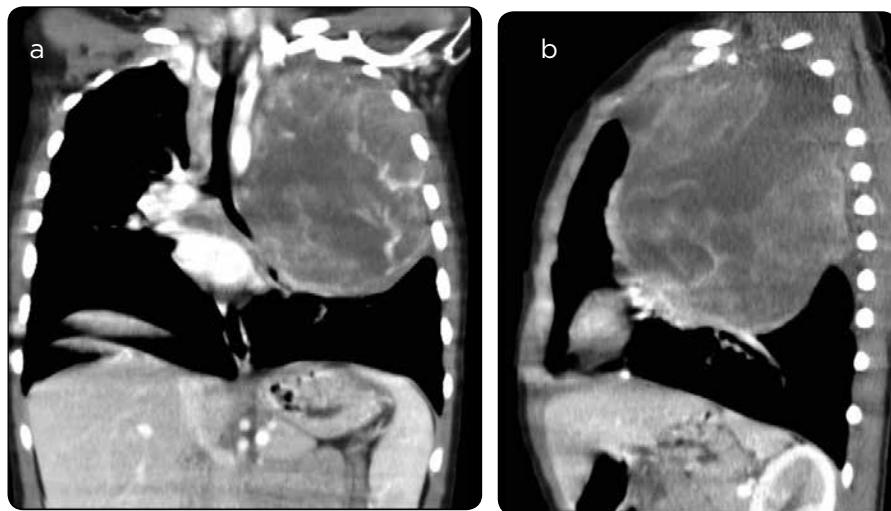


Figure 3. a and b) Mass with compressive effect on the left source bronchus which is displaced towards the caudal without complete occlusion of its light.



Figure 4. Picture of the product of the upper left pulmonary lobectomy, with a weight of 492.5 gr and measures 15 x 10 x 8 cm, in which is observed a mass of 11 x 10 x 8 cm well circumscribed, not encapsulated, of dark brown color, with area of continuity solution in one of its faces of 4.5 x 2.5 cm, through which protrudes yellow-brown material.

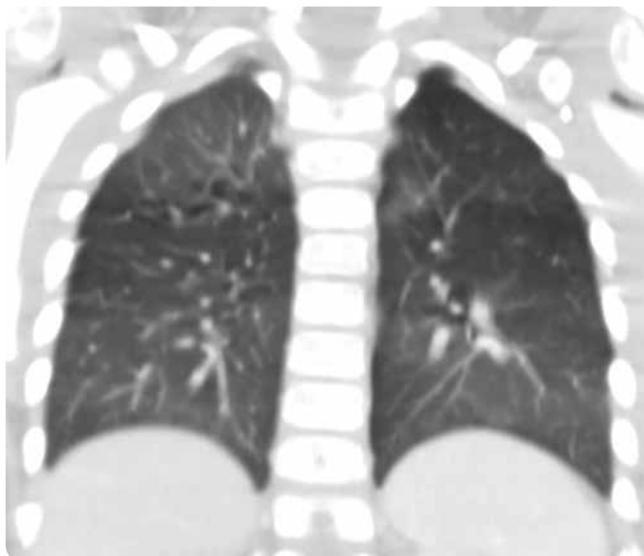


Figure 5. Coronal reconstruction of thorax CT with contrast medium, post-surgical control at 4 months, without evidence of recurrence or tumor residue.

## Discussion

Pleuropulmonary blastoma is a rare mesenchymal intrathoracic neoplasm corresponding to 0.5% of all primary malignancies of the lung (2). The prevalence is 1 per 250,000 live births and is part of the group of dystogenic tumors, such as Wilms tumor, hepatoblastoma and neuroblastoma (3). It was first described in 1961 by H. Spencer who suggested that it originated from mesodermal blastema, but since 1988 it has been recognized as an entity different from adult pulmonary blastoma to its histological characteristics of mesenchymal malignant stroma with differentiation in blastematosus and sarcomatous elements (4-6).

Approximately 2/3 of children diagnosed with pleuropulmonary blastoma are heterozygous for the DICER1 mutation, which is related to a ribonuclease useful in the development of tumor suppressor genes and genes. DICER1 syndrome associated with pleuropulmonary blastoma is found in 10% of patients, as well as their family members; likewise, cystic nephroma is the most common associated extrapulmonary tumor. Other extrapulmonary neoplasms recognised in relatives affected by the syndrome are adenoma and thyroid carcinoma, chondromesenchymal nasal hamartoma, embryonal rhabdomyosarcoma of the cervix and stromal tumours of the sexual cord in the ovary (7-8). According to Dehner, pleuropulmonary blastoma is classified into three types: Cystic (type I), is the least frequent and occurs in younger patients, with an average age of 10 months, so it can be diagnosed prenatally. Mixed (type II), occurs in older children with an average age of 34 months, and solid (type III), appears in the group of larger patients, with an average age of 44 months (1). A progressive malignancy from type I to type III has been described (5,9).

Clinically, these patients manifest respiratory symptoms: cough, dyspnea, fever, respiratory difficulty due to airway compression and also spontaneous pneumothorax associated with type I (cystic) has been described when the tumor ruptures. Initially establishing the diagnosis in these patients is difficult due to their low frequency and low specificity, which is why they are diagnosed as or empyemas. Therefore, the persistence of pulmonary consolidations that do not resolve with antibiotics requires additional studies to rule out an occult primary pulmonary tumor.

Pleuropulmonary blastoma is observed in images as a peripheral or pleural-based lung mass involving the right hemithorax in 70-80 % of cases (10); it usually occupies almost completely the affected hemithorax and may be confined in 15 to 25 % to the diaphragm or mediastinum, with mass effect in most cases represented by mediastinal displacement and the paraspinal band towards the contralateral side (11). Other concomitant findings are pleural effusion, pneumothorax and lack of extension to the chest wall, the latter useful for differential diagnosis with other pathologies (12).

Distant metastases have been more commonly described in the brain, spine, bone and lymph nodes and more rarely in the liver, pancreas, kidney, adrenal gland and soft tissues, although it is less frequent in type I and up to 30% for types II and III (11,13).

The differential diagnosis of intrathoracic opacity is extensive. Because primary lung tumours are rare in paediatric age, a congenital lesion or secondary lesion by primary tumour of the adrenal gland, thyroid gland, gonads, liver, kidney, soft tissue or bone is the first thing to be considered in the case of an intrathoracic mass (14).

If a primary pulmonary tumor is considered as differential, due to its solid character, seen in types II and III, associated with aggressive characteristics, rhabdomyosarcoma, undifferentiated sarcoma and Ewing sarcoma should be suspected, which share the property of invasion of the chest wall, although Ewing sarcoma is extrapleural and is not associated with pleural effusion. Up to 25% of PPBs present as an extrapulmonary mass attached to the parietal pleura, so the primitive neuroectodermal tumor or PNET, which often originates from the chest wall, should not be forgotten (12,15).

The inflammatory pseudotumor also enters the diagnostic possibilities given the appearance of lobed mass, with a tendency to be located in lower lobes. However, it is smaller than PPB, is associated with calcifications and its peak of presentation is in the second decade of life (16).

Neuroblastoma may also be another differential of intrathoracic location. It is located in the posterior mediastinum, invading the neural foramen and spinal canal, produces erosion of the ribs and contains calcifications (15).

PPB type I, or cystic, opens another arm of differential diagnoses, such as congenital pulmonary cysts (bronchogenic cysts, pulmonary sequestrations and congenital malformations of the airway). The prognosis of PPB is generally poor. However, local recurrence and distant metastases have been described more frequently in types II and III (14, 17).

5-year survival rates of 83 % for type I and 42 % for types II and III have been reported; however, some authors describe 10-year survival rates of only 8 %. Worst prognostic factors include: size greater than 5 cm, metastatic disease, pleural or mediastinal involvement, and thoracic lymph nodes positive for malignancy (14,17-19).

Given the malignant nature of PPB, the treatment of choice is complete surgical resection (14,18). If the diagnosis is established preoperatively the standard approach is thoracotomy and lobectomy (18).

In order to achieve negative resection edges, in most cases it is necessary to resect the entire pulmonary lobe because of the difficulty in differentiating normal parenchyma from parenchyma compromised by tumor (17, 18). Complete resection is essential to prevent local recurrence and improve prognosis (17).

There are very few cases of resection by thoracoscopy. It is uncertain whether tumor rupture significantly increases the risk of local recurrence (18). Only one case of tumour rupture has been reported during resection by thoracoscopy with local recurrence after 3 months at the incision site, so more experience is needed to evaluate the usefulness of minimally invasive approaches (18,20).

With respect to adjuvant postoperative chemotherapy, improvement in recurrence-free survival has been found in the surgery plus chemotherapy group versus the surgical resection group, although with no change in mean survival (11,14,18,19).

In cases of tumors with local extension that do not allow complete surgical resection, partial resection followed by neoadjuvant chemotherapy, imaging evaluation by computerized axial tomography (CT) and a second thoracotomy for complete resection are recommended. In patients with metastatic disease at the time of diagnosis, recurrent or residual disease, neoadjuvant chemotherapy and radiation therapy are recommended, although the role of the latter is unclear (14,20).

The aggressiveness of PPB is given by its early local recurrences and metastases, in which the time of recurrence varies from 3 to 53 months, so long-term surveillance with CT is necessary, especially for the central nervous system and bone (13, 17, 18). Although there is no consensus on the ideal method, imaging control is suggested at least every 6 months (18).

On the other hand, given that up to 25% prevalence of tumors in relatives of the patient with BPP has been described, studies should be initiated to look for tumors in close relatives, as well as extension studies in the patient due to the association with cystic nephroma (20-21).

## Conclusions

Primary pulmonary tumors in children are rare; however, faced with a large predominantly right lung mass, without extension to the chest wall, with solid, cystic or mixed component and pleural effusion, differential diagnoses should be considered in PPB, as well as in congenital pulmonary malformations of the airway, especially type I and IV. The treatment of choice associated with decreased recurrences is radical resection, as for congenital lung malformations of the airway due to the high risk of neoplastic involvement as they are indistinguishable in images and difficult to differentiate histopathologically.

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