CASE REPORT

Pleuropulmonary blastoma type II: a case report

Carlos Camilo Neto, MD; Sabrina Hashimoto Kato, MD; Laudreísa da Costa Pantoja, MD; Cecília Maria Lima da Costa, MD; Isabela Werneck da Cunha, MD, PhD

Abstract

Pleuropulmonary blastoma (PPB) is a rare embrionary mesenchymal neoplasm but is recognized as the most common pulmonary malignancy of childhood. It may present metastasis to the brain and also be indicative of other neoplasms in affected individuals or in their relatives. Being such a rare disease, it is considered a difficult diagnosis to be made. A 3-year-old female presented with fever and respiratory distress. At first, she had been treated for pneumonia with antibiotics for 14 days in another hospital with no response. Computed tomography (CT) scan showed a right lung/mediastinal mass. The patient was referred to our institution and a new CT-scan evidenced a complex mass of irregular borders, cystic areas and solid projections, along with a right pneumotorax. The mass was biopsied and hematoxylin-and-eosin (HE) stained histological sections showed a neoplasm composed of small and round cells with hyperchromatic nuclei and scant cytoplasm. The immunohistochemical profile demonstrated positivity for desmin, myogenin and Myo-D1, suggesting the diagnosis of rhabdomyosarcoma. After two weeks of hospitalization, the patient was clinically stable and initiated the first chemotherapy cycle. Surgical resection of the mass was performed and the HE slides demonstrated a neoplasm composed of anaplastic and condrossarcomatous cells with extensive necrosis. The correlation of clinical data, radiological and morphological features were conclusive of a PPB type II. The recognition and diagnosis of this entity is of great importance due to its clinical and prognostic particularities.

Keywords: immunohistochemistry, lung neoplasms, pleuropulmonary blastoma.

INTRODUCTION

Pulmonary neoplasms of childhood are rare and in 83.3% of the cases they are represented by metastases, especially in Wilms tumor and osteosarcoma[1]. Primary lung neoplasms in children are even more rare and pleuropulmonary blastoma (PPB) is the most common among them, representing approximately 57.1% of the cases[1,2].

PPB is an embrionary mesenchymal malignant neoplasm of the lungs and/or pleura affecting almost exclusively children and is very uncommon after the age of 12. It was first described as a distinct entity in 1988[3] and is histologically characterized by a variable combination of primitive cells with blastematous and sarcomatous features[4]. Until its description as a distinct and single entity and even a few years back, this neoplasm had already been designated as: pulmonary blastoma of childhood, pulmonary rhabdomyosarcoma, malignant mesenchymoma, myxosarcoma among others[5,6].

Department of Pathology, Hospital A.C. Camargo, São Paulo, Brazil.

Send correspondence to:
Carlos Camilo Neto.
Rua Taguá, 440, 1º andar. São Paulo - SP, Brazil. CEP: 01508-010.
Phone: 55 (11) 2189-5066.
E-mail: carloscamiloneto@yahoo.com.br

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Nowadays, it is still not considered a very well known entity with few statistical studies published in the literature and also a challenging diagnosis due to its clinical and pathological overlapping characteristics with other lesions. This neoplasm deserves attention mainly because of its clinical and prognostic particularities; therefore, a correct diagnosis is extremely important.

MATERIAL AND METHODS

Tissue specimens were fixed in 10% buffered formalin and embedded in paraffin. Histological sections were stained with hematoxylin-and-eosin (HE). Immunohistochemical studies were performed in paraffin-embedded tissue using a peroxidase polymeric system (Envision™ Flex High pH (Link) - Dako, Denmark) and 3 - 3' diaminobenzidine as a chomogen.

Case report

A three-year-old girl presented with fever and mild respiratory distress. The patient was treated with broad-spectrum antibiotics for 14 days, but had no clinical improvement, leading the medical team to request chest Computed Tomography (CT) scans that showed a mediastinal/right lung mass. She was transferred to our institution for clinical evaluation and treatment. The patient did not have any prior history of neoplasms, neither did her rela-

tives. Physical examination revealed poor condition of her teeth, onychomycosis and mild respiratory distress. New CT scans showed a complex mass partially delimitated, predominantly cystic but with septae and solid projections. The tumor measuring 67 mm in its greatest dimension associated with a large right lung pneumothorax, minimal pleural effusion and right upper and lower pulmonary lobes atelectasis. A CT-guided biopsy was performed.

HE stained sections of the tumor evidenced small cells with hyperchromatic nuclei, scant cytoplasm and ill-defined borders. There was mild to moderate cellular pleomorphism and evident mitoses (Figure 1A). The immunohistochemical profile demonstrated positivity for the following markers: MyoD1, desmin (Figure 2A-B) and myogenin. Markers such as Neuroblastoma, CD99, AE1/AE3, WT1, CD34 and PLAP were negative. (Table 1) This results lead to the diagnostic of an embrionary rhabdomyosarcoma.

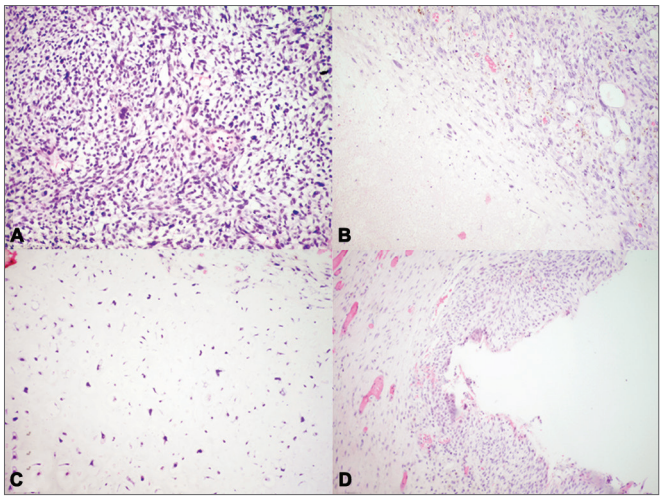

Figure 1. (A) Histological sections showing cystic area surrounded by small cells with hyperchromatic nuclei (HE x100). (B) Area of chondrosarcomatous differentiation (HE x100). (C) Histological sections composed of small cells with hyperchromatic nuclei, scant cytoplasm and mild to moderate cellular pleomorphism (HE x200). (D) Histological sections showing extensive areas of necrosis on the left and anaplastic cells on the right (HE x100).

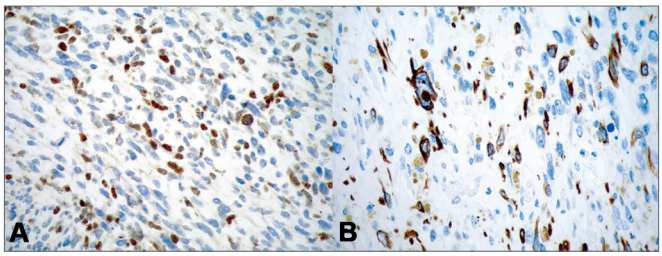

Figure 2. (A) Immunostaining for MyoD1 in a nuclear pattern (x400) and (B) Immunostaining for desmin in a cytoplasmic pattern (x400).

Table 1. Pannel of antibodies evaluated in the neoplasia (result findings in tumor cells).

Antibody	Source	Clone	Dilution	Results
AE1AE3	DAKO	AE1AE3	ready-to-use	negative
CK7	VENTANA	SP52	ready-to-use	negative
CK20	VENTANA	SP33	ready-to-use	negative
TTF-1	VENTANA	8G7G3/1	ready-to-use	negative
EMA	VENTANA	E29	ready-to-use	negative
Desmin	VENTANA	DE-5-11	ready-to-use	Focal positive
SMA	VENTANA	1A4	ready-to-use	Focal positive
Myogenin	DAKO	F5D	ready-to-use	Focal positive
MyoD1	DAKO	5.8A	1:25	Focal positive
CD34	VENTANA	QBEnd10	ready-to-use	negative
S100	VENTANA	4C4.9	ready-to-use	Focal positive
Neuroblastoma	DAKO	NB84a	1:50	negative
WT-1	VENTANA	6F-H2	ready-to-use	negative
CD99	VENTANA	13	ready-to-use	negative

Chemotherapy with vincristine, dactinomycin and ifosfamide was initiated following the staging and classification of the European protocol (Protocol EpSSG RMS2005). After the second cycle of chemotherapy, she evolved with compression syndrome of the upper mediastinum that was successfully treated with radiotherapy.

The patient underwent surgical resection of the right lower pulmonary lobe. The surgical specimen contained a tumor with 100 mm in its greatest dimension, featuring solid and extensive necrotic areas. HE stained histological sections evidenced a neoplasm composed of atypical cells showing moderate pleomorphism, hyperchromatic nuclei , extensive necrotic areas (Figure 1B), foci of chondrosarcomatous differentiation (Figure 1C) and large anaplastic areas (Figure 1B). Cistic areas were also noted (Figure 1D). The immunohistochemical profile of this current lesion demonstrated positivity for vimentin and desmin and negativity for myogenin, MyoD1, CK7 and AE1/AE3. Due to those microscopic findings (anaplastic areas associated with rhabdomyosarcomatous and chondrosarcomatous differentiation), associated with clinical and radiologic features, the final diagnosis was pleuropulmonary blastoma.

In order to stage the disease, CT scans were performed to assess abdominal and pelvic status and evidenced hepatomegaly, mesenteric lymphadenopathy and moderate amount of fluid in the peritoneal cavity.

The patient is currently receiving the same initial chemotherapy regimen plus doxorubicin.

DISCUSSION

PPB is a true desymbriogenic neoplasm of thoracopulmonary mesenchyma without malignant epithelial cells and histologically characterized by primitive blastema and malignant mesenchymal stroma that usually shows multidirectional differentiation, such as rhabdomyosarcomatous, chondrosarcomatous or liposarcomatous differentiation[7]. Pleuropulmonary blastomas were classified in types I, II and III in 1995 and this classification is still used by the World Health Organization (WHO)[8,9]. Type I lesions are entirely cystic, type II are solid-cystic and type III are solid and the respective median age at diagnosis for each type is 10, 33 and 44 months[5,10].

In children, pulmonary neoplasia should be suspected when the patient presents persistent cough, hemoptysis, recurrent pneumonia and wheezing[1]. It is very important to rule out metastatic lesion. Main PPB related symptoms described in the literature comprehend respiratory change, fever, thoracoabdominal pain and cough[5,7]. Idolfini et al. published a study of 11 cases in which they demonstrated diagnostic delays of up to 45 days due to unspecific clinical presentation[7].

The precise diagnosis of PPB is important due to its clinical implications for patients and their relatives. PPB is associated with a poor prognosis. Five-year survival rates are 83% for type I and 42% for types II and III. Recurrence rates are 14% and 46%, respectively[5,7]. Metastases occur in up to 30% of types II and III lesions, especially to central nervous system (CNS) and bone[1,5,7,11]. CNS metastasis rates may reach up to 44% of the cases[5]. In a familial context, this tumor predicts the occurrence of otherdiseases, such as cystic nefroma, sarcoma, medulloblastoma, thyroid neoplasms, leukemia, lymphoma and germ cell tumors, in the patient or their relatives in 25 to 38% of the cases[10,12].

PPB, clinically and radiographically, is the most common malignancy associated with lung cyst in childhood, especially type I lesions[10], thus, its main differential diagnosis is congenital cystic adenomatoid malformation (CCAM) which is represented by a respiratory epithelial cyst. The diagnosis depends mostly on morphology, so extensive sampling of the cyst is mandatory[1,5]. The present case showed the importance of an extensive sampling. The previous biopsy evidenced only the rhabdomyosarcomatous component which led to an erroneous diagnosis of embryonal rhabdomyosarcoma. Small biopsis should be evaluated very carefully in cases like this since other components such as blastematous areas and other mesenchymal differentiation are essential for the diagnosis of PPB. Synovial sarcomas and pulmonary blastomas are the main differential diagnoses of types II and III. Synovial sarcomas usually express pan cytokeratins and are negative for muscle markers such as desmin, myogenin and MyoD1. Also, they may show epithelial component that is not found in pleuropulmonary blastomas. Pulmonary blastoma presents epithelial, stromal and blastematous components and occurs almost exclusively in adults, although there is a case report involving a child[13]. Rhabdomyosarcoma and teratoma also figure as differential diagnoses of types II and III pleuropulmonary blastomas[5].

Due to its rarity, very few studies had described its molecular pattern. Gains of cromossome 8 and loss of 9p 21-24 have been the most common findings[14].

Progression from type I to type III may be observed[1,4,6] as reported in a 38 patient case study of PPB type I in which 9 cases recurred as types II/III[15]. Another evidence of progression lies in the fact that anaplasia is rarely seen in type I, opposed to types II and III that present this feature in 78% and 84% of the cases, respectively[10].

The diagnosis of PPB is very often compromised due to scant representation of the biopsy material, therefore, thorough sampling of the specimen along with careful morphologic and immunohistochemical evaluation of the material in association with clinical and radiological features are essential for a precise final diagnosis.

Recognition of this entity and its clinical course is of paramount importance in order to detect the disease in early stages, thus providing a better prognosis for the patient. Screening of the patient and family for associated diseases and neoplasms should be carried out.

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