

# Congenital pulmonary fibrosarcoma in a newborn with hypoglycemia and respiratory distress: case report

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**SUMMARY:** Şahin D, Koç N, Etker Ş, Güven Ş, Canpolat C. Congenital pulmonary fibrosarcoma in a newborn with hypoglycemia and respiratory distress: case report. Turk J Pediatr. 2010; 52: 325-329.

Although primary bronchopulmonary fibrosarcoma is a rare tumor, it may be characterized by the symptoms of acute respiratory distress occurring during the first moments of life in a newborn. It is one of the leading congenital malignant neoplasms of the lung, but is considered a borderline tumor since its biological behavior is much more favorable than that of adult fibrosarcomas. In the absence of metastases, complete resection is curative. Histopathological diagnosis is not simple, as the microscopic characteristics may be confused with benign fibromatosis or malignant mesenchymal neoplasms. In this case report, we present a case of congenital pulmonary spindle cell tumor showing the features of fibrosarcoma, and we discuss the differential diagnosis of spindle cell lesions localized within the thorax.

**Key words:** bronchopulmonary fibrosarcoma, congenital, hypoglycemia, newborn, respiratory distress.

Primary bronchopulmonary fibrosarcoma (BPFS) is rarely seen, but is the most common primary malignant congenital tumor of the lung<sup>1</sup>. These tumors may lead to serious respiratory distress, in the forms of status asthmaticus, respiratory distress syndrome, and fetal asphyxia<sup>2,3</sup>. The diagnosis of these tumors may be delayed because of some non-specific signs and symptoms such as cough, fever, hemoptysis, fetal anemia, and relapsing or non-curable pneumonia<sup>4,5</sup>. BPFSs present as an endobronchial mass, with some showing a polypoid form and others being localized intraparenchymally<sup>6</sup>. These tumors may be congenital or develop at different ages during childhood.

Although BPFS can be diagnosed using the advanced imaging methods, the definitive diagnosis can only be confirmed via cytological and histopathological assays. Difficulties may arise during the histological diagnosis of BPFSs, since the microscopic appearance is substantially similar to that of fibromatosis and malignant spindle-cell mesenchymal neoplasms<sup>7</sup>. The definitive and differential

diagnosis requires immunohistochemical investigation. Although BPFSs are malignant, they show a slow progression and have good prognosis if treated early. Because of their favorable prognosis after a total resection despite the tumors histopathologically showing cellularity and mitotic activity, they are considered as borderline tumors with low-grade malignancy, and total resection has been reported to be curative<sup>2</sup>.

## Case Report

Our case was a newborn that presented with respiratory distress and cyanosis during breastfeeding 5 to 6 hours after the delivery, and was admitted to the intensive care unit. A direct X-ray revealed an opacity of 5x4x3 cm in the middle part of the right lung, which was considered as pneumonia, congenital pulmonary cyst, or bronchogenic cyst, and subsequently an antibiotic therapy was initiated (Fig. 1). Since the radiological findings remained unchanged, a computerized tomography (CT) was taken, and surgical treatment of the lesion was recommended, with the diagnosis of bronchogenic cyst (Fig. 2).

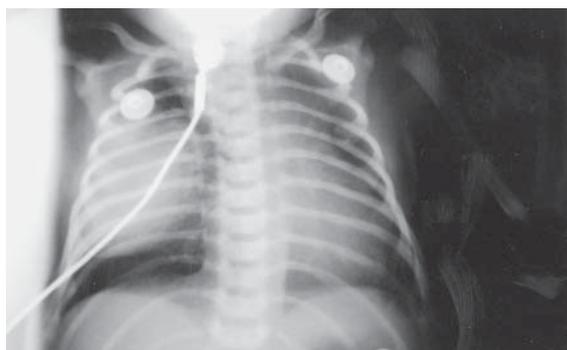


Fig. 1. A tumor in the middle part of the right lung on the preoperative direct posteroanterior X-ray.

Laboratory findings were as follows: erythrocyte count  $3.23 \times 10^6/\mu\text{L}$  (4.7-6.0), hemoglobin 10 g/dl (14-24), white blood cell count  $21.3 \times 10^3/\mu\text{L}$  (4.3-10.3), hematocrit 33% (42-52), C-reactive protein (CRP) 11.5 mg/dl (0-5), and blood glucose 21 mg/dl (normal: 40-60).

The exploration revealed a mass measuring 5x4x3 cm, involving the upper lobe of the right lung, having a cystic appearance, and covering a substantial part of the hemithorax. The mass was completely resected. There was no spread to the chest wall or mediastinum. After detecting the hypoplastic and atelectatic ventilation of the middle and lower lobes, the operation was terminated with a closed underwater drainage via the tube thoracostomy. The patient was supported through mechanical ventilation during the post-operative period, and there was no further problem with respiratory distress. During the follow-up, it was observed that the air cyst replacing the resected mass had completely resolved, and a



Fig. 2. Computerized tomography scan of the mass in the right lung.

limited contraction occurred toward that side in the mediastinum. (The patient's treatment was discussed in the Panel of Pediatric Oncology, Medical Faculty of İstanbul University and Medical Faculty of Marmara University, and was considered adequate and sufficient). During the first days of the surgery, the glucose level elevated to 40 mg/dl, and normalized to the physiologic level together with the other parameters on the following days. Macroscopic examination revealed no tumor within the surgical borders of the resected tissue. The cross-section showed a solid tumor tissue of 6x4x3 cm with a regular margin and off-white in color. Microscopic examination revealed a cellular tumor tissue composed of uniform spindle cells, clustered in long and intersecting fascicles (herringbone pattern), and collagen deposits in the extracellular areas (Fig. 3). The spindle cells had an elongated or oval nucleus, and marked cytoplasm, and showed 20 mitoses at the 10 high-power fields (Fig. 4). There was no pleomorphism, nuclear hyperchromatism, atypia or necrosis. Based on these morphological findings, the tumor was diagnosed as fibrosarcoma, and an immunohistochemical examination was performed to verify the diagnosis. A strong diffuse cytoplasmic staining was observed with vimentin (Fig. 5). There was no staining with cytokeratin, myoglobin, S-100, smooth muscle actin, or desmin. Therefore, the diagnosis of BPFs was definitive. The patient remains in complete remission 16 months after the surgical procedure.

## Discussion

When pulmonary lesions are observed radiologically in newborns and children, some

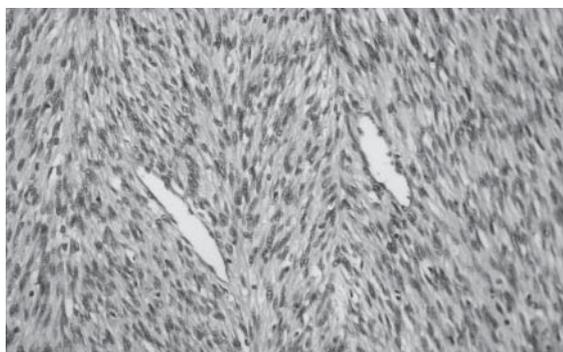


Fig. 3. Intersecting fascicles of spindle-shaped tumor cells (hematoxylin & eosin x 200).

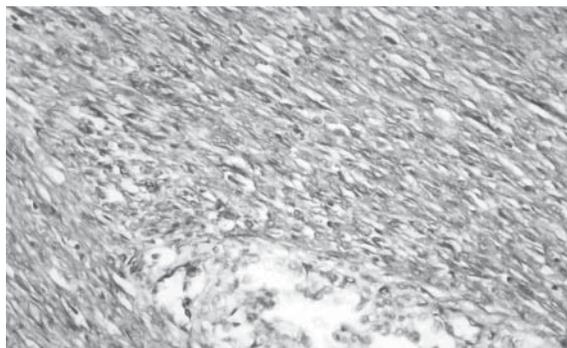


Fig. 4. Pulmonary alveoli in the left lower side, and a tumor cell showing a mitotic division next to the alveoli (hematoxylin & eosin x400).

age-specific congenital abnormalities, such as adenomatoid malformations and bronchogenic cysts as well as pneumonia, should be considered. Thus, in our case, the opacity in the upper and middle lobes of the right lung observed on the direct X-rays were diagnosed as pneumonia, and an antibiotic treatment was initiated. A subsequent CT scan verified the diagnosis of bronchogenic cyst, and led to the surgical treatment. During the childhood period, preoperative diagnosis of pulmonary masses is essential for scheduling a surgical treatment, as in adults. In the suspicious cases, an intraoperative pathological examination to determine whether the lesion is mesenchymal-derived is helpful in deciding whether or not to perform a lymph node dissection. In our case, the respective surgeon performed a radical surgical treatment considering the localization and structure of the mass. If the mass had been diagnosed histopathologically as pulmonary carcinoma (rarely seen in children), then an additional magnetic resonance (MR) imaging and another surgical procedure would have been required for the lymph node dissection. This case demonstrated that a preoperative pathological examination and perioperative frozen-section investigation are required in order to choose the accurate and proper surgical method.

A preoperative cytological and perioperative frozen-section-based diagnosis may not be easy in BPFSSs. During the frozen-section investigation, the pathologist may experience difficulty in differentiating such lesions from mesenchymal proliferations and fusiform-cell sarcomas. A pathologist should primarily keep in mind the possibility of

fibrosarcoma in newborns and infants. The microscopic appearance may substantially mimic fibromatosis and spindle cell malignant mesenchymal tumors<sup>7</sup>. In such cases, it would be sufficient to inform the surgeon that the tumor was mesenchymal-derived, and that a benign-malignant differentiation could not be made. The histopathologic differential diagnosis of fibrosarcomas should include plasma-cell granuloma, fibromatosis, leiomyosarcoma, malignant fibrous histiocytoma, malignant melanoma, Schwannoma, and spindle-cell carcinomas<sup>2,8</sup>. An immunohistochemical examination in addition to the morphological findings may be helpful for the differentiation from other sarcomas. Infantile fibromatosis, particularly its cellular variant (aggressive fibromatosis) is one of the most difficult lesions to diagnose. The signs of fibrosarcomas include hypercellularity, whether hypocellular collagenous structures are minimal or absent, contact between the nuclei of tumor cells, overlapping nuclei, hyperchromasia, marked nucleoli, frequent mitosis, necrosis, and infiltration into the vessel walls<sup>8</sup>. In order to differentiate from the other spindle-cell malignant tumors, the definitive diagnosis may require immunohistochemical, histochemical and ultrastructural investigations or molecular biological diagnostic methods in addition to the conventional histopathological findings. Demonstrating the silver-binding nucleolar organizing region (AgNOR) distribution has been shown to be useful to differentiate the low-grade fibrosarcomas from the benign fibrous proliferations<sup>9</sup>. The molecular analysis showing the ETV6-NTRK3 gene fusion has been reported to be the most useful method

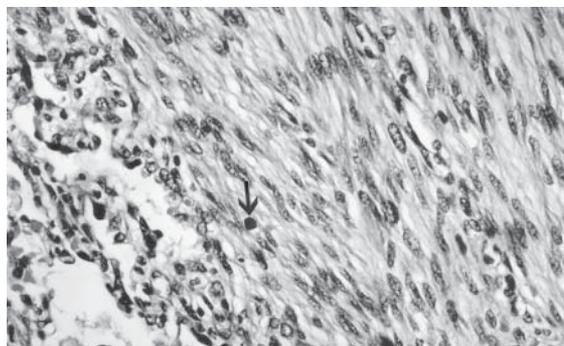


Fig. 5. Diffuse cytoplasmic staining of the tumor cells with vimentin (hematoxylin & eosin x 200).

in differentiating between the two entities<sup>10,11</sup>. Some authors suggested that it would be possible to decide whether these tumors are benign or malignant only through a prognosis follow-up for years, even if the clinical and pathological findings are available for diagnosis<sup>7</sup>.

Fibrosarcomas in the pediatric period, especially the retroperitoneal fibrosarcomas, may secrete insulin and similar substances, leading to hypoglycemia<sup>12</sup>. Although the insulin levels were not monitored in our case, hypoglycemia persisted in spite of the parenteral glucose administration (8 mg/kg/min). This may indicate a paraneoplastic syndrome caused by the bioactive peptides secreted from the neoplastic cells. Normalization of blood glucose levels 2-3 days after the resection supports our suggestion.

Congenital infantile fibrosarcomas should be considered as borderline tumors. The prognosis of these tumors is much better than that of fibrosarcomas in adults and other spindle-cell sarcomas in childhood<sup>7,10</sup>. It has been reported that congenital tumors have a better prognosis compared to those occurring in the pediatric period, while those showing endobronchial localization have a better prognosis than those showing pulmonary parenchymal localization<sup>6,13</sup>. Endobronchial resection and laser therapy are performed for the treatment of the tumors not spreading out of the bronchi (e.g. parenchyma) but causing airway obstruction, whereas surgical procedures including pneumonectomy or lobectomy are preferred for the treatment of intraparenchymal pulmonary fibrosarcomas<sup>14</sup>. Our case was congenital, showed intraparenchymal localization, and involved the upper lobe of the right lung.

Although surgical resection has been proposed to be curative for the non-metastatic cases, relapsing cases after the radical surgery have also been reported<sup>3,4</sup>. Radiotherapy and chemotherapy are preferred for the unresectable cases<sup>2</sup>. A combination of surgery, radiotherapy and chemotherapy may provide a survival rate of more than 78%<sup>6</sup>. In our case, a complete remission was achieved without applying any chemotherapy or radiotherapy after the surgical procedure. During the 16-month follow-up after the resection, the CT and MR imaging

scans revealed no mass in the lungs, thorax, or other organs.

In conclusion, BPFs may be congenital, or develop during the pediatric period, and are considered as borderline or low-grade sarcomas. These tumors have similar histopathologic features with benign proliferative lesions and spindle-cell sarcomas and carcinomas. The differential diagnosis of the tumors with similar morphological features can lead to histopathological misdiagnosis, and thus may require immunohistochemical, histochemical and ultrastructural investigations and molecular biological diagnostic methods, in addition to the conventional histopathological findings. In the newborns with hypoglycemia with a mass in the lung or other organs, the diagnosis of BPFs should be considered after some pathologies, such as maternal diabetes and insulinoma, are ruled out.

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