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Case Report

# Sudden death in a female child doe to undiagnosed pleuropulmonary blastoma – An autopsy case and review of literature

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## 1. Introduction

Pleuropulmonary blastoma (PPB) is a rare intrathoracic malignant tumor in children that is characterized by the proliferation of malignant stromal cells. PPB is diagnosed by histopathological examinations of biopsy or surgical specimens, combined with clinical data and imaging findings [1]. Cases of PPB have been reported in the fields of pediatrics, surgery, radiology and pathology [1–22]. However, to our knowledge, no reports of PPB have been published in the field of forensic medicine. We present for the first time an autopsy case of PPB in an infant that had not been diagnosed antemortem.

## 2. Case report

### 2.1. Clinical presentation

A 19-month-old girl without notable past or family history repeatedly cried in the evening, and had a fever of 39.3 °C. She vomited once and complained of chest pain with crying. Her mother considered these symptoms to be unusual, and thus brought the child to an emergency unit. Abdominal radiography showed the rectum filled with feces. After administration of an enema, a small amount of feces was evacuated. A mass in the right lung field was observed by chest radiography, but remained undiagnosed. She "vomited" bloody fluid when the patient was about to go home. CT scan results indicated intussusception. Therefore, a high-pressure enema was administered, the resulting hematochezia of which indicated that the intussusception had been successfully reduced. She was hospitalized for follow-up observation. Her body temperature was 38.1 °C on admission with heart rate was 188/min and respiration rate 42/min. The complete blood count showed a white blood cell count of 33,100/μL. It was decided that the mass in the right lung was to be examined by pediatric surgeons the next day or later. On examination the morning after admission, the patient's face had turned pale, and coldness was observed in her lower limbs. She had cardiopulmonary arrest on her way to another hospital. She was announced dead after arriving at the hospital. Autopsy was performed 2 days after death.

### 2.2. Postmortem CT findings

Postmortem CT images showed that there was a tumor occupying a significant part of the middle lung zone in the right thoracic cavity. The tumor was heterogeneous (Fig. 1). Some fluid was observed in the trachea and bronchi. There was no niveau in the cardiac cavity.

### 2.3. Autopsy findings

Weight and height of the body were within normal range (78.5 cm, 8.2 kg). Red-purple postmortem lividity was fixed on her back. Her abdominal skin color was light green, although other sites were pale. No lethal injuries were found. Red-brown colored fluid was observed in the left and right pleural cavities in the respective amounts of 5 ml and 15 ml. There was a moderate amount of green opaque fluid in the esophagus and trachea, and a well-defined tumor measuring 6 × 5 × 4 cm was observed in the upper or middle lobe of the right lung. The left lung weighed 100.5 g and the right lung weighed 166.5 g including the tumor (Fig. 2a). The removed lungs were wholly filled with 20% formalin solution injected through the trachea. Cut surfaces showed a grayish-white tumor with petechial hemorrhage and zonal necrosis after being fixed with formalin. There was no cystic structure in the lesion (Fig. 2b).

The heart weighed 46.6 g without malformation. There was 30 ml of clear red brown ascites. The small intestine contained a large amount of green or red-brown opaque fluid, and there were mucosal hemorrhages. A large amount of red-brown watery feces was observed in the large intestine. There was no intestinal invagination, and no other organs yielded notable findings.

Swab cultures of the nasal and bronchial mucosae revealed no appreciable bacteria. There was no increase in titers of viral antibodies in serum except mildly in RS viral antibody titers. Serum procalcitonin level was 13.8 ng/mL.

### 2.4. Histopathological findings

The lung tumor was surrounded by collagenous tissue. Polygonal

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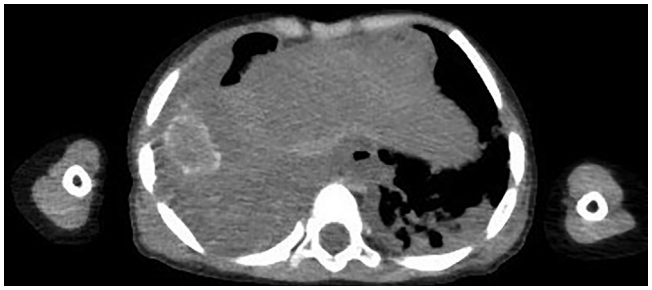

**Fig. 1.** Postmortem chest CT. There is a tumor occupying a significant part of middle lung zone in the right thoracic cavity.

shaped cells, which had oval or rod shaped nuclei with high N/C ratio, proliferated monotonously and diffusely (Fig. 3a–c). Abnormal mitoses were present in spots, and there were some multinuclear giant cells. The central part of the tumor included necrotic tissue with hemorrhage. Ectopic striated muscle tissue was observed in the stroma of the right lung apart from the tumor (Fig. 4a–c). There was accumulation of erythrocyte-containing fluid in the bronchioles of the right lung in and out of the tumor.

Immunohistochemical staining was positive for vimentin in the cytoplasm of the tumor cells. Desmin stained vascular smooth muscle cells in the connective tissue surrounding the tumor, although it was negative inside the tumor. AFP, S100 and Myf4 staining were negative. Phosphotungstic acid-hematoxylin (PTAH) staining of the right lung revealed thrombus containing tumor cells in the small blood vessels outside the tumor (Fig. 5). There was no aberration in other organs. From the clinical data, imaging findings, and histopathological findings, we diagnosed the cause of death in this patient as PPB. The MIB-1 (Ki-67) labeling index in the five hot spots (Genetic Lab Co. Ltd., Sapporo, Japan) were 9.4, 13.4, 14.4, 16.4 and 22.8% (mean: 15.28%).

## 3. Discussion

We experienced an autopsy case of a 19 month-old girl with a mass in the right thoracic cavity. We initially suspected the cause of death was a lung abscess following accidental aspiration of foreign bodies such as peanuts. Macroscopic observation, however, showed no abscess in the right lung after formalin fixation. The mass was a solid tumor with necrosis and hemorrhage. Histopathological study revealed a tumor surrounded by collagenous fiber, with diffusely proliferated polygonal shaped tumor cells. We diagnosed the mass as PPB with these findings. It was supported through the present case that combining the clinical data, imaging findings and histopathological findings is necessary for the proper diagnosis of PPB [1].

PPB is a rare intrathoracic malignant tumor, occurring during the fetal stage or infancy. There is no gender difference in incidence [23], and the tumor tends to occur on the right side of the lungs [2]. PPB was defined as a single neoplasmic category by Manivel et al. in 1988 [3]. Over 350 cases from the United States have been registered in the International PPB Registry (IPPBR) [4], and 41 cases have been reported in Japan [5–15]. The lesions are composed of immature mesenchymal cells that tend to differentiate into various kinds of cells, including striated muscle and bone cells.

PPB has been classified into three types according to the proportion of cystic and solid components: type I tumors are wholly cystic; type III are entirely solid; and type II have both components. It is considered that type I tumors develop into type II or III. Type I do not always progress to malignancy. Type “Ir” (regressed) is demarcated from type I, because a part of type I is non-progressive or regressed cystic lesions [4,16,17].

Typical microscopic findings of PPB are characterized by aggregation of primitive small cells. Immunohistochemical examination is non-essential but helpful for histological diagnosis. Muscle specific actin and desmin are usually positive in rhabdomyoblasts and cambium layer (undifferentiated small cells proliferated around the cysts). The chondrocyte nuclei stain for S100 [2]. Cytokeratin stains epithelial cells lining of cysts. The tumor cells express vimentin since they are undifferentiated mesenchymal cells. The cytoplasm of the tumor was stained for vimentin in this case. SMA (smooth muscle antigen) was used to stain capsular tissue, and desmin stained vascular smooth muscle cells in the surrounding connective tissue. Negative Myf-4 staining denied the existence of rhabdomyosarcoma. S100 staining of the tumor cells was also negative. Ectopic striated muscle tissue was observed in the stroma apart from the tumor. Striated muscle cells in non-neoplastic lung tissue might be due to morphogenetic errors [24].

PPB is highly associated with family incidence and other malignancies, and germline mutation of DICER1 contributes to the

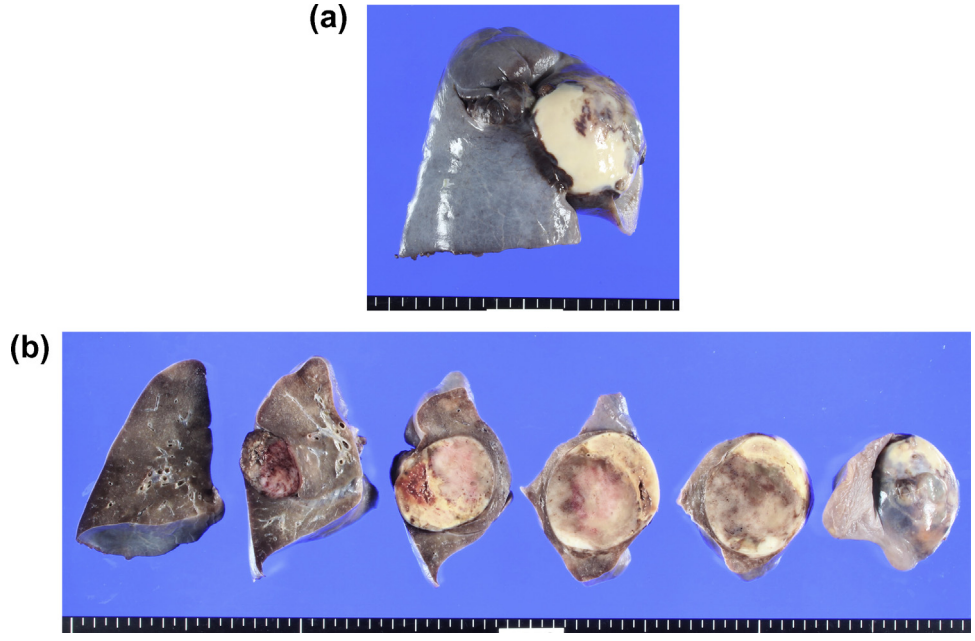


**Fig. 2.** (a) Gross appearance of the right lung. (b) The divided surfaces show a tumor measuring 6 × 5 × 4 cm in the upper lobe.