An infant with pleuropulmonary blastoma type II detected during the prenatal period

Naruki Higashidate, Kimio Asagiri, Suguru Fukahori, Shinji Ishii, Nobuyuki Saikusa, Yoshinori Koga, Naoki Hashizume, Motomu Yoshida, Saki Sakamoto, Yoshiaki Tanaka, Ken Tanigawa, Minoru Yagi

Department of Pediatric Surgery, Kurume University School of Medicine, 67 Asahi-machi, Kurume, Fukuoka 830-0011, Japan
Pathology, Kurume University School of Medicine, 67 Asahi-machi, Kurume, Fukuoka 830-0011, Japan

Pleuropulmonary blastoma (PPB) is a rare malignant pulmonary neoplasm observed during childhood. PPB is classified into three types according to the pathological findings: type I (purely cystic), type II (cystic and solid) and type III (purely solid). Only three cases of PPB diagnosed during the prenatal period have been reported in the previous literature, all of which involved PPB type I. We herein report the case of a female infant with PPB type II detected on maternal ultrasonography. The patient underwent surgical resection with adjuvant postoperative chemotherapy in the neonatal period due to persistent respiratory instability. According to the previous literature, the prognosis of type II and III disease is less favorable than that of type I. The present patient achieved 11 years of disease-free-survival. To our best knowledge, this is the first report of PPB type II diagnosed during the prenatal period.

© 2014 The Authors. Published by Elsevier Inc. All rights reserved.

A R T I C L E   I N F O
Article history:
Received 27 March 2014
Received in revised form 28 April 2014
Accepted 3 May 2014
Available online 19 May 2014

Key words:
Pleuropulmonary blastoma
Neonatal lung tumor
Prenatal diagnosis
Adjuvant chemotherapy

A B S T R A C T
Pleuropulmonary blastoma (PPB) is a rare malignant pulmonary neoplasm observed during childhood. PPB is classified into three types according to the pathological findings: type I (purely cystic), type II (cystic and solid) and type III (purely solid). Only three cases of PPB diagnosed during the prenatal period have been reported in the previous literature, all of which involved PPB type I. We herein report the case of a female infant with PPB type II detected on maternal ultrasonography. The patient underwent surgical resection with adjuvant postoperative chemotherapy in the neonatal period due to persistent respiratory instability. According to the previous literature, the prognosis of type II and III disease is less favorable than that of type I. The present patient achieved 11 years of disease-free-survival. To our best knowledge, this is the first report of PPB type II diagnosed during the prenatal period.

© 2014 The Authors. Published by Elsevier Inc. All rights reserved.

Pleuropulmonary blastoma (PPB) is a rare, progressive and aggressive malignant intrathoracic tumor observed during childhood [1,2]. Making a definitive diagnosis of PPB based on clinical manifestations and imaging studies can be difficult due to the wide spectrum of differential diagnoses, including congenital cystic adenomatoid malformation (CCAM) [3]. However, delayed diagnosis and treatment for PPB are sometimes associated with fatal outcomes. Only three prenatally diagnosed cases have been reported in the previous literature: the pathological diagnosis was type I in each case. We herein report the first case of PPB type II detected during the prenatal period.

1. Case report

A female was born at 38 weeks of gestation via induced vaginal delivery due to tumor compression of the mediastinum. A left-sided lung mass had been detected during the prenatal ultrasound testing. Immediately after birth, respiratory distress was detected and the patient required immediate intubation and mechanical ventilation. A chest X-ray showed a giant mass occupying the left thoracic cavity, with the mediastinum shifted to the right side (Fig. 1). Contrast-enhanced computed tomography (CT) revealed a tumor measuring 6 × 6 × 3 cm in size that was enhanced non-uniformly. Magnetic resonance imaging (MRI) showed a mixture of cystic and solid components, and intratumoral hemorrhage was suspected (Fig. 2). Several antibiotics were administered; however, the treatment was ineffective. The initial diagnosis was CCAM type 2 and twenty-two days after birth, thoracotomy was performed. The baby was placed in the right lateral decubitus position, and the skin incision was made at the level of the seventh costal cartilage between the parasternal line and the posterior axillary line. A tumor measuring 6 cm-in size occupied the dorsocaudal region of the left thoracic cavity, and the left lower lobe was shifted ventrally. The tumor originated from the pleura surrounding the hilum of pulmonis and connected with the pleura via the still, including the feeding artery. Removal of the tumor was undertaken with ligation of the still. The exact tumor size was 6.7 × 6.3 × 3.4 cm, with a weight of 86 g. Histopathologically, the tumor was primarily composed of diffuse proliferation of round to oval cells with hyperchromatic nuclei, prominent nucleoli and scant cytoplasm, accompanied by mild chronic active inflammatory infiltration. Mitotic figures were occasionally...
seen in the tumor cells. Cystic spaces lined with cuboidal and columnar epithelium were also observed in the low-power field. Immunohistochemically, the tumor cells were positive for vimentin, cytokeratin, lysosome and α-SMA. These findings were compatible with a diagnosis of PPB type II (Fig. 3). The patient recovered uneventfully during the perioperative period. She subsequently received VAC chemotherapy (Vincristine, Actinomycin and Cyclophosphamide) as adjuvant chemotherapy and has achieved a disease-free survival of 11 years as of today.

2. Discussion

PPB was first described in 1988 as a malignant immature tumor of the chest in children arising from the lung mesenchyme [1]. The pathological findings of PPB are similar to those of adult-type pulmonary blastoma in that the lesions are composed of blastoma and stroma, although PPB has no malignant epithelial component. Priest et al. classified 50 cases of PPB into three groups according to the histological features: type I (pure cystic), type II (cystic and solid) and type III (purely solid) [2]. The mean age at presentation of type I, II and III was 10, 34 and 44 months, respectively. Type I was found to be associated with a lower rate of recurrence than types II and III and included no metastatic lesions. In that report, the five-year survival rates of type I and the others were reported to be 83% and 42%, respectively. These findings suggest that the cystic type PPB tends to present earlier with a more favorable prognosis than solid-type PPB.

Interestingly, transitional cases from PPB type I to type II or III have been reported. In some cases, although the biopsy specimen showed type I features, the resected tumor was diagnosed as type II or III. In other cases, although the primary tumor was diagnosed as type I disease, the recurrent lesion was diagnosed as type III [4,5]. These findings suggest that some PPB cases exhibit characteristics of progression from type I to type II or III and that the prognosis deteriorates as the lesions transition to the solid type.

Fig. 1. Chest X ray at birth showed a giant mass occupying the left thoracic cavity.
International PPB registry (IPPBR) reported that, among 277 patients, nine (3.2%) had PPB in their family. Making a definitive diagnosis of PPB is often difficult because the differential diagnosis of congenital lung lesions includes a wide spectrum of disorders, such as CCAM, congenital peribronchial myofibroblastic tumors (CPMTs), congenital cystic adenomatoid or pulmonary airway malformation (CCAM-CPAM) and other rare tumors, including PPB. However, it is more difficult to distinguish malignant tumors from these lesions using prenatal imaging studies because the features of the above-mentioned diseases are complex. In the present case, the initial diagnosis was made as CCAM, and conservative therapy, including mechanical ventilation and the administration of several antibiotics, was given as primary treatment. Nevertheless, early surgical resection was fortunately performed due to the patient’s persistent respiratory distress, which revealed a large-sized tumor occupying the left thoracic cavity. Early surgical resection should be considered in patients with symptoms such as those observed in the present case, although the management of asymptomatic cases remains controversial. Careful evaluation and proper intervention are crucial in the management for congenital lung lesions, which include rare potentially malignant tumors, such as PPB. Complete surgical resection is the most important treatment for PPB. Recently, some authors have reported that postoperative adjuvant chemotherapy and radiotherapy provide more favorable outcomes than surgical resection alone, while other authors recommend the use of adjuvant chemotherapy in all cases of PPB [8,9]. Moreover, the effectiveness of radiation therapy after surgery for type II and III disease is contended [10].

Thus far, four cases of PPB, including the present case, have been diagnosed prenatally and treated with tumor resection [11,12]. The average gestational age at diagnosis and birth among these cases was 32.5 (21–40) and 38.5 (35–41) weeks, respectively. All cases were detected with maternal ultrasonography. Two patients had no respiratory symptoms at birth, whereas respiratory distress was detected in the other two patients, including the present patient. The initial diagnosis in three cases was CCAM, while that of the other case was not described. Two patients, including the present patient, with respiratory distress underwent tumor resection in neonatal period, while the other two cases underwent tumor resection at 20 and 4 months of age, respectively. The pathological diagnosis in the three previously reported cases was type I disease. On the other hand, the present case was diagnosed as type II. Adjuvant chemotherapy was given in the present case only, although another prenatally resected patient suffered from local recurrence and was treated with wedge tumor resection. No patients exhibited any metastatic lesions and survived throughout their observation period (Table 1). In the previous three cases, the pathological findings were all of type I and the patients underwent surgical resection at a relatively early age, including the neonatal period. These factors are thought to be associated with favorable outcomes. The present patient also demonstrated a favorable outcome despite

![Fig. 3. (A) Cystic spaces lined with cuboidal and columnar epithelium were observed in the low-power field (H&E stain × 100). (B) The tumor was primarily composed of diffuse proliferation of round to oval cells with hyperchromatic nuclei, prominent nucleoli and scant cytoplasm, accompanied by mild chronic active inflammatory infiltration. Mitotic figures were occasionally seen in the tumor cells (H&E stain × 400).](image)

**Table 1**

The characteristics of prenatally diagnosed PPB cases.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gestational age at diagnosis</th>
<th>Modality</th>
<th>Respiration before operation</th>
<th>Preoperative diagnosis</th>
<th>Age at operation</th>
<th>Tumor size</th>
<th>Pathological type</th>
<th>Adjuvant therapy</th>
<th>Observation period</th>
<th>Recurrence</th>
<th>Metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Our case</td>
<td>37 weeks</td>
<td>US</td>
<td>Distress, HFO</td>
<td>CCAM</td>
<td>22 days</td>
<td>$6.7 \times 6.3 \times 3.4$ cm</td>
<td>Type II</td>
<td>VAC</td>
<td>11 years</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>21 weeks</td>
<td>US</td>
<td>Asymptomatic</td>
<td>CCAM</td>
<td>20 months</td>
<td>Unknown</td>
<td>Type I</td>
<td>None</td>
<td>39 month</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>40 weeks</td>
<td>US</td>
<td>Distress, 100% O₂ hood</td>
<td>Unknown</td>
<td>2 days</td>
<td>Unknown</td>
<td>Type I</td>
<td>None</td>
<td>9 years</td>
<td>Resection</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>32 weeks</td>
<td>US</td>
<td>Asymptomatic</td>
<td>CCAM</td>
<td>4 months</td>
<td>$2 \times 1.5 \times 0.3$ cm</td>
<td>Type I</td>
<td>None</td>
<td>3 years</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

US, ultrasound test; HFO, high frequency oscillation; CCAM, congenital cystic adenomatoid malformation; VAC, vincristine, actinomycin D and cyclophosphamide.
receiving a diagnosis of type II PPB. We speculate that the early diagnosis made following the detection of the relatively large tumor and the administration of post-operative adjuvant chemotherapy may account for the favorable prognosis observed in the present case. One interesting finding in this case is that the patient was diagnosed with type II PPB during the prenatal period, which indicates that some cases of type II PPB may involve genetic abnormalities, such as DICER1 mutations rather than characteristics of progression from type I to type II or III. Further molecular biological investigations are needed to clarify the morphogenesis of PPB. In conclusion, we herein reported a rare case of PPB type II detected in the prenatal period. The possibility of PPB should be taken into consideration in the differential diagnosis of pediatric pulmonary disorders including cystic lung diseases.

References