Pleuropulmonary blastoma in adolescence: A rare tumor beyond first decade of life

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ABSTRACT

Pleuropulmonary blastoma (PPB) is a unique dysontogenetic and a primitive neoplasm occurring almost exclusively in the first decade of life, as a pulmonary- and/or pleural-based tumor with cystic, solid, or combined cystic and solid features. It is characterized histologically by a primitive, variably mixed blastematous and sarcomatous tissues. These tumors are usually associated with a poor prognosis. However, with a multimodality treatment approach, the survival of the patient can be prolonged. We herein report two cases of PPB in adolescence, a rare presentation beyond first decade of life with a short review of literature.

KEY WORDS: Adolescence, blastoma, pleuropulmonary, primitive

INTRODUCTION

In 1988, Manivel et al.[1] first described pleuropulmonary blastoma (PPB) as a distinctive tumor in young children, occurring almost exclusively in the first decade of life. Since then, individual cases as well as series of similar tumors in children have been reported with the diagnosis of PPB. International PPB Registry is maintaining a record of patients with PPB for last 20 years having published [N = 50] as well as unpublished [N = 128] registry series.[2] It has a rare occurrence beyond the first decade of life and only a few isolated cases in adults have been reported.[3-6] These tumors usually require a multimodality treatment approach for improving the survival including surgery, chemotherapy and radiation therapy. PPBs occurring in older age usually have a poor prognosis. We herein report a short series of two cases of PPB in adolescence, with one of them having a relatively long survival, an unusual presentation beyond the first decade of life.

CASE REPORTS

Case 1

A 14-year-old adolescent male presented with complaints of nonproductive cough for three months associated with dyspnea on exertion in July 2009. Computed tomography (CT) of the chest showed an approximately 6 × 5 × 3 cm sized heterogenous mass lesion in the right lower lobe [Figure 1a]. Possibilities were carcinoid, primitive neuroectodermal tumor (PNET) and sarcoma. Endobronchial biopsy was done, which showed nests of malignant cells with hyperchromatic, elongated nuclei and moderate cytoplasm. These cells were positive for vimentin on immunohistochemistry. A possibility of PPB was suggested. The patient underwent right middle and lower lobectomy. On cut sections, tumor was seen occupying approximately 90% of lower lobe and was greyish white in color with areas of cystic changes. Multiple areas of hemorrhage were also seen. On microscopy, plump to spindle-shaped cells arranged in short fascicles as well as storiform pattern were seen. The cells were showing moderate nuclear atypia, elongated nucleus, some showing nucleoli and moderate amount of cytoplasm with brisk mitoses. In between, there were vague nests of primitive blastemal cells. Based on these features, a diagnosis of PPB was given.

The patient was referred for radiotherapy, where he received a cumulative dose of 50 Gray (Gy) in 25 fractions.
Radiotherapy was completed in October 2009. The follow-up CT showed a heterogenous soft tissue in the right paravertebral location abutting the mediastinal pleura [Figure 1b]. In view of residual lesion, the patient received six cycles of chemotherapy (250 mg paclitaxel and 70 mg cisplatin) at 3-week intervals. The sixth cycle was completed in March 2010, and no residual lesion was seen in the follow-up CT.

The patient was on a regular follow up without any significant complaints. However, in September 2011, the patient started complaining of vague abdominal pain on and off. The ultrasound examination showed a heterogenous mass lesion in the left kidney. Fine-needle aspiration (FNA) was done under ultrasound guidance, which showed highly cellular smears and sheets of undifferentiated cells having high nuclear/cytoplasmic ratio. In addition to focal mesenchymal fragments, many mitotic figures and karyorrhexis were noted. On immunocytochemistry, cells were positive for vimentin and neuron-specific enolase (NSE) showed strong focal positivity. In addition, nuclear positivity for Wilms tumor (WT-1) was seen in about 50% of cells. A diagnosis of Wilms tumor was offered. The patient was referred to the urology department for the surgical consideration, however, was lost to follow up.

**Case 2**

An 18-year-old adolescent male patient was referred recently to our institute from a hospital with complaints of abdominal pain with recurrent fever for the last 4 months. A clinical possibility of a ruptured liver abscess in the right pleural cavity based on sonographic findings was documented in the records. The radiograph of the chest showed white-out right hemithorax. The patient underwent CT of chest and abdomen. The CT showed a large solid-cystic mass lesion with thick enhancing septae filling almost the entire right hemithorax and extending inferiorly, indenting upon the right hemidiaphragm and displacing the liver inferiorly. The mass was having loss of fat planes at places with the mediastinal structures, including trachea, heart, right innominate artery, and was compressing upon right main bronchus. Overlying ribs and soft tissues were normal with no extrathoracic extension [Figure 2]. Moderate pleural effusion was also seen. Radiologically, a possibility of sarcoma was suggested.

A percutaneous ultrasound (US)-guided FNA was performed. The aspirate was particulate and the smears were air-dried as well as alcohol-fixed and stained with May–Grünwald Giemsa and hematoxylin and eosin, respectively. A cell block was also prepared. On microscopy, the smears were cellular, and showed sheets of small variably shaped poorly differentiated cells. The cells were predominantly oval to spindle-shaped and a prominent perivascular arrangement was noted. The tumor cells had high nuclear: Cytoplasmic ratio, finely granular chromatin, inconspicuous nucleoli, and scanty eosinophilic cytoplasm with indistinct cell borders. Occasional scattered cells had cytoplasmic vacuolation [Figure 3]. Heterogenous component was not seen. Immunocytochemically, the tumor cells showed strong positivity for vimentin and focal positivity for smooth muscle actin [Figure 4]. Cytokeratin, Mic-2, and CD56 were negative. A cytological diagnosis of PPB was offered.

The patient developed progressive respiratory dysfunction and died approximately seven days after the diagnosis of tumor.

**DISCUSSION**

PPB, which is a rare aggressive malignant primary neoplasm of the pleuropulmonary mesenchyme occurring in early childhood associated with poor prognosis. Its occurrence beyond the childhood is exceptional. Only a few isolated cases of PPBs have been reported in literature in adult population. Table 1 summarizes the key findings of previously published cases in literature in adult population. There are three pathological types (type I, II, and III) of PPB based on gross and microscopic...
features. The median ages at diagnosis are 10, 34, and 44 months for types I, II, and III, respectively.\(^2,^7\)

The tumor may arise from the lung or it may be extrapulmonary, involving the mediastinum or parietal pleura. Our case showed the tumor filling nearly the entire right hemithorax in the second case, whereas it was central in location in the first case.

The tumor has no characteristic findings on imaging studies. Type I PPB presents as benign appearing air-filled lung cysts. It is to be kept in mind that type I PPB cannot be differentiated from other benign cystic lung lesions on imaging studies, which include congenital lung cysts such as congenital adenomatoid malformations.\(^2\) Type II and III PPB usually present as a large heterogenous masses, which may invade mediastinum, vessels, and diaphragm. They are frequently associated with pleural effusion and rarely involve lymph nodes. These radiological findings in varying proportions were present in our cases too. Type II PPB is a solid-cystic tumor, whereas type III PPB is solid tumor without epithelial-lined cystic spaces.\(^7\) In view of presence of solid-enhancing areas as well as nonenhancing cystic areas, the tumors in our cases were type II PPB radiologically. Type II and III PPB tumors can metastasize to central nervous system, bones, and liver.

Microscopically, there is presence of primitive blastema and a malignant mesenchymal stroma that often demonstrates heterologous elements such as cartilage differentiation. Myxoid components resemble embryonal rhabdomyosarcoma. Blastema components may show numerous mitoses and foci of necrosis, as seen in the resected specimen in the first case. Cystic component is lined by benign respiratory-type epithelium. Due to histologic variability in the solid component of the PPB, there can be a broad differential diagnosis. However, based on the some characteristic features such as cystic architecture, blastemal tissue, and other mesenchymal components including cartilage, PPB can be designated as a distinct entity.\(^3,^7\) The malignant mesenchymal cells are usually immunoreactive for vimentin, muscle-specific actin and desmin. However, vimentin positivity has been described as the only typical characteristic finding. The cells were vimentin positive in both of our cases, whereas actin positivity was seen in the second case only.

Clinically, the tumor equally affects both genders. In our series, both patients are males. Shortness of breath in the absence of other respiratory tract symptoms is the main symptom in most cases of PPB reported. A suspected pulmonary infection, including an empyema, is the most frequent clinical impression in these patients.\(^7\) Our first patient presented with respiratory complaints of nonproductive cough and dyspnea. However, the second patient presented with abdominal pain with recurrent fever for last 4 months and hence a pulmonary infection was not a clinical consideration.

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**Table 1: Clinicoradiological details of published cases of PPB in adult population**

| Reference number | Author            | Age in years | Gender | Clinical presentation                      | CT appearance                | Treatment given                |
|------------------|-------------------|--------------|--------|-------------------------------------------|------------------------------|-------------------------------|
| 3.               | Hill et al.       | 36           | Male   | Chest pain, cough, fever, weight loss     | Multilocular cystic lesion   | Surgery and chemotherapy      |
| 4.               | Liu et al.        | 43           | Female | Massive pleural effusion                  | Multicystic lesion           | Surgery and chemotherapy      |
| 5.               | Lee et al.        | 21           | Male   | Chest pain, mild dyspnea                  | Multicystic tumor            | Surgery only*                 |
| 6.               | Gönülü et al.     | 25           | Female | Dyspnea, irritative cough                 | Solid mass                   | Surgery and chemotherapy      |

*The patient was planned for chemotherapy after the surgery, however, he refused, PPB: Pleuropulmonary blastoma, CT: Computed tomography

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**Figure 3:** Case 2. Aspiration cytology of pleuropulmonary blastoma:
(a) cellular smear with prominent perivascular pattern (hematoxylin and eosin $\times 200$) (b) small ovoid to spindled cells with occasional cell showing cytoplasmic vacuolation, Inset: small cell with cytoplasmic vacuolation [May–Grünewald Giemsa (MGG) $\times 400$] (c and d) cell block showing oval to spindle-shaped cells with scanty eosinophilic cytoplasm with indistinct borders (MGG $\times 400$)

**Figure 4:** Case 2. Immunohistochemistry slides showing strong positivity of tumor cells for vimentin (a–c) and weak focal positivity for smooth muscle actin (d)

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PPBs require a multimodality treatment approach including surgery, chemotherapy, and radiation therapy.\[7\] Chemotherapy is based on the institutional practice, which includes either specific chemotherapeutic agents or their combination. The various agents that have been used include vincristine, actinomycin D, cyclophosphamide, doxorubicin, ifosfamide, etoposide, cisplatin, carboplatin, epirubicin, methotrexate, and 5-fluorouracil. However, no specific association has been shown between the survival and the chemotherapy used.\[7\] Our first patient received cisplatin–paclitaxel combination and showed a complete response (100% decrease) according to Response Evaluation Criteria in Solid Tumors (RECIST) criteria. Types II and III PPBs are aggressive tumors and even after a multimodality therapy have a survival rate of 62% at 2 years and 42% at 5 years.\[7\] Our first patient underwent multimodality treatment and had an overall survival of 27 months (from the diagnosis to the last contact). However, the second patient died within seven days due to progressive respiratory dysfunction even before the treatment could be started.

PPBs are familial childhood cancer with a high incidence of childhood cancers in close relatives (25%).[5,8] These include PPB, malignant germ cell tumor, medulloblastoma, thyroid neoplasia, and others.[5,8] No family history of childhood neoplasia was there in either of the index case. The patients with PPB are also at a higher risk of developing childhood cancers, as seen in the first case in which the patient developed renal Wilms tumor during the follow-up period.

To conclude, PPBs are primitive dysodontogenic neoplasms of childhood. Their occurrence beyond the first decade of life is a rare presentation. These neoplasms usually present with respiratory complaints with no specific radiological features on imaging. Pathologically, variably shaped poorly differentiated cells having a prominent perivascular arrangement are seen. The cells should show positivity for vimentin, actin, and desmin on immunohistochemistry. The patients are at a risk of developing primitive childhood tumors. Multimodality treatment helps in ensuring satisfactory clinical results and increasing the survival.

**REFERENCES**

1. Manivel JC, Priest JR, Watterson J, Steiner M, Woods WG, Wick MR, et al. Pleuropulmonary blastoma. The so-called pulmonary blastoma of childhood. Cancer 1988;62:1516-26.
2. International Pleuropulmonary Blastoma Registry. Available from: http://www.ppregistry.org/doctors/diagnosis.htm. [Last accessed on 2015 Jan 25].
3. Hill DA, Sadeghi S, Schultz MZ, Burr JS, Dehner LP. Pleuropulmonary blastoma in an adult: An initial case report. Cancer 1999;85:2368-74.
4. Liu AH, Zheng WY, Wu L. Pleuropulmonary blastoma in an adult women with pleurorrhea as the major clinical manifestation: Report of a case. Nan Fang Yi Ke Da Xue Xue Bao 2008;28:2241-3.
5. Lee CH, Kim KI, Kim YD, Lee MK, Kim JY, Park DY, et al. Pleuropulmonary blastoma in a young adult presenting as a ruptured cystic teratoma in radiology. J Korean Med Sci 2003;18:593-8.
6. Gönüllü G, Evrensel T, Kurt E, Aydin S, Bayram S, Aydin F, et al. Pleuropulmonary blastoma in an adult patient: Report of a case. Turk J Cancer 2007;37:158-61.
7. Priest JR, McDermott MB, Bhatia S, Watterson J, Manivel JC, Dehner LP. Pleuropulmonary blastoma: A clinicopathologic study of 50 cases. Cancer 1997;80:147-61.
8. Priest JR, Watterson J, Strong L, Huff V, Woods WG, Byrd RL, et al. Pleuropulmonary blastoma: A marker for familial disease. J Pediatr 1996;128:220-4.

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