Case Series

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Pleuropulmonary Blastoma: A Rare Malignant Lung Disease in Children

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ABSTRACT

Background: Pleuropulmonary blastoma (PPB) is a very uncommon, mesenchymal malignant tumor in the chest cavity that occurs mostly in children before preschool age (less than 6 years old), while it is the most common cause for primary pleural and lung tumor in children and adolescent malignancy. **Aim**: To increase the awareness about the diagnosis of PPB in children. **Methods**: Six Pleuropulmonary blastoma cases were diagnosed at Basra Oncology Center in the south of Iarq and registered at Basra Specialist Children's Hospital. The first case was diagnosed in 2012 and the last case was diagnosed in 2020, where their characteristics, clinical and pathological features, methods of treatment, and relapse and survival outcomes were retrospectively evaluated. **Results**: Male to female ratio being 1:1; most of the patients were less than five years old. Most of the cases were poor prognosis type II/III (mixed/pure solid). Three cases were type II and the other three cases were type III, and in spite of forceful treatment by multimodality, involving surgery, chemotherapy, and radiotherapy, have grave prognosis and the death rate was 33.3%. **Conclusions**: PPB is an uncommon neoplasm, but it is an aggressive disease having a poor outcome. Its recurrence is high in spite of intensive surgical excision of tumor mass being used, which is the corner stone of PPB, along with chemotherapy and/or radiotherapy. Especially in younger children, it causes severe morbidity.

Keyword: Pleuropulmonary blastoma, Children, lung, malignant disease

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INTRODUCTION

Pulmonary blastoma (PB) is an uncommon lung tumor. The incidence of its occurrence is approximately less than 0.5% of primary intrathoracic malignancies. Less than 1000 cases have been reported in the world since its first description given by Barnett and Barnard in 1945.[1]

The morphology of this tumor has a similar form to the embryonal structure of the lung, which was historically described under a uniform medical term until distinct entities were recognized,[2] and because it can originate from the lung or pleura, it's termed as pleuropulmonary blastoma (PPB).[3]

It occurs in an exclusive manner in children and mostly involves local evolution with some cases presenting as metastasizing and aggressive tumors.[4]

While PB in adults is more common than children's type of (PPB), PB occurs commonly in the middle-aged and is typically associated with symptoms and signs similar to lung cancer. It is divided into two groups depending on histopathological features: type (1) monophasic PB,

which is called well-differentiated fetal adenocarcinoma (WDFA), and type (2), which is classic biphasic PB (CBPB) containing tissue of both fetal adenocarcinoma (type 2 is typically low grade) and primitive mesenchymal stroma.[5] These three subgroups (PPB, CBPB, and WDFA) have overlapping genetic abnormalities, the original pathological grouping, and histological characteristics.[6]

Primary pulmonary neoplasms are rare in children. One such tumor, pleuropulmonary blastoma (PPB), is highly aggressive and malignant, very rare, and originates from either the pleura or lungs. It occurs mainly in children aged less than 6 years.[7]

Dehner et al. classified PPB into three subgroups in 1995 as type I (cystic), type II (mixed cystic and solid), and type III (pure solid).[8] The median diagnosis age, type I, occurs in infants (10 months) in contrast to type II (34 months) and type III (44 months).[9] Type II and type III have unfavorable prognosis, while type I is more favorable than others.[8] Most type I PBBs progress to types II and III. But not all cystic type I PPBs progress to the more malignant types. These “regressed” cystic types are designated as type I regressed (type Ir).[10]

Previously, PPB Type II was incorrectly called “extra-renal Wilms tumor” because it is morphologically similar to Wilms tumor.[11]

PPB is associated with a rare hereditary condition related to DICER1 gene mutation, which presents with an unusual pneumothorax. The aim of this study is to increase awareness, to recognize this rare entity in its early course. And it leads to local relapse and distant metastasis, so that genetic condition is predisposed to a variant neoplastic condition called DICER1 syndrome [8]. It has also been shown to be linked with a disorder of the long arm of chromosome 8.[12]

The risk of the present neoplasm is in direct proportion with the increase in age, so the incidence of PPB before the age of 10 years is 5.3% and before the age of 60 it is 31.5%.[13]

The recommended treatment depends on the type of PPB. Type I regressed (type Ir) is treated only by follow up and does not need chemotherapy while type I (cystic type) PPB treatment includes surgical excision and chemotherapy. For type II (mixed type) and type III (solid type) tumors, the treatment depends on the size of the tumor. If it is an operable tumor, aggressive surgery is used and then adjuvant chemotherapy. While the large type II and type III tumors are inoperable and treated by starting neoadjuvant chemotherapy, the aim is to reduce the tumor size usually by more than 90%, followed by aggressive surgical resection. The recommended protocol of chemotherapeutic agents is the IVADO regimen (Ifosfamide, Actinomycin D, Vincristine, and Doxorubicin), and if it metastasizes, the recommended treatment consists of all three modalities (chemotherapy, surgery, and radiation therapy).[14]

MATERIALS AND METHODS

Six Pleuropulmonary blastoma cases were diagnosed at Basra Oncology Center in the south of Iarq and registered at Basra Specialist Children's Hospital. The first case was diagnosed in 2012 and the last case was diagnosed in 2020, where their characteristics, clinical and pathological features, methods of treatment, and relapse and survival outcomes were retrospectively evaluated. Children are classified according to the age into the following groups:

- Birth up to 36 months (<3 years old)
- 37 months up to 144 months (3 years old– <12 years old)
- 144 months up to 192 months (12 years old–16 years old).[15]

RESULTS

Over the last 10 years, 6 patients with PPB have been admitted to the center. Per the distribution data of the 6 cases, according to the gender 3 were male and 3 were female (50% males and 50% females).

As given in Table 1, the most occurring ages with PPB in our study were less than and equal to 36 months of age (66.6%), and 2 cases were of those more than 36 months of age (33.3%).

The histopathological distribution was cystic/solid (type II) in 3 (50%) patients, solid (Type III) in 3 (50%) patients, while no cases were diagnosed as type I.

Two cases were diagnosed in 2012; one case was diagnosed in 2013, so 50% of the cases were diagnosed before 2015, and the other three cases were diagnosed in 2016, 2019, and 2020.

Table 2 shows all patients with PPB had SOB and cough (100%). Five cases had fever (83.3%) and one patient had sweating (16.6%) while no patient with PPB had cyanosis. The most common location of PPB was on the left side of the chest (4 cases, 66.6%). In the other two cases, it occurred on the right side (33.3%).

All PPB patients (100%) at the center were treated by surgical excision, chemotherapy, and radiotherapy, using chemotherapy in the form of VIVA protocol (vincristine, ifosfsmide, doxorubicin, and actinomycin).
During follow up only two patients showed recurrence of PBB (33.3%). The recurrence of PPB more in type III (33.3%) than in type I and type II (16.6%).
During follow-up of patients with PPB, 33.3% were dead and 66.6% were still alive.

Table 1: Age distribution of cases diagnosed with PPB.

Age	No.	Percentage
< 36 months	4	66.6
37 up to 144 months	2	33.3
144 up to 192 months	0	0

Table 2: Incidence of signs and symptoms in PPB.

Symptoms and Signs	No.	Percentage
Fever	5	83.3
Shortness of breath	6	100
Cough	6	100
Cyanosis	0	0
Sweating	1	16.6

DISCUSSION

In our study, the male: female ratio for PPB sex distribution was 1:1, which matches Oliveira et al.'s work[16] who took 10 cases of PPB and the male: female ratio was (5:5) which also matches Zhang Na et al.'s work[17] who took 41 patients with PPB and the M:F ratio was 20:21, which shows 0.95:1 incidence.
Most cases of PPB occur at the age of three years old and are less similar to that occurring in Zhang et al.'s work.[17] In most cases, the age was less than three years old.

Our study on PPB revealed no type I and the type II to type III ratio was 3:3. The result is not in agreement with Messinger et al.'s work [18], which shows 350 patients had one-third of each type (35%) because in our society there are a low number of cases and there is a delay of diagnosis due to low pediatrician awareness about the signs and symptoms of PPB. However, our study is highly in agreement with Nahid et al.'s work [19], which showed type II and type III (80%) have high incidence than type I. In this study, the most common clinical symptoms were respiratory distress such as SOB and cough which matches Indolfi et al.'s work.[20] It involved 11 cases, and the most common clinical feature was also respiratory distress. [21]
All patients in our study were treated by surgical excision of tumor mass, which was followed by chemotherapy and radiotherapy. This was not significantly in agreement with Ömer et al. 's work [21], and radiotherapy was not included in the treatment protocol for PPB, while it was significantly in agreement with the work of Indolfi et al. [20]

Most cases in our research show the location of PPB on the left side of the chest (4/6 of cases, i.e., 66.6%). That is the same as that occurring in Bu et al.'s work [22], which showed 29 cases of PPB were located on the left side of the chest. The most common recurrence of the disease was of type II and type III, rather than in type I. That result agrees with those of Messinger et al. [18] and Priest et al. [23] The result in Priest et al.'s work shows the recurrence of type I PPBs was 14% while of type II and III PPBs it was 46%.
The prognosis is regression. So many patients with type I will have histopathological progression to type II and typeIII, which have poor outcome, increased incidence of relapse, and most patients pass away, which show the same results as those of Messinger et al. [18]

CONCLUSIONS

PPB is an uncommon neoplasm, but it is an aggressive disease having a poor outcome. Its recurrence is high in spite of intensive surgical excision of tumor mass being used, which is the corner stone of PPB, along with chemotherapy and/or radiotherapy. Especially in younger children, it causes severe morbidity. Most PPB cases are diagnosed at a late stage so the pediatrician must create awareness about any children having respiratory symptoms and the seriousness of PPB. Most of the cases have poor prognosis due to delay in diagnosis, so we need early diagnosis facilities.

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