

Endobronchial pulmonary blastoma – an unusual presentation of a rare lung malignancy and review of literature

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Abstract

Biphasic pulmonary blastoma (BPB) is an extremely rare highly aggressive malignant tumour that arises from fetal lung tissue and has the classical biphasic histology of epithelial and mesenchymal components. It is usually seen in adults with a slight

predominance among males and smokers. Previously grouped along with well-differentiated fetal adenocarcinoma (WFA), and pleuropulmonary blastoma (PPB), now it is considered a separate variant and grouped under sarcomatoid neoplasms. Symptoms include chest pain, cough, hemoptysis and it is asymptomatic in at least one-third of the cases. A biopsy is essential for diagnosis and surgical excision is the treatment of choice. Prognosis is poor with 5-year survival less than 20% and recurrence occurring within 12 months of surgery. An aggressive multimodality approach is required for its management and active follow up surveillance is needed to look for recurrence.

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Introduction

Biphasic pulmonary blastoma (BPB) is a rare lung neoplasm comprising 0.25-0.5% of primary lung malignancies with a very aggressive course and poorer prognosis [1,2]. It was initially described by Barnett *et al.* [3] in 1952 and since then approximately 300 cases have been reported in the literature [4]. Morphologically, it resembles fetal lung tissue of gestation age less than 16 weeks and has typical biphasic histology (epithelial and mesenchymal components) [5]. Despite having fetal lung tissue origin, it is seen predominantly in adults [2]. Due to its rarity, non-specific clinical symptoms, subtle radiological findings, variable histology, rapid progression, and poor prognosis, the diagnosis and management is challenging. Here, we describe a rare case of a classical BPB with endobronchial spread and a brief review of the literature.

Case Report

A 30-year-old Indo-Aryan male, chronic smoker, with no previous co-morbidities was admitted to our hospital with complaints of cough with minimal expectoration, right-sided chest pain, and shortness of breath on exertion for the last four months. He also had multiple episodes of mild hemoptysis in the last two months. On admission, he had tachycardia, tachypnoea with accessory respiratory muscle use, was normotensive and had slightly reduced peripheral oxygen saturation (SpO₂- 93% on room air). Arterial blood gas (ABG) on ambient air revealed respiratory alkalosis and mild hypoxemia (PaO₂-70mm Hg). Respiratory system examination disclosed decreased chest expansion and absent breath sounds in the right hemithorax. Chest radiograph showed an opaque right hemithorax (Figure 1A). Contrast-enhanced computerized tomog-

raphy (CECT) of the thorax revealed a right-sided large homogeneous mass (9.3 cm) with endobronchial spread involving right main bronchus causing an ipsilateral mediastinal shift and mediastinal lymphadenopathy (Figure 1B). After obtaining informed consent, ultrasound-guided (USG) transthoracic biopsy was done. However, transthoracic biopsy was non-contributory.

Video bronchoscopy and endobronchial biopsy was performed. White light bronchoscopy (WLB) revealed a fleshy endobronchial mass in the right main bronchus (RMB) (Figure 2 A,B). Multiple endobronchial biopsies were taken and sent for histopathology (HPE). Hematoxylin and Eosin (H&E) stained sections showed a tumour with biphasic morphology comprised of irregular elongated glands and cellular mesenchymal component. The glands are lined by low to tall columnar, focally stratified cells with hyperchromatic nuclei, inconspicuous nucleoli and scanty cytoplasm. Few small supra-nuclear vacuoles are noted. The mesenchymal component shows nuclear pleomorphism with irregular hyperchromatic nuclei and scanty cytoplasm (Figure 3 A,B). Focal stromal vacuolisation is noted. On immunohistochemistry (IHC), the malignant glandular component displays thyroid transcription factor-1 (TTF-1) nuclear immuno-positivity (Figure 3C) indicating pulmonary origin and is negative for alpha-smooth muscle actin (SMA) and vimentin while the malignant mesenchymal component is immuno-positive for vimentin (Figure 3D) and alpha-SMA (Figure 3E) and negative for TTF-1. Hence, a diagnosis of pulmonary blastoma was rendered.

Whole-body positron emission tomography-computed tomography (PET-CT) was done for staging and resectability status. PET-CT showed a dense FDG avid large homogeneous mass in the right hemithorax measuring 10.8 cm with SUV uptake 14.8 HU and FDG avid right paratracheal lymph node (SUV- 11.1HU) (Figure 4 A,B). Staging was done similar to non-small cell cancer (NSCLC) and was labelled as stage III-B (T4N2M0) [6]. An integrated multimodality approach involving a team of Pulmonologists, Oncophysicians, and Oncosurgeons was formed and a multidisciplinary discussion (MDD) was initiated to decide on further management. In view of TNM stage III-B and involvement of carina (a relative contraindication for pneumonectomy), it was decided to initiate neoadjuvant chemotherapy and reassess for surgery after 3 cycles of chemotherapy. The patient and his family were explained regarding the decision of the MDD. He was put on conventional chemotherapy regimen (cisplatin and etoposide) and asked to follow up for after completing 3 cycles of chemotherapy.

Discussion

Pulmonary blastomas are unusual primary lung malignancies comprising less than 1% of all lung tumours. It was poorly understood because of its biological behaviour and initially referred to as

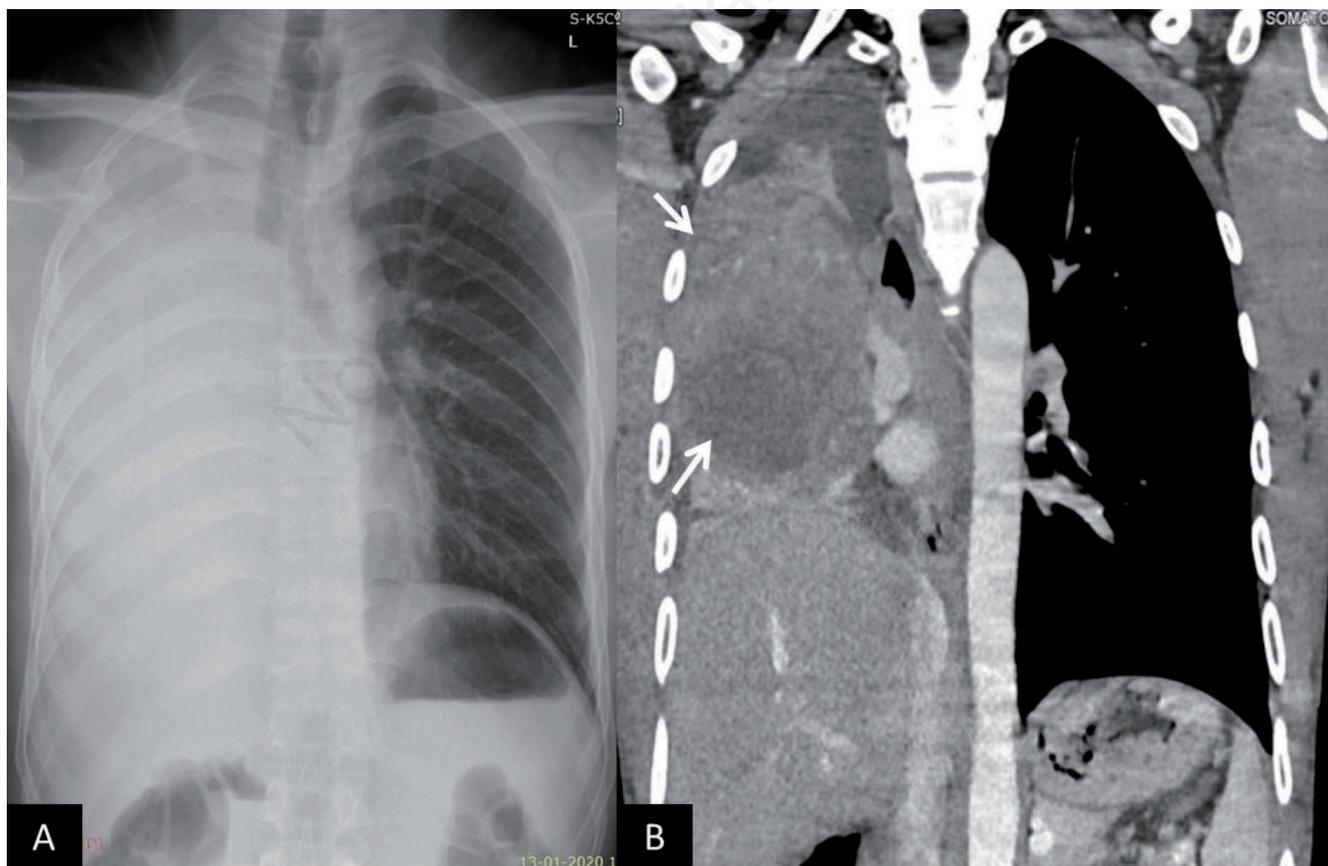


Figure 1. A) Chest radiograph showing opaque right hemithorax with mediastinal shift. B) Coronal reformatted CT images showing heterogeneously enhancing large mass lesion occupying almost the right hemithorax (arrows) with infiltration into the right main bronchus and causing passive collapse of underlying right lung.



Figure 2. A,B) White light bronchoscopy revealing a fleshy endobronchial mass in right main bronchus (blue arrow). C) Endobronchial biopsies taken with fenestrated cup forceps (red arrow).

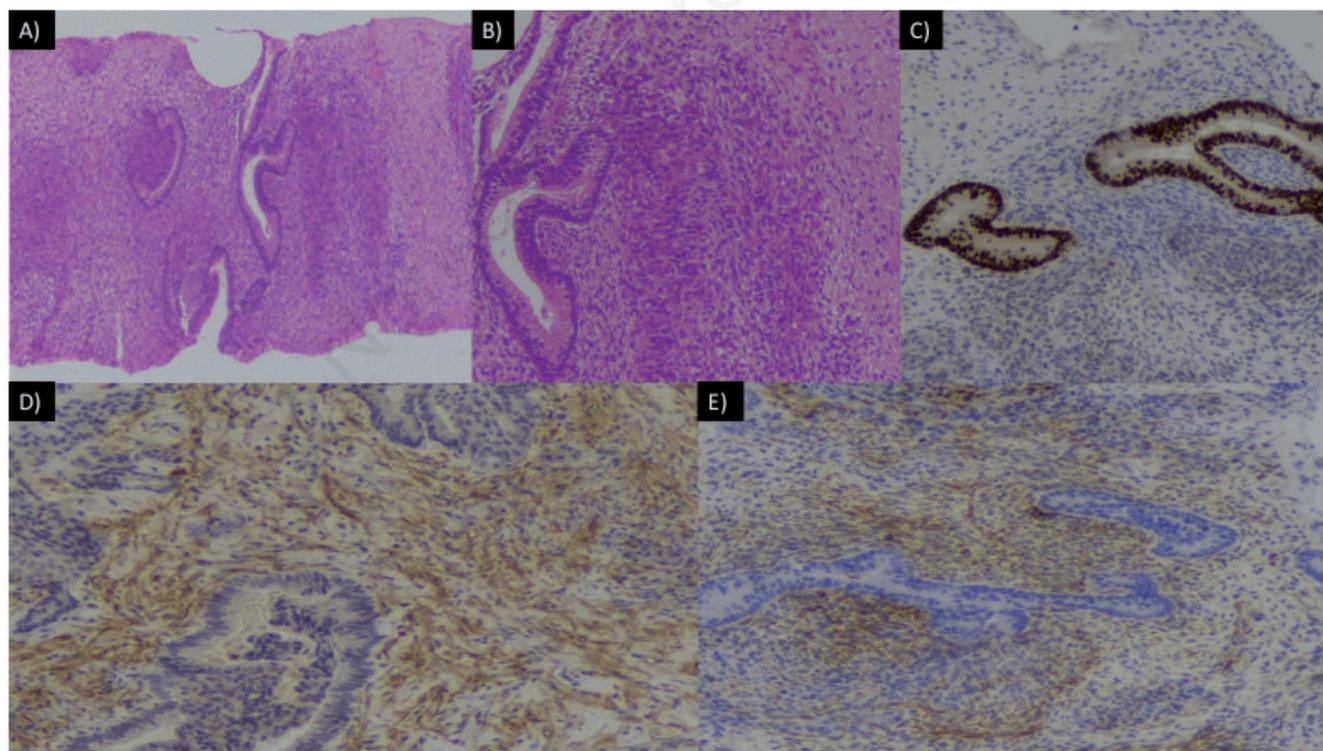


Figure 3. A) Biopsy showing an admixture of elongated irregular glands and cellular mesenchymal component; the glands are lined by columnar cells with tall columnar hyperchromatic nuclei, H&E stain, 4x. B) Biopsy showing glands lined by hyperchromatic focally stratified nuclei with few supranuclear vacuolations, H&E stain, 10x. C) IHC for TTF1 showing intense nuclear immunopositivity, DAB-H, 10x. D) IHC for vimentin showing cytoplasmic positivity in the mesenchymal component, DAB-H, 10x. E) IHC for alpha-SMA showing cytoplasmic positivity in the mesenchymal component, DAB-H, 10x.

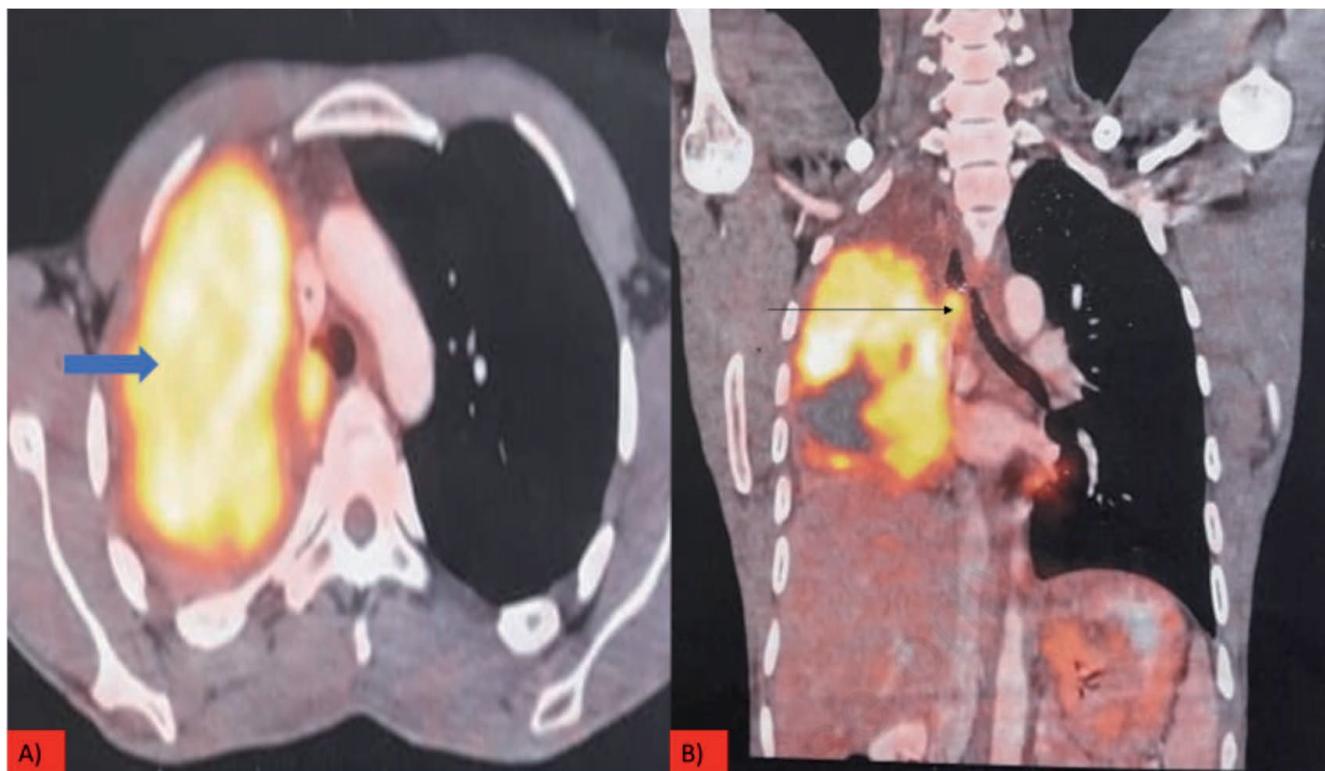


Figure 4. A) PET-CT showing FDG avid mass with ipsilateral paratracheal adenopathy (blue arrow). B) Coronal reformatted PET-CT image confirming right bronchial tree and carinal involvement (black arrow).

an embryoma [3]. Later it was found that the tumour arises from fetal lung tissue and was labelled as pulmonary blastemas. This was further classified into 3 subtypes by Koss *et al.* [7]. These include biphasic pulmonary blastoma, monophasic pulmonary blastoma with predominant epithelial expression (W DFA), and pleuropulmonary blastoma (PPB) with mesenchymal expression. WHO classifications (1999 and 2004) separated BPB from W DFA and PPB and are now grouped under sarcomatoid carcinomas [8]. Classical BPB typically occurs in adults with an average age of onset at 40 years with a slight male predisposition (2:1) [9]. There are no identifiable risk factors, but there appears to be a strong correlation with cigarette smoking [10]. Nearly 40% of cases are asymptomatic and detected during incidental imaging [7]. Among symptomatic cases, common symptoms include cough, hemoptysis, chest pain and dyspnea due to tumour compressing the bronchi and/or pleura. Although pleural and chest wall extension have been described in the literature [11], endobronchial involvement has not been reported previously to the best of our knowledge.

Radiology shows a large well defined homogenous solitary mass with smooth margins, almost always unilateral and peripherally located close to the pleura [12]. Due to its proximity with the pleura, bronchoscopy and biopsy is diagnostic in only one-fourth of the cases. Ultrasound/CT guided transthoracic biopsy serves as an excellent modality in the diagnosis [13]. Histopathological diagnosis of BPB is difficult due to its pleomorphic histology but requires a high degree of suspicion when there is cytological heterogeneity with a mixture of malignant epithelial and mesenchymal cells [5]. There is no separate staging system for pulmonary blastoma and it is reasonable to stage

them in the same way as NSCLC. Distant metastasis by hematogenous spread to brain, bone, liver, kidney, pancreas, and adrenal glands has been described in the literature. The role of PET-CT is not well studied and may help predict operability and relapse after surgical excision. Pulmonary blastomas are intensely FDG-avid which could be attributed to the presence of fetal lung tissue [14].

Surgery is the treatment of choice and complete surgical excision is the only curative treatment [15]. A mean survival of 33 months was noted after surgical excision compared to less than 2 months in unresected disease. In surgery, Larsen and colleagues [9] found that local resection had a better survival than pneumonectomy. Blastomas are relatively chemo- and radio-resistant and may be useful in the relief of palliative symptoms [2]. Chemotherapy had a mere 16% response rate [9]. However, neoadjuvant chemotherapy combined with postoperative radiotherapy and chemotherapy have shown a better prognosis [16]. Among chemotherapeutic agents, cisplatin and etoposide are preferred. Recently, a combination of ifosfamide, carboplatin, and etoposide popularly known as the *ICE protocol* was used as an effective treatment of pulmonary blastoma. Complete remission was noted at 3 months follow up after 6 cycles of ICE [17]. BPB has a poor prognosis with nearly 2/3 of patients die within 2 years and an estimated 5-year survival is 15-30% [2,10]. Factors responsible for poor prognosis include tumour size >5 cm, metastasis, completeness of resection and tumour recurrence. The recurrence rate is high the first year after resection with nearly 43% of cases have a recurrence and after one year, recurrence usually does not occur [18].

Conclusions

Our report highlights an atypical presentation of adult pulmonary blastoma and alerts pulmonologists the importance of an integrated multimodality approach. Surgical excision is curative and regular follow up is advised. In inoperable cases, conventional chemotherapy or the *ICE regimen* can be considered. Despite the best management, prognosis is poor and inversely related with the delay in diagnosis.

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