Unresectable Middle Mediastinal Biphasic Pulmonary Blastoma

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Abstract. *We report a case of a young male who presented with an unresectable, centrally-located classic biphasic pulmonary blastoma (CBPB) involving his bilateral mainstem bronchi and esophagus and a synchronous right testicular seminoma. CBPB is a rare and aggressive tumor that most commonly presents as a solitary mass in the periphery of the lung. Surgical resection is the preferred treatment for CBPB, as chemotherapy and radiation have demonstrated limited effectiveness. In the current case, four cycles of cisplatin, ifosfamide, and etoposide with concurrent radiotherapy resulted in a favorable response at three months. Currently he optimal treatment for unresectable pulmonary blastomas remains undefined.*

Classic biphasic pulmonary blastoma (CBPB) is a rare and aggressive tumor that most commonly presents as a solitary, peripheral lung mass in patients approximately 40 years old (1). Surgical resection is generally considered the optimal treatment, though chemotherapy and radiation have been used in cases of unresectable disease and as adjuvant therapy (1-4). We report on a case of an unresectable CBPB that presented synchronously with a right testicular seminoma that was treated with airway stenting and concurrent chemoradiotherapy.

Case Report

A 43 year-old non-smoking Caucasian male with a past medical history of diabetes mellitus and bipolar disorder presented with a six-week history of hemoptysis, shortness of breath, and weight loss. Computed tomography (CT) of the chest with intravenous contrast demonstrated a 6.7×4.7 cm heterogeneous mediastinal mass centered in the sub-carinal region, nearly occluding the right mainstem bronchus but not involving the upper lobe bronchus, extending into the left mainstem bronchus, and surrounding the esophagus (Figure 1). There were no parenchyma lung tumors present to suggest this represented a nodal metastasis. Tumor markers were notable for an alpha-fetoprotein (AFP) level of 115 ng/ml (reference range 0-10 ng/ml) and a β-human chorionic gonadotropin (βHCG) level of 6 miu/ml (reference range 0-5 miu/ml). Flexible and rigid bronchoscopy was performed for tissue diagnosis and to recanalize the right mainstem bronchus. A studded 12×40 mm right mainstem silicone stent with a hole fashioned to allow right upper lobe aeration was left *in situ*.

Pathological analysis of the tumor demonstrated a malignant neoplasm composed of immature spindle cells and high grade blastomatous and chondrosarcomatous elements, consistent with a CBPB (Figure 2). Within the chondrosarcomatous and blastomatous portions, primitive glandular elements resembling fetal lung tissue were present. The blastomatous component was positive for vimentin, glial fibrillary acidic protein, synaptophysin and focally for thyroid transcription factor 1 (TTF-1). The immature spindle cell component of the tumor stained positive for desmin and focally for cytokeratin 8/18 and A1/A3. The glandular component stained positive for cytokeratin 8/18 and A1/A3. S-100 protein stained mainly the chondromatous areas. All three tumor components were positive for vimentin and B-catenin. Tumor cells were negative for CD17, placental alkaline phosphatase, AFP, P53 and CD30.

Magnetic resonance imaging of the brain was negative and there was no evidence of retroperitoneal lymphadenopathy on CT. A testicular ultrasound demonstrated a 2.5 cm mass replacing the right testicular parenchyma. One week later, the patient underwent right radical orchiectomy, revealing a classic seminoma. Resection of the mediastinal CBPB was not possible due to the extensive involvement of the bilateral bronchi and esophagus. A treatment regimen consisting of four cycles of cisplatin, ifosfamide, and etoposide (VIP) was chosen due to its efficacy in both the pulmonary blastoma and testicular seminoma. This was administered concurrently with 40 Gy external-beam radiation in 20 fractions with a favorable response at 3 months.

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Discussion

Pulmonary blastoma is a rare and aggressive malignancy that accounts for 0.25-0.5% of all primary lung tumors (3). The term blastoma reflects its histological resemblance to fetal lung tissue (3). Pulmonary blastomas have been divided into three sub-groups: CBPB, well -differentiated fetal adenocarcinoma, and pleuropulmonary blastoma (1-3). CBPB is characterized by a mixture of malignant epithelial and mesenchymal tissues, and is considered a sub-type of sarcomatoid carcinoma (1, 3). CBPBs most often present as a large, symptomatic mass causing cough, hemoptysis, fever, and chest pain in the fourth or fifth decade of life (1). However, up to 17% of patients have been reported to be asymptomatic (1). Imaging most frequently reveals a peripheral lung mass, with only about 25% of cases involving the cartilaginous airway (1, 2).

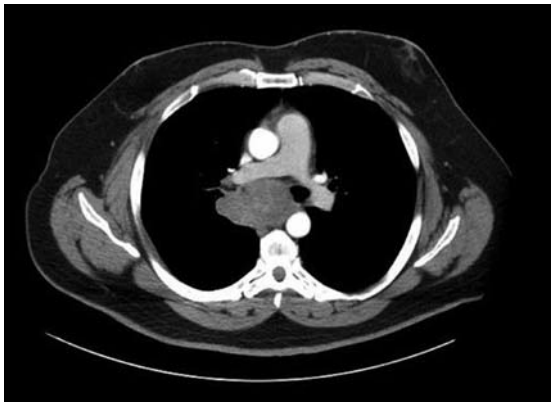

Figure 1. *CT scan of the classic biphasic pulmonary blastoma involving bilateral mainstem bronchi and esophagus.*

While our patient presented with typical symptoms, his tumor was unusual in that it was centrally located in the middle and posterior mediastinum. Although several cases of CBPB involving the anterior mediastinum have been reported and CBPB can metastasize to the mediastinum, this is the first known case of CBPB presenting exclusively in the middle and posterior mediastinum (1, 4). In one previously reported case of CBPB, the patient had a left hilar mass that grew into the anterior mediastinum (4). In another, the patient presented with an anterior mediastinal mass compressing the left main pulmonary artery; it was roughly 60-70% CBPB with rare elements of teratoma, seminoma, and embryonal carcinoma, which also led to elevated AFP and β-HCG (4, 5). Although reports have described blastomatous and seminomatous elements arising within the same tumor (5) and synchronous testicular seminoma and mediastinal choriocarcinoma (6), synchronous CBPB and seminoma have not been described in the same patient, as in the present case.

The optimal treatment for localized CBPB is surgical resection (1). However, the current patient's tumor was unresectable due to the extensive involvement of the right and left mainstem bronchi and esophagus. Compared to resection, chemotherapy and radiation are generally considered less effective for the treatment of CBPB (3). Larsen reported a 16% chemotherapy response rate and minimal response to radiotherapy in 43 patients (3). Koss observed that chemoradiation did not result in long-term survival, but did prolong life by an average of 11 months in patients with recurrent disease (1). No evidence exists supporting the efficacy of one cytotoxic regimen over another, but cisplatin-based therapy is often chosen due to its known effect on primitive tumors (3).

The chemotherapy regimen of cisplatin, ifosfamide, and etoposide (VIP) was chosen for its dual activity against the seminoma and CBPB. Germ-cell tumors including seminomas have demonstrated responsiveness to a VIP regimen, leading to 2.5-year progression-free and overall survival rates of 85% and 93%, respectively, for poor-risk germ cell tumors (7). Furthermore, VIP may offer an advantage in patients with underlying lung disease, as alternative chemotherapy regimens such as bleomycin, etoposide, and cisplatin may induce pulmonary injury (7). Additionally, some authors have recommended cisplatin and etoposide-based regimens for the treatment of CBPB, with a reported mean survival of 14.7 months (8). Long-term remission has been described using adjuvant cisplatin-based chemoradiation for a case of locally-invasive CBPB with incomplete surgical resection (8). In another case, cisplatin plus etoposide with radiation therapy reduced the pulmonary blastoma size, allowing for resection to be performed (9).

The prognosis for patients is generally poor with CBPB (1-5). Two-thirds of patients die within two years of diagnosis and the overall 5-year survival is 16% (3). The most significant prognostic factor for survival in pulmonary blastomas is histological classification, as patients with a CBPB are more likely to die from their tumors than those with well-differentiated fetal adenocarcinoma (1). For CBPB, tumor size, extent of surgical resection, and metastasis at initial presentation also predict survival (1).

In summary, CBPB is a rare and lethal malignancy that frequently appears in the lung periphery and is generally treated with surgical resection (1). In the current patient, CBPB presented in the middle and posterior mediastinum synchronously with a testicular seminoma. Due to extensive airway and esophageal involvement, the patient was treated with concurrent chemoradiation with a favorable early response. The optimal treatment for unresectable pulmonary blastomas remains undefined.

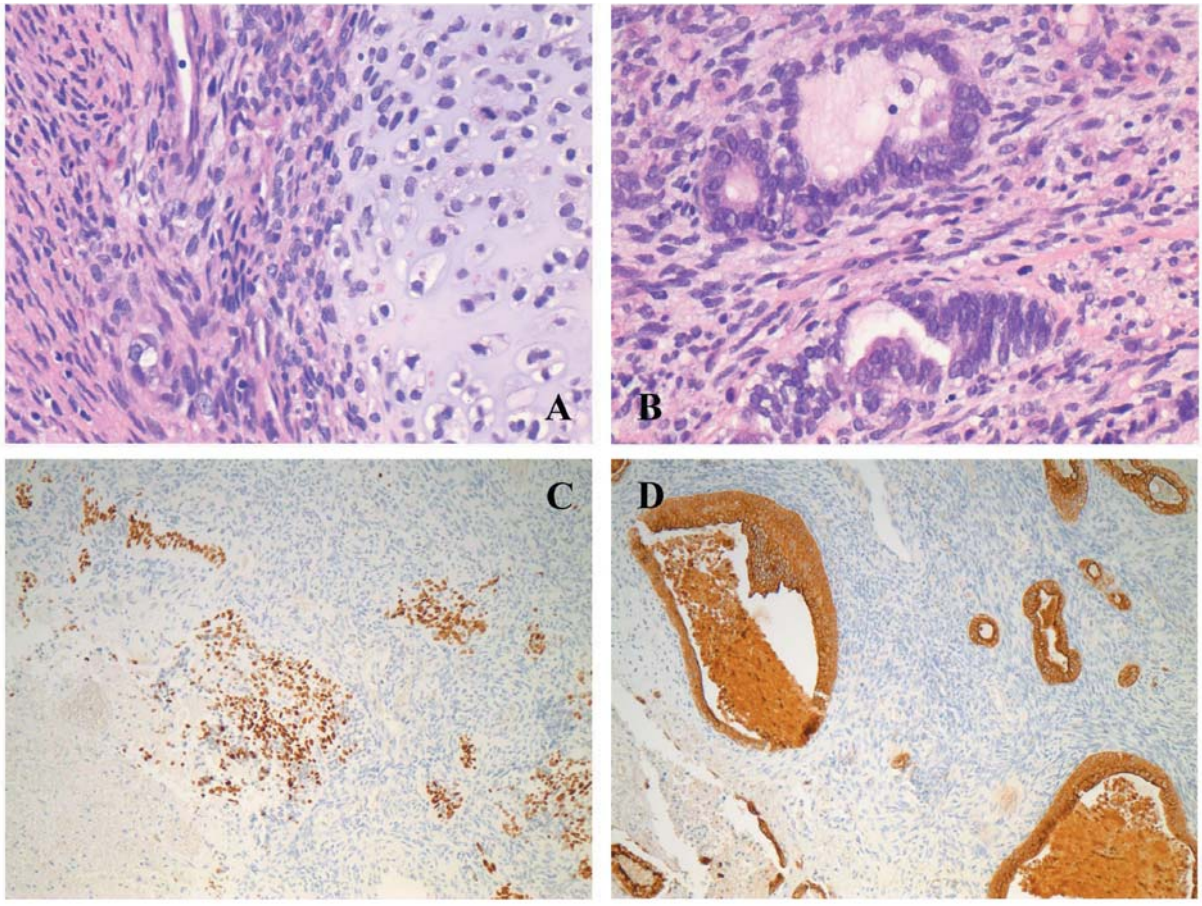

Figure 2. *A. Chondromatous area on the right and sarcomatous area on the left; B. Primitive glandular elements resembling fetal lung; C. Blastomatous component focally positive for TTF-1; D. Glandular component stained positive for cytokeratin 8/18.*

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