A 31-Year-Old Woman With Hemoptysis and an Intrathoracic Mass

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A 31-year-old woman presented with 3 months of hemoptysis (one-half cup daily), left chest pain, and intermittent expectoration. The sputum was described as having a “cheeselike” appearance, occurring every 5 to 6 days. She reported mild shortness of breath for 2 months but no weight loss, night sweats, or fevers. Her chest pain was episodic in nature and occasionally pleuritic. She denied nausea, vomiting, rashes, or joint pain. Her menses were regular and of normal quantity. Six years prior, she presented to another institution with an acute onset of hemoptysis and underwent left internal mammary arterial embolization. A diagnosis was not established, and she was lost to follow-up. The hemoptysis had subsided following the embolization but now returned.

She underwent a left eye enucleation at age 4 years for retinoblastoma. She received no radiation, chemotherapy, or subsequent genetic evaluation. She reported no pneumonia, foreign-body aspiration, or coagulopathy. She was a former smoker (5 years), occasionally drank alcohol, and denied illicit drug use. She was from Denver and had not traveled outside of the United States. There were no risk factors for TB. She took no medications. There was no family history

of retinoblastoma, other malignancies, or pulmonary disease.

The physical examination included: temperature, 37.8°C; pulse, 64 beats/min; BP, 122/70 mm Hg; respiratory rate, 14 breaths/min; and oxygen saturation, 97% while breathing room air. She was thin and in no acute distress. There was a left prosthetic eye. An oropharyngeal examination revealed normal dentition and an absence of mucosal lesions. The neck was supple without masses or lesions. Cardiovascular exam revealed a normal S1, physiologically split S2, and no gallops, murmurs, or pericardial rub. Lung examination revealed decreased breath sounds over the anterior left thorax with early inspiratory crackles. The abdominal, lymphatic, and skin examinations were normal. Strength was normal.

The WBC count was 10.0×10^3 cells/ μ L with 64% neutrophils, 24% lymphocytes, 6% monocytes, and 6% eosinophils; hemoglobin 14.1 g/dL; hematocrit 42.2%; and platelet count 296×10^3 cells/ μ L. The serum electrolytes, liver function tests, coagulation studies, and urinalysis were normal. HIV testing was negative. The chest radiograph is shown in Figures 1 and 2, and the CT scan is shown in Figure 3.

What Is the Differential Diagnosis?

The patient has a large, solitary, parenchymal mass in the left hemithorax. The chest radiograph (Figs 1, 2) showed a heterogeneous left paracardiac mass with central calcifications and embolization coils within the left internal mammary artery. A chest CT scan (Fig 2) showed a large 7×7 cm complex mass in the left anterior hemithorax containing fat, nonfat soft tissue, and osseous structures with partial lingular atelectasis. The thyroid gland appeared normal, and there were small bilateral axillary reactive lymph nodes. The presence of continued hemoptysis suggested a communication between the mass and an adjacent bronchus, and her transient improvement following embolization of the left internal mammary

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FIGURE 1. Posteroanterior chest radiograph.

artery suggested altered vascular architecture. The possibilities include the following: (1) a benign or malignant parenchymal tumor, (2) a tumor located in

FIGURE 2. Lateral chest radiograph.

the anterior mediastinum, (3) a fungal or mycobacterial infection, (4) a lung abscess, or (5) a hydatid cyst.

The leading possibilities are an anterior mediastinal mass or a benign solitary parenchymal tumor. The absence of constitutional symptoms, lymphadenopathy, and further radiographic lesions argued against a diffuse or rapidly growing metastatic disease. The patient had no history of exposure to TB, and the mass involved the inferior and anterior aspect of the thorax, making TB less likely. A lung abscess of this size with bronchial communication more likely than not would result in fevers, purulent and foul-smelling sputum, and weight loss. In addition to the solid structure and marked heterogeneity of the computed tomographic image, there was no exposure history suggesting the possibility of a hydatid cyst.

Hamartoma is the most common benign lung tumor, accounting for 75% of all benign lung nodules and 5% to 10% of solitary pulmonary nodules. Hamartomas most often present in the sixth or seventh decades^{1,2} but can occur in young adults as well. The diameter is usually < 6 cm,^{1,3} but they have been reported as large as 25.5 cm.⁴ The mass in this patient had a heterogenous appearance with a radiographically apparent focus of calcification. Calcification has been reported to occur in 3% to 32% of hamartoma cases but tends to have a punctate or “popcornlike” pattern.^{1,5,6} Calcification can also occur in other benign pulmonary tumors, including plasma cell granulomas and desmoid tumors. Plasma cell granulomas, also referred to as an inflammatory pseudotumor, most often present in childhood or adolescence and usually do not exceed 6 cm in transverse diameter.⁷ Desmoid tumors most often arise from the chest wall and invade surrounding structures, although they sometimes arise from the lung parenchyma.⁸

An intrapulmonary or mediastinal lipoma is unlikely to have this CT scan appearance because they tend to have uniform fatty attenuation. Additionally, intrapulmonary lipoma more often occurs on the right and in middle-aged men.⁹ Pulmonary leiomyoma would also have a homogenous radiographic appearance.¹⁰ Finally, in a young woman with recurrent, episodic hemoptysis, pulmonary endometrioma should be considered. Radiographically this presents as small pulmonary nodules and not a large heterogenous mass.^{11,12}

It was difficult to determine based on the CT scan appearance whether this large complex mass originated from the anterior mediastinum or from the lung parenchyma. Thymoma, the most common anterior mediastinal mass, rarely has calcification, and if it occurs, the calcifications are small, curvilinear, or punctate.¹³ Invasive thymomas are rare, but

sometimes they can extend into the lung causing hemoptysis.¹³ This is an unusual presentation of lymphoma because there are no systemic symptoms or diffuse lymphadenopathy. A mediastinal or intrapulmonary teratoma can present as a large, heterogeneous mass with fat, soft tissue, and osseous structures, and can invade an adjacent bronchus. Occasionally patients can expectorate tissue from an intrabronchial tumor, which could account for this patient's cheese-like sputum.

What Should Be Done Next?

This patient had hemoptysis with recurrent symptoms. She was hemodynamically stable and did not have a coagulopathy. Although a tuberculin skin test should be performed and sputum could be examined for the presence of atypical cells or infection, the next logical step is to obtain tissue for a histologic diagnosis. Consideration should be given to performing a bronchoscopy to determine whether there is endobronchial involvement. Although surgical resection is not required for many hamartomas, the large size, bronchial invasion, and persistent symptoms caused by this mass represent indications for surgical resection. The sampling error of a percutaneous needle aspiration or transbronchial biopsy in such a heterogeneous lesion is sufficiently high. Thus, surgical resection is recommended.

What is the diagnosis?

Diagnosis: mature intrapulmonary teratoma

The results of the workup revealed the following. Her tuberculin skin test was negative. At the time of surgery, a fiberoptic bronchoscopy was performed and did not reveal any abnormalities. Next, the patient was intubated with a double-lumen endotracheal tube, and a left lateral thoracotomy incision at the fifth intercostal space was undertaken. The large heterogeneous mass appeared to originate from the lingula and was adherent to the mediastinal pleura and the anterolateral chest wall. During surgical manipulation of the mass, several hairs were noticed within the endotracheal tube. A complete lingulectomy was performed along with excision of an encapsulated $7 \times 5.5 \times 6.5$ -cm mass without complication. Pathologic evaluation revealed a thick, fibrous capsule with visible areas of calcification. The internal contents of the mass were separated into loculations by the fibrous capsule and included areas of a green-yellow granular substance with intermixed hair, soft adipose tissue, and a mucous white substance. Histologically, the resected specimen displayed a mature, intrapulmonary teratoma; it specifically showed well-differentiated tissues derived from all three germinal layers: respiratory, pancreatic, and intestinal epithelium from endoderm, pilosebaceous units from mesoderm, and hair follicles and squamous epithelium of skin from the ectoderm (Figs 4, 5).

DISCUSSION

Teratomas are usually benign but are sometimes malignant tumors composed of tissues that originate from pluripotent stem cells and are foreign to the site

from which they arise. It is believed that the remnant pluripotent stem cells have undergone ectopic migration during embryonic development. Teratomas are defined by the presence of at least two of the three embryonic germ layers: endoderm (respiratory and intestinal epithelium), mesoderm (fat, cartilage, bone, smooth muscle), and ectoderm (skin, hair, sweat glands, teeth). Histologic examination of the tumor in this patient revealed all three embryonic germ layers (Figs 4, 5).

Teratomas are the most common mediastinal germ cell tumors.^{14,15} Germ cell tumors make up 10% to 15% of all anterior mediastinal masses in adults.^{15,16} Other germ cell tumors include seminomas, embryonal cell carcinomas, endodermal sinus tumors, and choriocarcinomas. After the sacrococcygeal area in children and the gonads in adults, the mediastinum is the most common site for these tumors.

Although the majority of intrathoracic teratomas arise from within the mediastinum, they can also arise rarely from an intrapulmonary source and abut, but not directly involve, the mediastinum. Intrapulmonary teratoma has been reported in 81 cases.¹⁷⁻⁵¹ In the third to sixth gestational week, thymic tissue is derived from the third pharyngeal pouch and the ventral side of the foregut, respectively. Intrapulmonary teratomas are believed to occur when primordial thymic tissue migrates along the course of the developing lung bud. This theory has been supported by reports of thymic tissue present in surgically resected teratomas.³¹ These tumors have been described in patients from 10 months to 65 years of age, although the majority occur in childhood or adolescence. Men and women are affected equally.

FIGURE 3. CT scan of the thorax.

FIGURE 4. Hematoxylin-eosin-stained image from the resected intrathoracic mass demonstrating skin with hair follicle and sebaceous glands on the right. There is laminated keratin material on the left. Original magnification $\times 200$.

Approximately 33% of patients with intrathoracic teratomas have symptoms. These include fever, cough, hemoptysis, chest pain, weight loss, or superimposed lung abscess. Occurring in nine of 81 reported cases (11%), hair expectoration, or trichoptysis, is believed to be pathognomonic for bronchial extension of intrathoracic teratoma. Trichoptysis has been reported to occur with both mediastinal⁵² and intrapulmonary teratomas.^{17,22,26,33,37} The other reported cause of trichoptysis is reconstructive surgery following resection of a laryngeal tumor.⁵³ The expectorated hair from teratomas is usually white, perhaps due to a lack of maturity of the pigment-producing cells within the tumor.¹⁷ Detection of endobronchial hair in the absence of trichoptysis, as was the case here, has the same significance (bronchial communication).¹⁹

FIGURE 5. This hematoxylin-eosin-stained section demonstrates cartilage on the right and pancreatic acini on the left. Original magnification $\times 200$.

All intrathoracic teratomas have been shown to produce proteolytic or digestive enzymes that can lead to invasion and rupture into adjacent structures.⁵⁴ Rupture into the tracheobronchial tree, the pleural space, the pericardium, the aorta, and the superior vena cava have been reported and obviously is a clear indication for surgery.⁵⁵ In addition, these tumors may be associated with atelectasis, bronchiectasis, and postobstructive pneumonia.^{33,48}

The radiographic presentation of intrathoracic teratoma is most often a localized mass in the anterior mediastinum. Involvement of the middle or posterior mediastinum can occur. The vast majority of tumors have smooth or lobulated, but well-defined, margins. The heterogenous attenuation suggesting soft tissue, fluid, fat, and calcium is often sufficient evidence to diagnose these tumors on CT scan; however, calcification is not always present and has been reported in only 26% of mediastinal teratomas in one series.¹³ Because of the heterogenous architecture, a fat-fluid level is sometimes seen. An air-fluid level can be present that initially suggests cavitation but actually results from a communication of the teratoma and the bronchus.

The prognosis and natural history of the teratoma depends on the presence or absence of immature tissue and the age of the patient. Approximately 80% of teratomas are mature. Immature teratomas appear in infancy and childhood and are often treated successfully with surgical excision, although they can, in rare instances, recur and metastasize.¹³ Immature teratomas in adults often have an aggressive course and a poor prognosis. Less commonly, a mature teratoma can develop a focus of carcinoma, sarcoma, or malignant germ cell tumor, and is then referred to as a "malignant teratoma" or "teratocarcinoma."¹³ Teratocarcinomas can result in death within a few months of diagnosis as a result of local spread or distant metastasis, and therefore surgical excision of all suspected teratomas is recommended. Chemotherapy may be associated with improved survival in some cases of metastatic teratocarcinoma.^{56,57} In contrast, in resected mature teratomas, recurrences have not been described. Histologic examination of the resected mass is essential to determine whether a small focus of immature tissue or remnants of another germ cell tumor, carcinoma, or sarcoma are present. Notably, dense adhesions may be present at the time of surgery due to the leakage of fat into the mediastinum or the presence of functioning endodermal pancreatic tissue. With extensive teratobronchial communication, lobectomy or even pneumonectomy may be required.

The history of prior retinoblastoma in our patient increases the risk of subsequent malignancies, including sarcomas, melanomas, and central nervous system neoplasms.⁵⁸ To our knowledge, there are no cases of childhood retinoblastoma with subsequent teratoma.

Although there was a negative family history in this case, there is a small but significant possibility of a heritable form of the disease.

This patient presented with recurrent, severe hemoptysis due to a teratoma arising from an intrapulmonary source. It likely resulted from an embryologic migration of tissues from the third pharyngeal pouch. The potential to contain malignant tissue, produce digestive enzymes, and invade surrounding structures is identical to the more common mediastinal teratomas. Her hemoptysis indicated an endobronchial communication. Other clinical findings supporting endobronchial involvement include visualization of hair and/or sebum via bronchoscopy, as well as hair expectoration or trichoptysis. The fact that she had undergone left internal mammary artery embolization 6 years prior with amelioration of hemoptysis for several years suggests that the teratoma developed additional systemic blood supply following the embolization. Calcification and a heterogenous appearance of the mass on CT imaging is highly suggestive of this diagnosis. Definitive diagnosis and treatment require surgical resection.

Clinical Follow-up

The patient was discharged from the hospital 4 days after surgery and was without chest pain or hemoptysis 2 weeks later. Although the patient appeared to have a benign teratoma, given her history of retinoblastoma and the risk of subsequent malignancy, she was referred to a medical geneticist for further evaluation, education, and management.

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