Clinical-pathologic conference in general thoracic surgery: Pulmonary blastoma

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Case Presentation

Dr Force: A 46-year-old woman initially presented to a local emergency room in February 2002 with shoulder and back pain. She had a chest radiograph that demonstrated an abnormality. A computed tomographic (CT) scan of the chest was performed to characterize this lesion. Her medical history was unremarkable and her surgical history was significant for a basal skin cancer that was removed from her left eyebrow and a left breast lumpectomy for a benign lesion.

Dr Glazer: The chest radiograph is remarkable for a well-defined mass within the left upper lobe, which is well visualized on this CT scan (Figure 1). It has slightly lobulated borders and it abuts the lateral chest wall with no obvious rib destruction or chest wall invasion. It is relatively homogeneous except for some small low attenuation areas laterally, which may represent areas of necrosis within the mass. There is no calcification and no fat within the mass (Figure 2). There is a mildly enlarged lymph node in the right hilum, but no other lymphadenopathy seen. No other pulmonary nodules or effusions were seen (Figure 3) and the images in the upper abdomen were normal.

Dr Force: The patient subsequently underwent a fine needle aspiration of this lesion at an outside hospital, which revealed a fetal type adenocarcinoma or pulmonary blastoma. She then underwent an extensive radiographic workup that included a CT scan of the abdomen and pelvis, which showed some small hepatic lesions and a large mass in her pelvis that looked like it was coming from the uterus. She had a right upper quadrant ultrasound that showed the liver lesions to be consistent with simple cysts. She also had an MRI of her brain and a PET, which failed to show any evidence of metastases.

Dr Siegel: The F-18 fluorodeoxyglucose positron emission tomography (FDG-PET) study demonstrates fairly intense uptake in the left upper lobe mass (Figure 4). The standardized uptake value in this mass was 13, which is well in the malignant range. There were no metastases identified on this study; however, in reviewing the study today, there is a suspicion of faint uptake in mediastinal lymph nodes, but there appears to be no correlate for those nodes on the CT. There is very faint uptake

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Figure 1. Preoperative chest radiograph.

Figure 2. Preoperative chest computed tomography, mediastinal window.

in the pelvic mass, which was tremendously displacing the bladder. That is nonspecific, and it is certainly consistent with a benign leiomyoma of the uterus.

Dr Cooper: Did you think that the uterine lesion was benign?

Dr Force: It was thought that it was consistent with a leiomyoma. However, I'm not sure how well PET can differentiate between a sarcoma versus myoma versus carcinoma.

Dr Siegel: The bigger problem would be with false positive results, because some leiomyomas have increased FDG uptake on PET.

Dr Cooper: If this should turn out to be a benign metastasizing leiomyoma, it doesn't make any difference because you're going to take out the pulmonary lesion anyway. Is there anything that you could have turned up in the pelvis that would have altered how you managed the pulmonary lesion? It sounds like the answer is no.

Figure 3. Preoperative chest CT, lung window.

Figure 4. Preoperative FDG PET imaging.

Dr Force: I think if she had a leiomyosarcoma in the uterus, that would need to be dealt with. However, the negative PET findings made a leiomyosarcoma very unlikely. There was a distinct difference in PET uptake between the lung and the uterine lesion. Since the workup for metastatic disease was negative, the patient was taken to the operating room, where she underwent a bronchoscopic examination, which showed no endobronchial abnormalities. A limited posterolateral left thoracotomy was performed. When the left side of the chest was entered, inflammatory adhesions were seen tethering the tumor to the pleura, but the tumor actually fell away from the pleura quite easily. The visceral pleura did not appear to be grossly involved by the tumor. We initially started the dissection in the fissure and sent off some interlobar lymph nodes as well as some peribronchial lymph nodes for a frozen section. These came back negative for metastatic disease. We completed the left upper lobectomy, and the patient was transferred to the recovery unit. She did very well and was discharged home on the sixth postoperative day. Perhaps we could review pathology at this point.

Figure 5. Surgical pathology gross photo.

Figure 6. Surgical pathology histologic photo.

Dr Ritter: Here is the lobectomy specimen and the cross-section of the tumor (Figure 5). As you can see, the tumor is in the periphery above the pleura and the tumor itself is tan with central necrosis and hemorrhagic areas. This is typical of this type of tumor. It is well circumscribed, and a high-power view shows that it is composed of gland-like spaces and columnar cells (Figure 6). The cells of this tumor have atypical nuclei as well as subnuclear vascularization, which looks like a secretory type of endometrium. The other morphologic feature of this kind of tumor is the presence of squamoid nests of cells called morules (Figure 7).

Dr Force: Looking at these slides, one can see how these tumors got their names as fetal type because they had characteristics similar to fetal lung.

Dr Ritter: There are three types of tumors that are included in a group with the name “pulmonary blastomas.” There are monophasic and biphasic types and then there is a pleuropulmonary blastoma. The latter is a tumor that Dr Louis Dehner described about 15 years ago. It is actually a different sort of entity. It is usually seen in children and is similar to other kinds of childhood blastomas. It looks like Wilms tumor and has associations with other kinds of childhood malignant tumors such as rhabdomyosarcoma. The monophasic pulmonary blastoma is the type of tumor that this patient has.

Dr Force: Is that the same thing as a well-differentiated fetal adenocarcinoma?

Dr Ritter: Those terms are used synonymously. Having looked at autopsy lungs from fetuses, I think that it looks more like endometrium than it does like fetal lung, and a lot of people have made that comparison. Most patients with this tumor are in their 30s and 40s, which is quite a bit younger than is seen with “typical” lung cancer. Most of the patients are smokers and I don’t think it has ever been reported in anybody less than 10 years of age.

Figure 7. Surgical pathology histologic photo.

Dr Roper: In the childhood cases you were talking about, is that generally called lipoblastoma because it is essentially benign?

Dr Ritter: No, that is something different. The lesion in children is really a very aggressive malignancy. It has features of other childhood tumors such as rhabdomyosarcoma or some other childhood sarcoma and, again, may have a familial association.

Dr Govindan: I was under the impression that this was just a variation of pleural pulmonary blastoma?

Dr Ritter: If you do molecular studies on these, you can see that they express Clara cell antigens or surfactant so they look like they come from distal airway cells, like bronchiolar or alveolar epithelium. These mark like carcinomas, as opposed to the pleuropulmonary blastomas, which seem to be some kind of sarcomatoid lesion that probably comes from primitive fibroblastic cells.

Dr Force: These tumors also have a much better prognosis than pleuropulmonary blastomas.

Dr Ritter: Also a much better prognosis than the biphasic ones, which are even less common. I think in 10 years

we have only seen about three or four of those tumors. These cases behave about the same as any form of lung cancer, stage for stage. In most of the patients the tumor is T2 sized by the time it is discovered. But most of these tumors are way off in the periphery of the lung like this.

Dr Cooper: I don't think I have seen one of these so called pleuropulmonary blastomas. Are they associated with pleura or is that a histologic description?

Dr Ritter: No, most of them are subpleural and may present as a pleural mass. The pleuropulmonary blastoma is almost exclusively a pediatric condition. We see these rare lesions frequently because Dr Dehner, the chief of pathology, runs the pleuropulmonary blastoma registry. We have seen only one adult with a pleuropulmonary blastoma. Unless you operate on children, you will never see this lesion.

Dr Force: Dr Govindan, I know that you evaluated this patient for neoadjuvant therapy. What do you think is the role of preoperative therapy for larger lesions, perhaps T3 tumors or those with nodal metastases? Do you treat them like adenocarcinomas?

Dr Govindan: I reviewed this subject rather extensively over a year and a half ago when I was referred a patient that Dr Ritter just mentioned. The patient had advanced disease and had already received a variety of chemotherapy agents. There have only been a few studies looking at chemotherapy and radiation in these tumors and they usually report a poor outcome. Given the morphology of the tumor and the fact that the patient appeared to have T2 N0 disease, we elected to treat it like adenocarcinoma of the lung, which is, I think, what most oncologists would do. In the patient being discussed, we elected not to administer any induction therapy because we thought she had a favorable lesion amenable to complete resection. As it turned out, she had a T2 N0 lesion. If this were classified as a non-small cell lung cancer, she would be eligible for an adjuvant chemotherapy protocol. Since the diagnosis is pulmonary blastoma, I don't think we can make a compelling argument for any further treatment.

Dr Force: To sum up this rare tumor, pulmonary blastoma comprises only 0.5% of all lung cancers. This tumor was first recognized by Barret and Barnard in 1945 and was termed embryoma of the lung due to its similarity to fetal lung tissue. This tumor was shown to have both epithelial and mesenchymal components. The term embryoma of the lung was renamed pulmonary blastoma (PB) by Spencer in 1961 in his report of three additional cases.¹ Kradin identified a subgroup in 1982 consisting only of an epithelial component. This tumor is now known as well-differentiated fetal adenocarcinoma (WDFA). Manivel identified a second

subgroup in 1988. This tumor, called pleuropulmonary blastoma (PPB), was shown to occur in children and consisted of only malignant mesenchymal cells. Pulmonary blastoma is now recognized in three forms: one biphasic type (PB) and two monophasic types (WDFA and PPB).^{2,3}

The majority of patients with PB and WDFA are adults with a median age of 40 years. PPB, on the other hand, usually presents in childhood with a median age of 3 years. Although the small number of cases prevents defining an exact causative agent, the majority of patients have a history of tobacco use. Congenital cystic lung disease has been suggested as a predisposing factor in the case of PPB. Presenting symptoms are similar to those of bronchogenic carcinoma and consist of respiratory complaints, chest pain, pleural effusion, and pneumothorax. No serum tumor markers have been shown to be consistently elevated in these tumors.⁴

Anatomic resection, lobectomy, or pneumonectomy is the treatment of choice for monophasic and biphasic pulmonary blastomas. Case reports on the use adjuvant chemotherapy, usually cisplatin based, and adjuvant radiation have reported a wide range of response rates; but, the overall numbers are too small to draw any definitive conclusions. The overall survival for all three types of tumor is poor with only 33%, 16%, and 8% of patients alive at 2, 5, and 10 years, respectively. Among the subgroups, PPB has the worst prognosis. WDFA appears to have the best prognosis with a median survival of almost 3 years. Some investigators have suggested that WDFA can be separated into high and low grades based on several histopathologic features. The patients with low-grade lesions tend to have a considerably longer survival than those with high-grade tumors.⁵

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