A young man with a large lung mass

Steven Praske,[1] David Bradshaw,[1] John Roberts,[2] John Childs[2]

[1]Pulmonary and Critical Care Medicine Department; [2]Pathology Department, Naval Medical Center San Diego, USA

Abstract

A 27-year-old man presented with a large solitary lung mass. Transbronchial lung biopsy and lobectomy specimens showed malignant melanoma. A thorough search for a primary melanoma lesion, including an ophthalmic exam and a dermatologic exam with special attention to the skin, mucous membranes, genitals, perineum, scalp, and nails showed no lesions suspicious for a melanoma. The diagnosis of primary malignant melanoma of the lung was considered. Whole-body positron emission tomography scan with computed tomography fusion imaging at the time of diagnosis showed no evidence of tumor outside the chest, and the diagnosis of primary malignant melanoma of the lung was confirmed. The prognosis of patients with this exceedingly rare neoplasm is poor, though surgical intervention may be warranted in some cases.

Case Report

A 27-year-old man was referred to the pulmonary clinic for evaluation of a large right lung mass. Fifteen months earlier, he had been treated with oral antibiotics for community acquired pneumonia at an outside facility. The chest radiograph report from that hospital described a 3 cm *mass-like* opacity in the superior segment of the right lower lobe; however, follow-up imaging was not performed. His symptoms resolved, and he was well until two weeks prior to pulmonary referral when he developed a cough productive of yellow sputum. One week later, scant hemoptysis occurred. There was no other significant past medical history. Review of systems was positive only for a reduced appetite, but no weight loss. He had smoked five cigarettes daily for the preceding ten years. Prior to military service as a seaman, he had worked as a welder at a steel plant for seven years. He had no recent travel outside the United States. An annual tuberculin skin test required for all military members was negative nine months earlier.

Physical examination

The patient was a fair-complected caucasian male who appeared in no distress. His vital signs were normal. He weighed 136 pounds and the BMI was 20.14 kg/m2. Although thin, muscle wasting was not apparent. The chest exam revealed diminished breath sounds, crackles and dullness to percussion over the lower right hemithorax. The cardiovascular exam was normal. There was no palpable cervical, axillary, or inguinal lymphadenopathy. The skin, testicular, oropharyngeal, and rectal exams were also normal.

Laboratory findings

A complete blood count, basic metabolic panel, coagulation studies, and liver enzymes were all within normal limits. Serologic studies for endemic fungal infections including coccidioidomycosis, histoplasmosis, and cryptococcus were negative.

Diagnostic tests

Pulmonary function testing was notable for mild proportionate reductions in the forced expiratory volume in one second (FEV1) and forced vital capacity (FVC), yielding a normal FEV1/FVC ratio. The diffusing capacity for carbon monoxide (DLCO) and static lung volumes were normal. A chest radiograph obtained on the day of pulmonary consultation showed a very large, well-circumscribed mass lesion in the right lower lobe (Figure 1). The lesion showed heterogeneous enhancement on the intravenous contrast-enhanced computed tomographic (CT) scan and measured 10.4 by 5.8 cm in its greatest transaxial dimensions (Figure 2). A solitary 2.1×1.7 cm right hilar lymph node was also present (*not shown*). Whole-body combined positron emission tomography (PET) with CT fusion imaging was performed two weeks later and showed localized abnormal uptake in the mass (standard uptake value [SUV] 6.8) and right hilar lymph node (SUV 2.41) (Figure 3). The adrenal glands, kidneys, bowel, and skeletal structures were normal. A brain magnetic resonance imaging (MRI) (not shown) was negative.

Fiberoptic bronchoscopy showed blood in the right lower lobe bronchus and a friable endobronchial lesion extending out of the lateral basal segment. Brush, lavage, and biopsy specimens were obtained (Figure 4A). Two weeks later, the patient underwent thoracotomy and right lower lobectomy (Figure 4B). The tumor displayed cytopathologic and immunohistochemical features typical of malignant melanoma. Specifically, in both the transbronchial lung biopsy and the lobectomy specimen, the histological sections showed diffuse sheets of malignant cells with marked nuclear pleomorphism, cytologic atypia, prominent nucleoli, and characteristic cytoplasmic melanin production. Additionally, there were abundant intranuclear cytoplasmic invaginations. Regional peripheral zone lymph nodes showed isolated atypical cells suspicious for isolated melanoma cells. Immunohistochemistry plays an important role in confirming the diagnosis. The combination of positive staining for S-100 and HMB-45 markers, with negative staining for keratin, strongly supported the diagnosis of melanoma.

Correspondence: Steven Praske, Naval Medical Center San Diego, Pulmonary Medicine, Suite 301, 34800 Bob Wilson Drive, San Diego, CA 92134-3301, USA.
Tel: +1.619.602-2813 - Fax: +1.619.532-7625.
E-mail: steven.praske@med.navy.mil

Key words: lung, neoplasm, melanoma.

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

Conflicts of interests: the authors declare that they have no conflicts of interests.

Received for publication: 5 September 2011.
Revision received: 24 January 2012.
Accepted for publication: 25 January 2012.

Chest Disease Reports 2012; 2:e4
doi:10.4081/cdr.2012.e4

Discussion

Primary malignant melanoma of the lung (PMML) is an exceedingly rare neoplasm. According to a case report and review published in 2009, only 30 cases have been reported in the English literature.[1] Only eight cases of PMML were identified in the Armed Forces Institute of Pathology's (AFIP) extensive Pulmonary Tumor Registry from 1950-1995.[2] PMML accounted for only 0.01% of lung tumors.[2] Seven of the eight cases were male, although a literature review from the Mayo clinic[3] found an even gender distribution. The mean age of patients in the Mayo review was 54 years with a range of 29 to 90 years.[3]

Distinguishing PMML from the much more common melanoma metastatic to the lung is difficult. An analysis of 7564 patients diagnosed with melanoma at Duke University Cancer Center showed that 12% developed

lung metastases, and 25% of these were solitary pulmonary nodules.[4] Allen and Drash proposed three histologic criteria to distinguish primary melanoma of the lung from metastatic disease. These included: (i) junctional change with nesting of melanoma cells just beneath the bronchial epithelium, (ii) invasion of bronchial epithelium by the malignant cells in an area without epithelial ulceration, and (iii) an obvious melanoma beneath the above described changes.[5] The inability to demonstrate an intraepithelial component or nevus associated with the invasive component, however, should not exclude the diagnosis of PMML. Overgrowth of the invasive component and ulceration of bronchial epithelium could account for the absence of an in situ lesion in some cases. Because of this possibility, Wilson and Moran[2] did not include the presence of an intraepithelial component or nevus in their diagnostic criteria. In fact, only four out of the eight cases from the AFIP series exhibited an intraepithelial component.[2] Furthermore, based on reports of intraepithelial growth of metastatic melanoma to the lung,[2] the authors felt that the presence of an situ component is an unreliable criterion to establish a primary pulmonary origin. Given the shortcomings of a histologic approach to diagnosis, Jensen and Egedorf[6] proposed clinical criteria to define PMML. These criteria address the difficulty with classification and are widely accepted in contemporary PMML literature.[1,2,3,7,8,9] Four clinical criteria are required to make a diagnosis of PMML:[3-6] (i) A solitary lung mass or nodule; (ii) Typical histopathology confirmed by immunohistochemistry and/or electron microscopy; (iii) No prior history of melanoma or excision/fulguration of a cutaneous, mucous membrane, or ocular lesion unless the pathologic examination explicitly ruled out a melanoma; (iv) No demonstrable melanoma outside the chest at the time of diagnosis.

Our case fulfilled each of these clinical criteria and is properly considered a primary malignant melanoma of the lung. A thorough search for other possible sites of a primary melanoma lesion included a dilated ophthalmic exam performed by an ophthalmologist and a detailed inspection of the skin and mucous membranes by a dermatologist, with

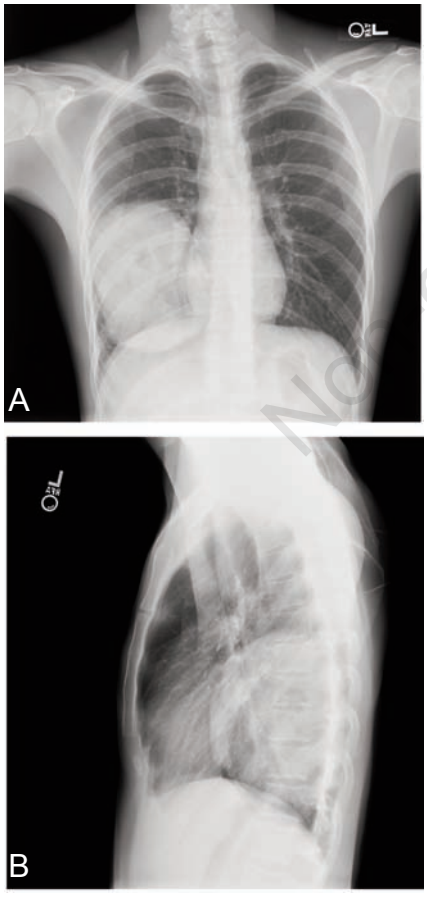

Figure 1. Chest radiograph. A) PA view. B) lateral view.

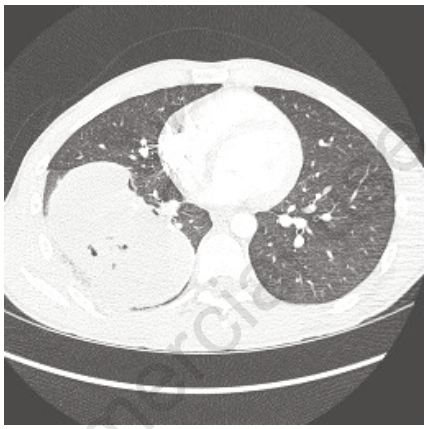

Figure 2. Chest computed tomography with contrast demonstrated an ovoid-shaped mass localizing to the right lower lobe and notable for internal air suspicious for necrosis. Splaying of the anterior basal and lateral basal segments of the right lower lobe bronchus is evident.

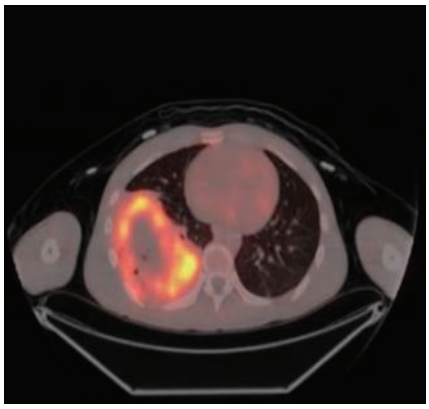

Figure 3. Combined positron emission tomography and computed tomographic scan fused images showed a hypermetabolic right lower lobe mass with central hypoactivity consistent with necrosis. The standard uptake value (SUV) was 6.2.

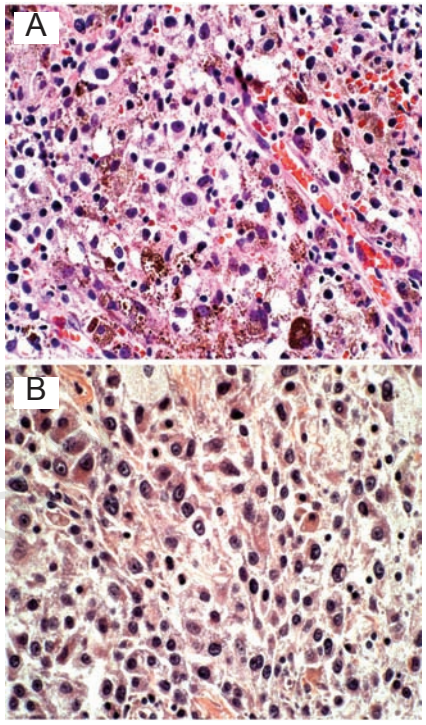

Figure 4. A) Transbronchial lung biopsy (TBLB) demonstrated sheets of atypical cells with moderate nuclear pleomorphism, irregular nuclear membranes, prominent nucleoli, increased nuclear-to-cytoplasmic ratios, and smokey pigmented cytoplasm (hematoxylin-eosin stain, original magnification X 40). B) Lobectomy specimen showed markedly atypical cells cytologically similar to those in the preceeding TBLB. Additionally, several cells in this field displayed prominent intranuclear cytoplasmic invaginations (hematoxylin-eosin stain, original magnification X 40).

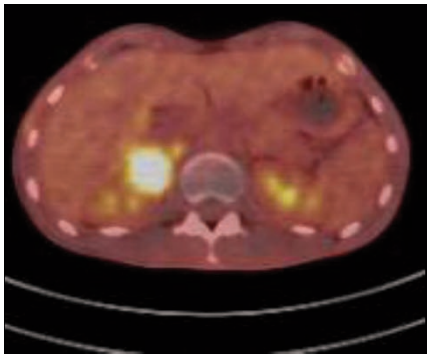

Figure 5. Combined positron emission tomography and computed tomographic scan 6 weeks after the initial study showed a new 4.7x4.6 cm hypermetabolic (SUV 10.9) soft tissue mass involving the right adrenal gland.

special attention to the perineum, oral mucosa, genitals, scalp, and nails. There were no lesions suspicious for melanoma, nor signs of a regressed melanoma. Finally, the whole body PET/CT performed at the time of diagnosis showed no evidence of tumor outside the chest.

The pathogenesis of PMML is uncertain. Melanocytes have been identified in the larynx and esophagus, which along with the lower respiratory tract, are derived from the sixth branchial arch.[2] Thus, it plausible that PMML is derived from benign melanocytes which have migrated with the respiratory tract during embryogenesis.[2] Other theories include melanogenic metaplasia in submucosal bronchial glands and melanocytic differentiation of other cell types (*i.e.* neuroendocrine) within the lung.[2,7]

The prognosis of patients diagnosed with PMML is poor and a majority of patients die of metastatic disease (median 14 months after resection in the AFIP series).[2] Of the 30 reported cases in the English literature, 25 had surgical resection and only eight were free of disease at the time they were reported (range 18 months to 11 years).[1] Although mortality is high, the observed long-term survival in a few patients seems to warrant an aggressive surgical approach. The case series from Duke University Cancer Center that included 945 patients with pulmonary metastatic melanoma demonstrated that even if the tumor later proves to be a metastasis from an undetected primary lesion, resection in patients with a solitary lung metastasis yielded a 20% five year survival versus 4% in those with similar disease, but no resection. In the same series, median survival was 1.6 years in those with a solitary metastasis treated with resection versus 0.6 years in unresected patients with a single lung mass.[4]

Among patients with stage IV metastatic melanoma, the standard recommended therapy according to the American Joint Committee on Cancer (AJCC) is single agent chemotherapy with dacarbazine.[10] In addition to dacarbazine, the only other FDA-approved systemic therapy for metastatic melanoma is high-dose interleukin-2 (IL-2). Neither agent has been shown to significantly improve survival in phase III trials. High response rates with adoptive cell therapy in very selected patients has been observed and stated to range between 49% and 72%.[10] This process involves isolating specifically sensitized antitumor lymphocytes from the patient's tumor or stimulating lymphocytes *in vitro* with autologous melanoma cells. The antitumor lymphocytes are then cultured in vitro and expanded to large numbers. After a regimen of non-myeloablative, lymphocyte-depleting chemotherapy, and total body irradiation, the tumor-infiltrating lymphocytes are transferred to the host in conjunction with high-dose IL-2. This therapeutic approach is exclusive to the National Cancer Institute in Bethesda, Maryland.

Clinical course

One month after undergoing thoracotomy and right lower lobectomy showing clear tissue margins, the patient presented to his oncologist with recurrent hemoptysis. Physical examination showed a new 1.5 cm mass in the posterior oropharynx, which proved to be melanoma by biopsy. A second PET/CT showed a new hypermetabolic 4.7×4.6 cm right adrenal mass (Figure 5) and two hypermetabolic foci in the small bowel. None of these lesions was present on the PET or CT scan performed just six weeks earlier. Several days later he underwent a partial small bowel resection for an obstructing mass shown to be metastatic malignant melanoma. A repeat brain MRI showed a new lesion in the right parietal lobe, also worrisome for a metastasis. He died 4 ½ months after diagnosis.

Conclusions

Primary malignant melanoma of the lung is rare. To our knowledge, this is the youngest patient ever diagnosed with PMML. Diagnostic criteria include (i) a solitary lung tumor (ii) typical histopathology confirmed by immunohistochemistry and/or electron microscopy (iii) no past history of melanoma or excision/fulguration of skin, mucus membrane, or ocular lesions unless proven not to be melanoma, and (iv) no demonstrable tumor outside the chest at the time of diagnosis. Prior to considering surgical resection, a thorough search for an occult primary lesion and other sites of metastases should be conducted. Melanoma is characterized immunohistochemically by the presence of S-100 and HMB 45 antigens and the absence of staining for cytokeratin. Prognosis in patients with PMML is poor, however, an aggressive surgical approach may be warranted based on observations of long-term survival in a few resected PMML patients and the observation that resected patients with a solitary lung metastasis from a primary cutaneous melanoma outlive those whose lung tumor was not resected.

References

1. Maeda R, Isowa N, Onuma H, et al. Primary malignant melanoma of the lung with rapid progression. Gen Thorac Cardiovasc Surg 2009;57:671-4.
2. Wilson RW, Moran CA. Primary melanoma of the lung: a clinicopathologic and immunohistochemical study of eight cases. Am J Surg Pathol 1997;21:1196-202.
3. Ost D, Joseph C, Sogoloff H, Menezes G. Primary pulmonary melanoma: case report and literature review. Mayo Clin Proc 1999;74:62-6.
4. Harpole DH Jr, Johnson CM, Wolfe WG, et al. Analysis of 945 cases of pulmonary metastatic melanoma. J Thorac Cardiovasc Surg 1992;103:743-8; discussion 748-50.
5. Allen MS Jr, Drash EC. Primary melanoma of the lung. Cancer 1968;21:154-9.
6 Jensen OA, Egedorf J. Primary malignant melanoma of the lung. Scand J Respir Dis 1967;48:127-35.
7. Reddy VS, Mykytenko J, Giltman LI, Mansour KA. Primary malignant melanoma of the lung: review of literature and report of a case. Am Surg 2007;73:287-9.
8. Jennings TA, Axiotis CA, Kress Y, Carter D. Primary malignant melanoma of the lower respiratory tract. Report of a case and literature review. Am J Clin Pathol 1990;94: 649-55.
9. Kundranda MN, Clark CT, Chaudhry AA, et al. Primary malignant melanoma of the lung: a case report and review of the literature. Clin Lung Cancer 2006;7:279-81.
10. Garbe C, Eigentler TK, Keilholz U, et al. Systematic review of medical treatment in melanoma: current status and future prospects. Oncologist 2011;16:5-24.