Acute respiratory failure mimicking acute respiratory distress syndrome due to parenchymal infiltration by metastatic melanoma

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Abstract: Malignant melanoma is the most aggressive form of skin cancer and carries a predisposition for metastasis to many different organs. Pulmonary dissemination is common, most often presenting as multiple discrete pulmonary nodules. While a variety of other intrathoracic patterns can occur, diffuse parenchymal infiltration causing acute respiratory failure is an extremely rare manifestation of metastatic disease. We present a case of an otherwise healthy man who developed rapidly progressive respiratory failure mimicking acute respiratory distress syndrome due to melanomatous infiltration of the lung parenchyma and airways.

Keywords: metastasis, cancer, acute respiratory distress syndrome, tumor, hypoxemia, melanoma.

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CASE PRESENTATION

An otherwise healthy 34-year-old male smoker presented initially with a right axillary nodule, for which excisional biopsy revealed melanoma. A full skin and soft-tissue examination elicited no evidence of primary disease, and a whole-body positron emission tomography (PET)/computed tomography (CT) scan was free of metastases. Complete axillary lymph node dissection demonstrated involvement in 12 of 20 nodes by metastatic melanoma. Postsurgical CT imaging revealed no residual disease, and preparation was made for adjuvant chemotherapy and radiation with curative intent.

Two weeks later, while awaiting treatment, the patient developed pleuritic chest pain, dyspnea, and cough with black sputum. After 1 week of escalating symptoms marked by progressive breathing difficulty, he presented to the hospital. Examination showed a thin man in respiratory distress, with oxygen saturation of 88% on room air. He lacked jugular venous distention, and subsequent central venous pressure measurement was 4 cmH₂O. Lung auscultation revealed bilateral crackles with diminished basilar breath sounds. Skin examination demonstrated a well-healed right axillary scar without other lesions, and the remainder of his examination was normal. White blood cell count was 13.8×10^9 cells/L, and arterial blood gas showed pH 7.35, pCO₂ of 48 mmHg, and pO₂ of 64 mmHg

on 6 L of supplemental oxygen. Serum testing was otherwise unrevealing, including a B-type natriuretic peptide level of 27 ng/L. Chest radiograph (Fig. 1) revealed bilateral airspace opacities.

The patient was treated for presumed pneumonia with antibiotics and cautious intravenous fluids due to limited respiratory reserve. Oxygen requirements and work of breathing increased, resulting in intubation on hospital day 2. Chest CT (Fig. 2A, 2B) revealed bilateral ground-glass opacities with dense basilar consolidation and was negative for pulmonary emboli. Initial bronchoscopy showed normal airways and minimal dark secretions and yielded negative microbiologic and cytologic evaluations on bronchoalveolar lavage.

Over the subsequent 48 hours, the patient's status continued to decline. A chest radiograph from hospital day 4 (Fig. 2C) demonstrated worsening bilateral airspace disease, at which time oxygen requirements had increased to 100% F_iO₂ with a resulting P_aO₂/F_iO₂ ratio of 84, necessitating positive end-expiratory pressure of 14 cmH₂O. The patient became progressively more difficult to ventilate, with worsening lung compliance resulting in plateau pressures measured at 35 cmH₂O. Antibiotics were broadened, and he was managed with low tidal volumes for presumed acute respiratory distress syndrome (ARDS). Attempts at

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Figure 1. Portable chest radiograph obtained on hospital day 1, demonstrating bilateral, lower lobe–predominant airspace consolidations.

diuresis were unsuccessful due to low urine output and worsening renal function. Repeat bronchoscopy was performed to assess for alternate etiologies on hospital day 5. Endobronchial examination demonstrated multiple raised, darkly pigmented airway lesions (Fig. 3A), newly developed since the time of initial bronchoscopy. Endobronchial biopsy (Fig. 3A) showed atypical hyperchromatic cells that stained positive with S-100 and melan A, consistent with endobronchial metastases from melanoma. Despite aggressive support, his respiratory status continued to dete-

riorate with progressive multiorgan failure, ultimately resulting in death on hospital day 6.

On autopsy (Fig. 3C, 3D), evaluation of the lung parenchyma revealed diffuse infiltration of the alveoli/ducts, airways, and interstitium with metastatic melanoma. Tissue lacked signs of diffuse alveolar damage or hyaline membranes to suggest ARDS, and there was no evidence of interstitial disease or infectious processes, including opportunistic pathogens. Histologically, the cause of death was most consistent with respiratory failure due to diffuse melanomatous infiltration of the lung parenchyma. Metastatic spread was also found in multiple other organs, including the heart, liver, adrenals, intestines, and intra-abdominal lymph nodes.

DISCUSSION

Malignant melanoma is an aggressive form of skin cancer that can spread rapidly and unpredictably to virtually any organ. The most common sites of metastasis are the skin and subcutaneous tissues, lymph nodes, lungs, liver, and brain.^{1,2} Pulmonary dissemination occurs in greater than 70% of cases of metastatic disease, with melanoma responsible for 5%–15% of all metastatic lesions to the lungs.^{1–4} The manner of pulmonary spread is variable, with combined patterns frequently present. The most common pattern is multiple discrete parenchymal nodules, seen in greater than 90% of metastatic cases.^{2,5} Other thoracic manifestations include solitary nodule, lymphangitic tumor spread, adenopathy, pleural effusion, extrapleural

Figure 2. A, B, Representative sections from a chest computed tomography scan performed on hospital day 2 following intubation, revealing bilateral ground-glass opacities and dense basilar consolidations. Contrast evaluation was negative for pulmonary emboli. C, Portable chest radiograph obtained on hospital day 4, demonstrating worsening bilateral airspace opacification.

Figure 3. A, Image from second bronchoscopy taken from the left upper lobe bronchus. Arrows indicate darkly pigmented endobronchial lesions. B, Endobronchial biopsy (original magnification, $\times 400$; hematoxylin and eosin stain) demonstrating irregularly shaped hyperchromatic cells with large nuclei. S-100 and melan A staining confirmed the diagnosis of metastatic endobronchial melanoma. C, Autopsy specimen (original magnification, $\times 100$; hematoxylin and eosin stain) demonstrating extensive alveolar and ductal infiltration by metastatic melanoma. D, Autopsy specimen (original magnification, $\times 200$) demonstrating positive S-100 staining. A color version of this figure is available online.

mass, and bone lesions.² Endobronchial melanoma without visible parenchymal disease is less common but reported, and it can first manifest as bronchial obstruction with resulting atelectasis.⁶ Most often, lung metastases are first detected on radiographs prior to development of pulmonary symptoms.³

In addition to these varied presentations, previous authors have described a miliary, nodular “snowstorm” pattern of metastasis that appears to carry a graver prognosis, with survival said to be 1–5 months.^{2,3,5} This rare pattern of dissemination occurs in less than 8% of cases of metastatic melanoma to the lungs. However, the micronodular description of the miliary presentation ap-

pears to be distinct from the rapid, diffuse airway and alveolar infiltration seen in our case.

Other malignancies have been associated with parenchymal infiltration by malignant cells leading to respiratory failure.⁷ The pattern is best described with primary non-small-cell lung cancer, most notably adenocarcinoma, as well as hematologic malignancies, including lymphoma and leukemia.^{8–10} Respiratory failure in these malignancies has been proposed to be due to either direct cellular infiltration of the alveoli or a secondary inflammatory reaction with resulting capillary leak.^{7,10} There is limited literature reporting a similar pattern in melanoma. Dwyer et al.⁵ described an individual who developed progressive respi-

ratory insufficiency 1 year after initial diagnosis of melanoma and eventually died of multiorgan failure 6 days after a diagnostic open-lung biopsy. Radiographic and pathologic descriptions were similar to those in our case. However, our case had several distinctive features, including rapid progression soon after presumptive complete resection, severity of illness, and bronchoscopic appearance with brisk development of endobronchial metastases.

In summary, we describe a case of newly resected metastatic melanoma presenting with acute respiratory failure. Our patient presumably harbored microscopic melanoma that was not apparent on postsurgical imaging, providing a source for rapid endobronchial and alveolar infiltration, leading to the brisk development of an ARDS-like picture ultimately resulting in death 6 days after presentation. The case highlights the need for consideration of malignancy as a potential imitator of ARDS and adds melanoma to the list of cancers that can present in this manner. In melanoma patients, especially when more common etiologies of respiratory failure have been ruled out, malignant infiltration of the lung parenchyma should be considered as a potential etiology.

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