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Case report

Dark sputum: An atypical presentation of primary pulmonary malignant melanoma

Alida Filippini [a, *], Fausto Zorzi [b, 2], Claudio Bna' [c, 3], Antonio Arnaboldi [a, 1], Tony Sabatini [a, 1]

[a] Department of Internal Medicine, Gastroenterology and Digestive Endoscopy, Poliambulanza Hospital Clinical Institute, Via Bissolati 57, 25124 Brescia, Italy
[b] Department of Pathology, Poliambulanza Hospital Clinical Institute, Via Bissolati 57, 25124 Brescia, Italy
[c] Department of Radiology, Poliambulanza Hospital Clinical Institute, Via Bissolati 57, 25124 Brescia, Italy

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A B S T R A C T

Primary melanoma of the lung is an extremely rare clinical entity. We found only 32 cases reported in literature, and in two of these multiple brain metastases were present. We describe a case of primary lung melanoma with brain and skin metastases that presented with an initial clinical diagnosis of pneumonia.

A 55-year-old white man presented with cough productive of dark sputum and fever. A chest x-ray showed a right lung infiltration. After failure to respond to usual treatment for pneumonia, bronchoscopy examination and CT scan revealed a right pulmonary mass. The CT-guided biopsy confirmed a diagnosis of malignant melanoma. The primary lung origin of the tumor was demonstrated by the characteristic junctional pattern of melanoma cells. Further evaluation revealed metastases in the brain and in skin.

Primary lung melanoma is an uncommon neoplasm that may be confused with more conventional types of lung cancer. Careful interpretation of histopathological information in correlation with all other clinical, laboratory and imaging studies may be needed to establish a diagnosis. Evaluation for metastases should include looking at the eyes, brain, skin. Due to the small number of cases reported in literature, there is no experience on the management and the prognosis of the disease.

Introduction

Malignant melanoma (MM) involving the respiratory tract is nearly always metastatic in origin. Primary malignant melanoma of the lung is uncommon, has a poor prognosis and only few cases have been reported [1,4]. Extra-pulmonary origin of the tumor including occult primary tumors must be excluded before considering this diagnosis. The proposed clinical and pathological criteria to define a primary lung melanoma [2,13,15] are often difficult to fulfill. Our case of lung MM with multiple brain and skin metastasis is among the first reported in literature.

Case report

A 55-year-old white male lawyer presented to the emergency department with a fever, persistent cough and shortness of breath beginning five days earlier. Past medical history revealed no previous serious illnesses. The patient never smoked.

Chest X-ray showed a right upper lobe infiltrate. Blood testing revealed leukocytosis and a high C-reactive protein. A diagnosis of right sided pneumonia was made and the patient was admitted to the hospital's Internal Medicine Department. Antibiotic therapy was started but fever and symptoms failed to respond. Due to the persistence of the symptoms and the presence of graysh/black sputum, chest computed tomography was performed. This revealed mixed ground-glass and lobar consolidation involving the right superior lobe, with associated air bronchograms and thickened interlobular septa, patchy areas of ground-glass in the middle and inferior lobe with air bronchograms and thickened interlobular septa and multiple bilateral nodules of varying size.

* Corresponding author. Department of Internal Medicine, Gastroenterology and Digestive Endoscopy, Poliambulanza Hospital Clinical Institute, Via Bissolati 57, 25124 Brescia, Italy. Tel.: +39 0303515556; fax: +39 303518224.
E-mail address: alida.filippini@libero.it (A. Filippini).
[1] Tel.: +39 0303515556.
[2] Tel.: +39 0303515065.
[3] Tel.: +39 0303515043.

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Tumor markers were within the normal range. Bronchoscopic examination showed a bulging lesion in the bronchus of the lower left lobe, and BAL revealed presence of melanocytes.

Careful skin examination showed a small lesion at the left shoulder and another at the left limb. The patient underwent surgical removal of the two lesions. The histopatological report described aggregates of atypical melanocytes within the dermis with thinning of the epidermis, no lateral extension of atypical melanocytes within the epidermis, absence of inflammatory infiltrate and junctional activity. This was reported as a characteristic pattern of metastatic malignant melanoma (MM). A CT scan of the brain revealed multiple secondary lesions. Detailed neurologic evaluation revealed the absence of any clinical neurological deficit. Comprehensive ophthalmologic examination showed no evidence of ocular melanoma.

A CT guided lung biopsy showed submucosal malignant epithelioid cells with large amounts of acidophilic cytoplasm and prominent nuclei. Dark brown pigment was observed in some of the tumor cells (Fig. 1). Mitotic figures were prominent. Immunohistochemical staining demonstrated positivity for pan-melanoma, S-100 protein, Vimentin, and HMB45 (melanoma marker), and were negative for cytokeratin (CK), epithelial membrane.

A diagnosis of primary lung malignant melanoma with multiple pulmonary, cerebral and skin metastases was made. The patient was referred to the local University Melanoma Center where he was treated with chemotherapy and immunotherapy. Despite therapy, the patient died three months after the diagnosis.

Discussion

Worldwide, approximately 160,000 new cases of melanoma are diagnosed each year, and about 41,000 melanoma related deaths occur annually [1]. Malignant melanoma mainly occurs on the skin, but has also been described in other mucosal sites and organs, including oral cavity, paranasal sinuses, esophagus, larynx, vagina, anorectal region, and liver [2,3].

Melanocytes are not normally found in the lower respiratory tract. Some likely explanations regarding the presence of melanoma in the lung are [2,8,13] the following: migration of benign melanocytes during embryogenesis. proliferations of melanocyte and melanocytic in the larynx and esophagus, melanogenic metaplasia in the submucosa [7,8].

Primary malignant melanoma of the lung is an extremely rare non-epithelial neoplasm that accounts for only 0.01% of all primary lung tumors [4].

To date, only 32 cases of primary pulmonary MM have been reported [5,6,7,9,10] and in only two were present multiple brain metastases [5,10,11]. The mean age at diagnosis is 57 years (range 41–82) with male prevalence. Lung MM are frequently endobronchial and manifest with cough, hemoptysis, lobar collapse, post-obstructive pneumonia [2] and in 30% of cases are found as incidental finding on chest x-ray.

Lung is one of the most common sites of metastasis of MM of extrapulmonary origin with an incidence of 70–82%. Usually primary pulmonary malignant melanoma (PMM) appears as solitary or multiple discrete nodules, and diffuse interstitial infiltrative pattern is rare and can be misdiagnosed due to more commonly accompanying conditions including pulmonary edema or drug-induced pneumonia [12]. Both endobronchial and lymph node involvement are common in this type of melanoma in contrast to melanoma that has metastasized to the lung [2].

To define PMM, Allen and Drash and others [2,13] proposed the following clinical and pathological criteria: 1. Junctional changes like “dropping off” or “nesting” of melanoma cells just beneath the bronchial epithelium. 2. Invasion of the bronchial epithelium by melanoma cells. Malignant melanoma associated with the epithelial changes. 3. No evidence of cutaneous, mucous membrane or ocular melanoma 4. The lesion should be a solitary lung tumor. 5. Absence of any other detectable tumor at the time of diagnosis. 6. No history suggestive of a previous melanoma [8].

Primary skin MM usually presents with marked epidermotropism, normally extending beyond the margins, no modification of epidermis at periphery, inflammation and adjacent melanocytic nevus with dysplasia, inconspicuous angiotropism and lymphatic invasion [15,16]. In our case the skin lesions were characterized by hyperplasia of epidermis at periphery, angiotropism and lymphatic invasion ; on the contrary epidermotropism, inflammation or autoaggression and the presence of melanocytic nevus around were absent. This pattern is indicative of cutaneous metastases of melanoma.

The optimal treatment of primary malignant melanoma of the lung remains to be determined. Some studies demonstrated a better prognosis for surgically-treated patients [14]. In our case various chemotherapeutic agents, including immunotherapy with interleukin-2 was used, but the patient died three months after the diagnosis.

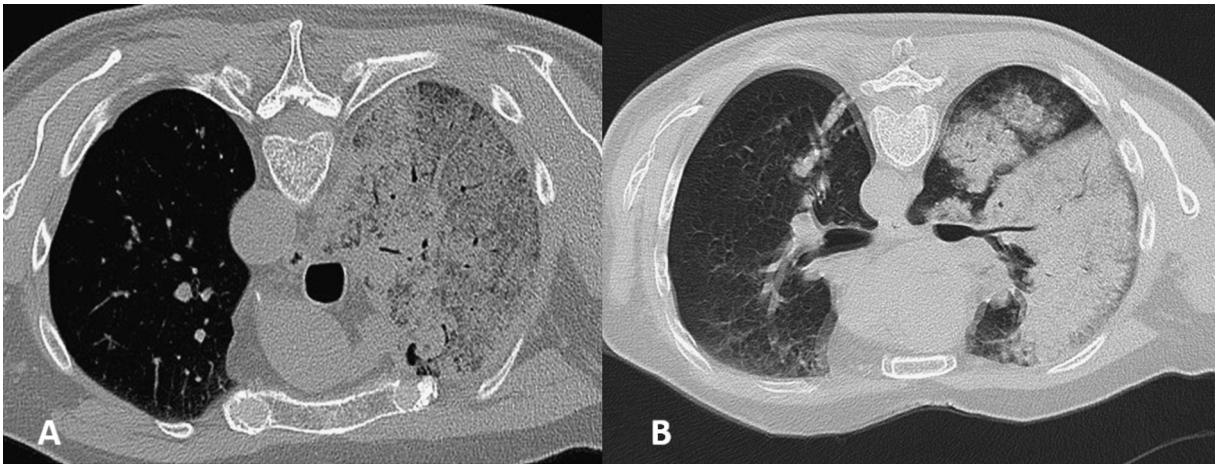

Fig. 1. Chest CT scan. **A-** Chest CT scan showes mixed ground-glass and lobar consolidation involving the right superior lobe, with associated air bronchogram and thickened interlobular septa. **B-** Chest CT scan showes ground glass with crazy paving appearance in the inferior right lobe and consolidation of superior right lobe, with air bronchogram.

Conclusion

Primary pulmonary malignant melanoma should only be diagnosed after detailed evaluations to exclude any extra-pulmonary origin. Histopathologic and clinical criteria have been proposed and should be applied in order to characterize a tumor as a primary pulmonary malignant melanoma.

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