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Case report

Beyond the skin – A rare case of primary pulmonary melanoma and endobronchial aspergilloma

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ABSTRACT

Melanoma is an aggressive skin tumor, but it may be present in other locations. Primary lung melanoma and endobronchial aspergilloma are rare entities.

The authors report a case of a 72-year-old, asthmatic woman, with worsening of her respiratory complaints. Imaging revealed finger in glove sign at the left hemithorax. Bronchoscopy revealed an elongated mass with evidence of *Aspergillus*. Despite endoscopic mass removal, the patient maintained the nodular imaging at the left hemithorax. She underwent thoracic surgery, and the histological evaluation identified malignant melanoma. After undergoing a thorough evaluation, we excluded other melanocytic lesions, and assumed the diagnosis of primary malignant lung melanoma.

This case demonstrates a rare association between endobronchial aspergilloma and primary lung melanoma, raising awareness of considering the co-existence of lung tumor in the presence of endobronchial aspergilloma, and showing endobronchial aspergilloma mimicking malignant lesions.

1. Introduction

Malignant melanoma (MM) is an aggressive skin tumor originating from melanocytes. MM may present in other, non-cutaneous locations, such as the eye, mucous membranes, meninges, adrenal glands, paranasal sinuses, biliary tract, or the lung [1,2]. The eye is the most non-cutaneous location affected by the melanoma [2,3].

Melanocytes derive from the neural crest, and during the embryonic devolvement, melanocytes may migrate to the lung [1]. These ectopic melanocytes can undergo malignant transformation. Non-cutaneous forms of MM are more aggressive [2,3].

Most cases of lung MM are associated with metastasis of skin lesions. Primary lung MM is rare, representing about 0.01% of all cases of primary lung cancer cases and 0.4% of melanomas [3]. Lung MM incidence does not differ by gender and has a mean age of

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presentation around 50 years [4].

2. Case report

The authors present the case of a 72-year-old non-smoker woman with a history of arterial hypertension, dyslipidemia, gastro-esophageal reflux, allergic rhinitis and controlled asthma with budesonide 160 μg/formoterol 4,5 μg 2 inhalations twice daily and montelukast 10 mg once a day. She had no previous surgical history.

The patient presented with a 6-week history of wheezing, mild productive cough with mucous sputum, and hemoptysis. She denied fever, chest pain, dyspnea, night sweats, and weight loss.

The patient was afebrile (36.5 °C) at the physical examination, with a blood pressure of 128/60 mmHg and a pulse of 80 bpm. She was eupneic with oxygen saturation of 97% on room air, pulmonary auscultation revealed bilaterally dispersed wheezing and rhonchi. She had no other abnormal findings.

The laboratory tests revealed 15000/μL leukocytes 9008/μL (60.5%) neutrophils, 170/μL (1.1%) eosinophils, 4310/μL (28.7%) lymphocytes, 1410/μL (9.4%) monocytes, hemoglobin 14.2 g/dL, platelets 227,000/μL, C-reactive protein 0.0 mg/dL, total IgE 17 UI/mL. The HIV serology result was negative.

Chest imaging revealed an elongated mass measuring about 3.4 cm in the left upper lobe. Suggestive of mucocele with a "finger in glove" pattern (Fig. 1a–c).

Bronchoscopy showed a gloved-finger gelatinous mass emerging from the sub-segmental apical-posterior bronchus of the left upper lobe (Fig. 2a). The endobronchial mass was almost removed with the biopsies performed. Bronchoalveolar samples were negative for microbiological and mycobacteriological cultures. Anatomopathological examination revealed fungal structures compatible with *Aspergillus*, and was negative for malignant cells (Fig. 2b).

The prick test was negative for *Aspergillus fumigatus*. Galactomannan and serum precipitins to *Aspergillus* spp. (*fumigatus, niger, flavus* and *terrus*) 8.8 mg/L (<44 mg/dL) were negative.

The patient began taking 200 mg of itraconazole twice daily for 6 months.

One month later, in the follow-up assessment, she presented clinical improvement but without radiological changes.

Based on these findings, we examined the hypothesis of an endobronchial aspergilloma associated with a malignant lesion.

Because the patient refused to repeat bronchoscopy, a ^{18}F-FDG positron emission tomography CT was performed, revealing an increased uptake identifying a mass in the left lung with apparent bronchial continuation, with a SUV equal to 19. With no other

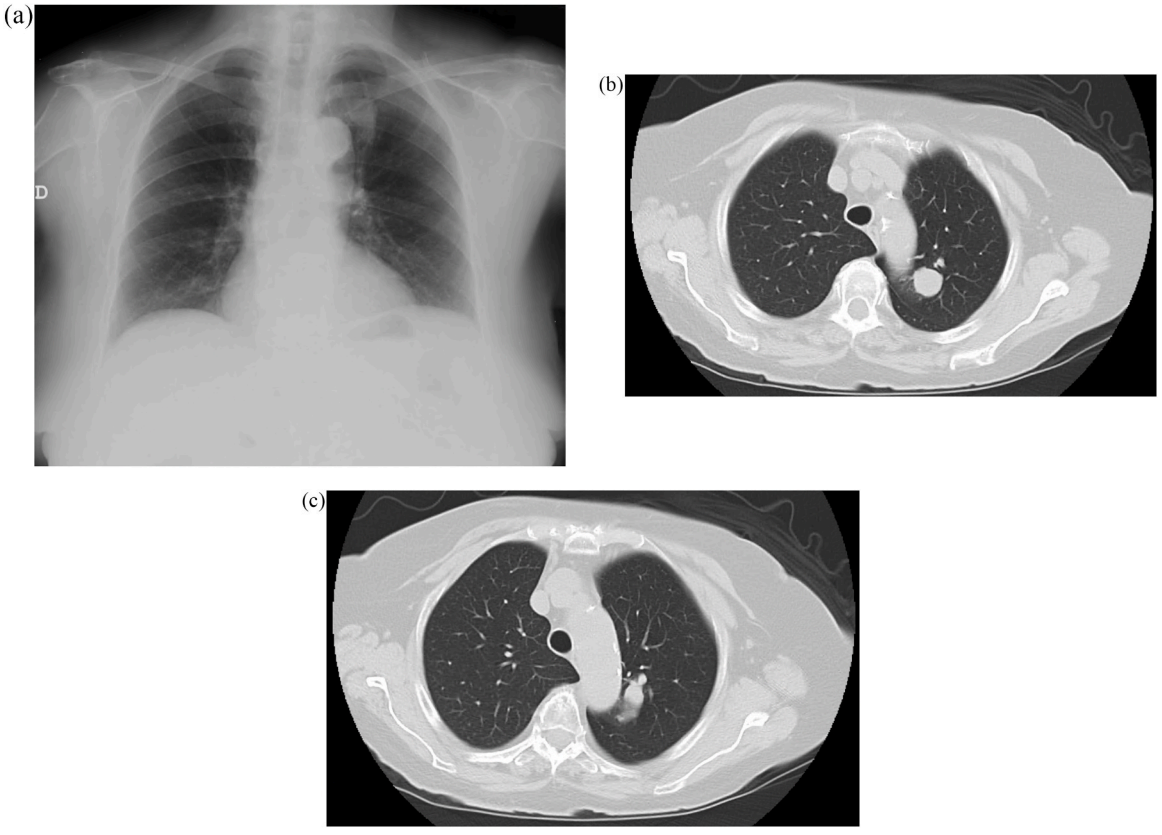

Fig. 1. a) Chest x-ray showing upper left opacity. b and c) Chest CT axial cut lung window: showing in the upper left lobe an elongated mass measuring 3.4 cm long.

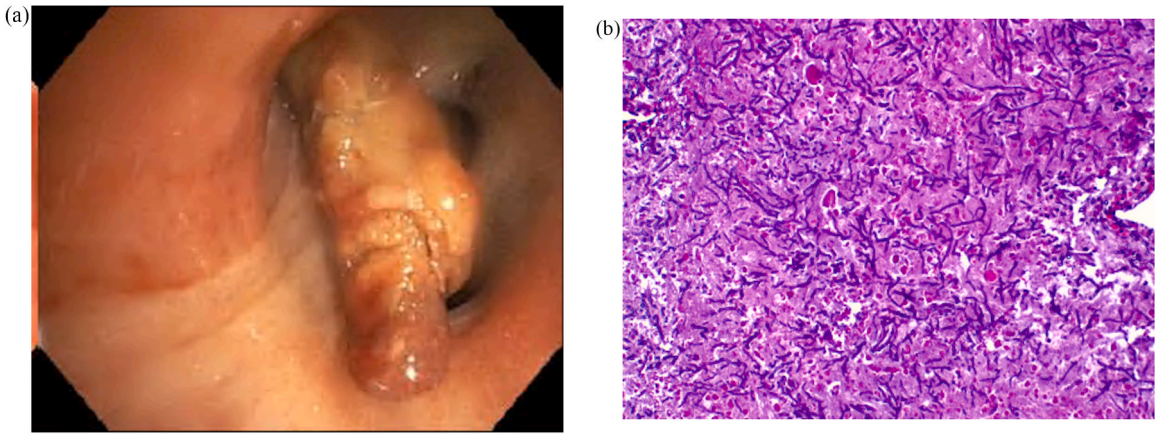

Fig. 2. a) Digitiform mass emerged from the apico-posterior of the upper left bronchus, and b) Hematoxylin and eosin staining image, with 100× magnification, showing fibrino-necrotic exudate with numerous fungal structures, characterized by hyphae with frequent 45° septation and branching, with a diameter of 2.5–4.5 μm.

relevant changes.

Head CT images had no relevant brain alteration or paranasal sinus abnormality.

About 3 months after bronchoscopy, the patient underwent a wedge resection of the left upper lobe.

The surgical specimen measured 10 x 5 x 4 cm with no gross lesions. The surgical specimen was subjected to an extemporaneous examination, given an enormous amount of mucus, the pathological evaluation was difficult and prolonged. The thoracic surgeon decided to complete surgery without preliminary results, but preserving the possibility of a second surgical approach based on the pathology result.

Anatomopathological examination identified a 4 cm nodule, well delimited and friable. Histology revealed a malignant

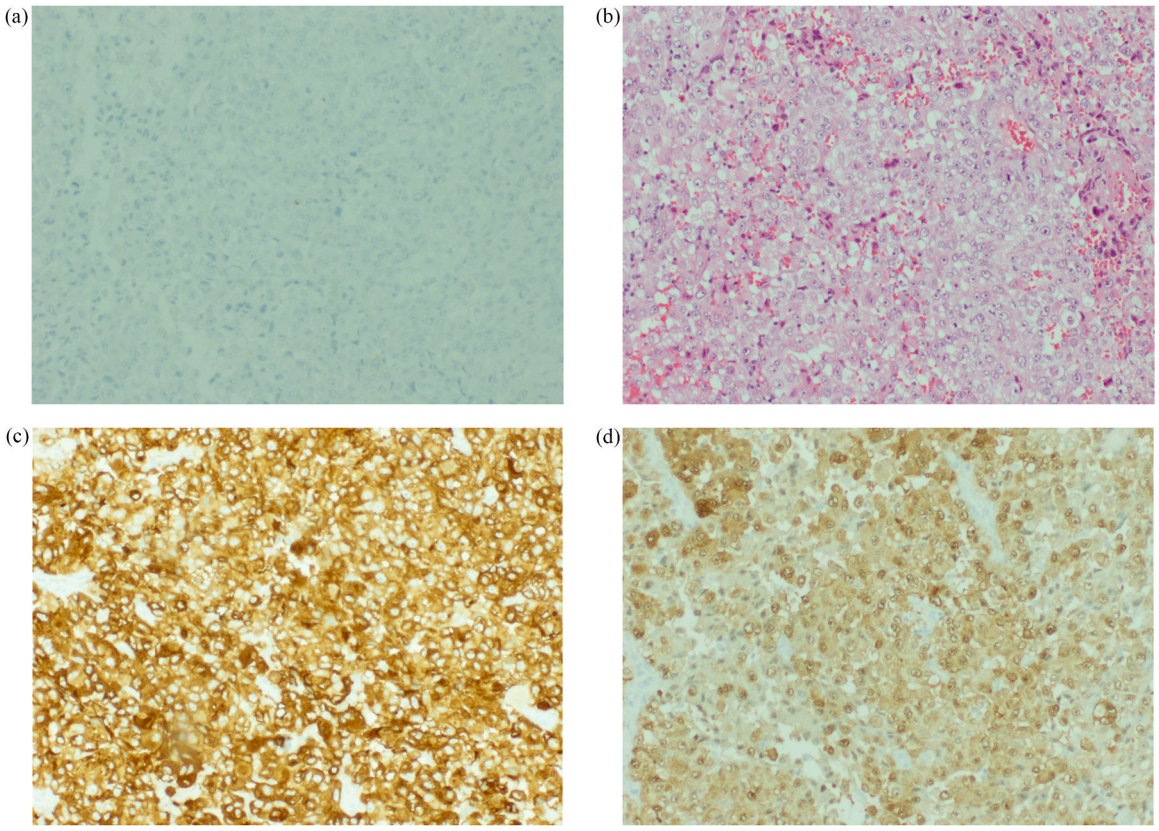

Fig. 3. Magnification 10 × 10. a) Hematoxylin and eosin staining of tumor cells. b) AE1/AE3 negative staining. c) The cytoplasm of malignant cells stained positive with antibodies against S100, and d) Melan A.

pleomorphic neoplasm, with extensively necrotic and hemorrhagic multinodular morphology, with large cells with clear cytoplasm and eosinophilic and finely granular cells. Large perimembranous concentrated chromatin nuclei with clear center alongside other plasmacytoid nuclei, the nucleoli are prominent eosinophilic. Brownish pigmentation and numerous pigmented macrophages were observed on the periphery of the nodule. No fungal structures were found in the surgical specimen.

The immunohistochemical study was positive for: Vimentin, S100 and Melan A. Being negative for: CK7, TTF1, P40, CD56, CD45, CK8/18, CKB12, AE1/AE3 (Fig. 3 a-d).

The neoplasm did not infiltrate the pleura or surgical pulmonary margins. Angioinvasion was not observed. Morphological evaluation and immunohistochemical and molecular profile revealed malignant melanoma without BRAF gene mutation.

The patient underwent a multidisciplinary evaluation. The eyes, skin, scalp, and genital and perianal regions were thoroughly evaluated, without evidence of melanocytic lesions. Oral cavity and nasal cavities were also free from suspicious mucosal alterations.

Given these findings, we assumed simultaneous primary lung melanoma and endobronchial aspergilloma.

Surgery was required to dissect the lymph nodes and lobectomy. Due to the ongoing SARS-CoV-2 pandemic, there was some delay until the start of systemic therapy and surgery. As a result of rapid clinical deterioration, the patient died of brain metastasis after 9 months of symptom development, with no further surgery or chemotherapy.

3. Discussion

For the diagnosis of primary lung MM, it is essential to rule out metastatic lung lesions. To establish the diagnosis, it is essential to meet clinical and immunopathological criteria. Thus, the presence of: solitary lung lesion is essential, confirmation by immunohistochemistry being imperative; no previous history of surgical excision of skin, mucous or ocular lesions; absence of tumor in another location at the time of diagnosis and absence of a history suggestive of melanoma [2]. It is important to exclude other melanotic tumors, such as medullary thyroid carcinoma and pigmented neuroendocrine carcinoma [3].

Endobronchial aspergilloma is a rare disease. It is a noninvasive form of aspergillosis that can mimic lung cancer. The literature reports some cases of endobronchial *Aspergillus* fungus balls associated with endobronchial tumors. In the presence of this form of aspergilloma, the co-existence of lung tumor should be suspected. A second bronchoscopy must be performed to evaluate the clinical response to treatment. Optimal treatment and duration is not yet established [5,6].

As the patient refused to repeat bronchoscopy, it was not possible to assess the effect of therapy on endobronchial aspergilloma. However, no fungal structures were found in the surgical specimen, which suggests a good response to itraconazole.

The patient met all defined criteria for the diagnosis of lung MM. The best therapeutic approach for lung MM is not clear, given the rarity of cases [2]. However, the literature emphasizes the importance of an aggressive, multifaceted approach with pneumonectomy or lobectomy with lymph node dissection, radiotherapy, chemotherapy, and immunotherapy [3].

The prognosis of lung MM is very unfavorable, most patients survive about 18 months [3].

4. Conclusion

The reported case is of special interest because of the rarity of both associated pathologies, and because endobronchial aspergilloma can obscure underlying malignant lung disease.

The present case highlights the importance of considering this neoplasm in the differential diagnosis of primary lung cancer. As it is extremely rare, its therapeutic approach is not well established. Therefore, we share our experience in order to contribute to future case approaches.

Patient consent

Written informed consent was obtained from the patient's family.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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