Spontaneous regression of pulmonary metastatic melanoma

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Abstract
Spontaneous regression of metastatic melanoma is a rare event with only 76 cases having been reported since 1866. The precise mechanism of regression remains unknown. We present a case of a man with spontaneous regression of pulmonary metastatic melanoma confirmed on histopathology accompanied by reduction in fluorodeoxyglucose-activity on serial positron emission tomography/computed tomography scan.

Introduction
Spontaneous regression of malignancy is defined as “complete or partial disappearance of the malignant tumour in the absence of all treatment” [1]. Spontaneous partial regression of primary melanoma is well-recognized with 10–35% of melanoma showing histological changes [2]. Complete regression of metastatic melanoma is rare, with only about 0.23% of cases having been reported [1, 2].

Case Report
A healthy 83-year-old male, a lifelong non-smoker, was found to have an incidental 15 mm left upper lobe lingula segment lung nodule as part of the investigation of peripheral neuropathy. Computed-tomography-guided biopsy demonstrated malignant melanoma, immunohistochemistry was positive for S-100 and Melan-A (Fig. 1A). The initial FDG (fluorodeoxyglucose) positron emission tomography/computed tomography (PET/CT) scan (Fig. 2A) showed increased uptake in the left upper lobe lesion with an SUV of 3.4, and mild uptake in the small hilar and mediastinal lymph nodes. No endobronchial lesions were seen on bronchoscopy. Endobronchial ultrasound-guided fine-needle aspiration of the mediastinal nodes showed no malignant cells. No cutaneous melanoma or other sites of metastasis were identified.

Serial PET/CT scans were performed at 3 and 6 months as part of the treatment planning workup, which confirmed no progression of disease, but the left upper lobe nodule SUV (standardized uptake value) had reduced to 0.9 at 6 months (Fig. 2B). Video-assisted thoracoscopic surgery wedge resection of the left upper lobe lesion was performed 8 months after initial diagnosis. Histopathology showed scattered completely infarcted and necrotic ghost outlines of cells seen within the nodule with no viable cells present. Stains for S-100 and Melan-A were negative. Stains with Mason Fontana and Melanin bleach confirmed the presence of melanin pigment within the necrotic cells (Fig. 1B). Postoperative CT chest confirmed the left upper lobe nodule had been completely resected with no new pulmonary nodules.

The final diagnosis was spontaneous regression of pulmonary metastatic melanoma confirmed on histopathology accompanied by reduction in FDG-activity on serial PET scan.s
Discussion

Spontaneous regression of metastatic melanoma is a rare event. A recent review summarized a total of 76 cases reported in the literature since 1866 [1]. The majority were regression in cutaneous and lymph node metastases, whereas regression of pulmonary metastases has only been reported in 10 cases. Spontaneous regression of metastatic melanoma occurs equally in both genders in all age groups. In comparison to spontaneous regression of primary melanoma, the ratio of male to female is 2:1 [1]. The prognosis of regression of primary melanoma is debatable, with some studies suggesting this to be generally an indicator of poor prognosis, and others suggesting a favorable outcome.

While this might be explained by differing criteria for defining histological regression, the prognostic significance of regression remains controversial [2].

The mechanisms of spontaneous regression of melanoma are unknown. Possible etiologies have been postulated, including infection, operative trauma, hormonal influences or immunologic factors [1]. It has been suggested that surgery and infection could be acting as mediating factors of regression by increasing the individual’s natural defenses against the tumor. Immunological studies have demonstrated that T cells are able to recognize melanoma antigen and induce apoptosis. Infiltration of inflammatory cells, especially lymphocytes can be seen on histology of regressing melanoma [1, 3].
PET is sensitive (83%) and specific (85%) in detecting metastasis of melanoma [4]. FDG PET/CT imaging aids in disease staging and prognostication, but its use in monitoring disease progression or treatment response is less well defined [5]. FDG uptake in tumor cells reflects metabolic activity which can be quantified by the SUV. A value exceeding 2.5 is considered highly suggestive of malignancy. Our case demonstrates a clear reduction in the SUV on serial imaging, which is in keeping with reduction in tumor metabolic activity, most likely through cell necrosis as seen in the resected specimen.

To our knowledge, this is the only case report of spontaneous regression of melanoma with evidence of serial reduction in FDG-avidity on PET/CT imaging, and confirmed on histopathology.

**Disclosure Statements**

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

**References**

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