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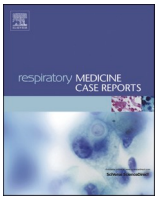

Case Report

# Endobronchial melanoma metastasis. A rare relapse

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ABSTRACT

Melanomas are skin derived malignant tumors exhibiting extreme diversity during disease progression in terms of time and site of metastasis. This is a rare case of a 68 year old, former smoker male, with a history of a cutaneous head melanoma which was treated 20 years ago. He presented with dyspnea and mild hemoptysis. On examination a solid mass found at the right lower lobe. Bronchoscopy performed and biopsies taken revealing endobronchial metastatic melanoma. Tissue genomics revealed two rare mutations. Finally patient received a doublet of immunotherapy and targeted therapy regiments. To the best of our knowledge this is a rare case of endobronchial metastasis 20 years after the treatment of the primary site. After so many years elapsed it is difficult to make a differential diagnosis between metastasis and a second primary endobronchial melanoma. Surgery and bronchoscopic modalities are promising only if they can be combined with immunotherapy and targeted therapies which are the game changers regarding the treatment of the disease.

## 1. Introduction

Melanomas are highly aggressive and invasive tumors, usually deriving from the skin [1]. The primary cutaneous tumor, generally has no major metastatic trends [2], to specific organs. It tends to progress locoregionally to the skin or lymph nodes and distally to organs preferably to the liver, brain, GI and the lungs [3,4]. Although late melanoma recurrence is a well recognized clinical phenomenon, endobronchial metastases and specifically delayed ones are extremely sparse [5]. Median time to endobronchial metastasis was calculated to 48 months after the discovery of the primary tumor [6]. This paper enlightens a case of a probable endobronchial metastatic melanoma 20 years after the primary tumor site treated, which, to the best of our knowledge, is one of the most delayed melanoma metastasis ever documented.

## 2. Case report

A 68 year old male former smoker (20 pyrs, quitted 20 years ago) presented with hemoptysis, dyspnea on exertion and low grade fever. Symptoms first encountered about a month before the hospital admission. The patient had a history of controlled arterial hypertension and head melanoma, which was surgically treated with regional nodal removal 20 years ago. Unfortunately, there were no histologic or surgical records from that period. The patient received no adjuvant treatment and he had been followed up by his dermatologist for five years with no clinical signs of relapse. The bloodwork during admission showed increased inflammation markers

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(white blood cells, CRP). On physical examination low blood oxygen saturation (94 %) and crackles on the right hemithorax detected. Patient underwent a chest x ray revealing a right hilar lesion and a chest CT scan which clearly depicted a right lower lobe solid mass with bronchial obstruction [Fig. 1a]. Patient had no other lesions nor enlarged regional, hilar and mediastinal lymph nodes [Fig. 1b]. The lesion was centrally located with a diameter 3,5cm × 4cm and the patient offered a EBUS bronchoscopy. Just below the superior segment bronchus of the right lower lobe (RB6) an exophytic grey mass was identified occluding the right lower bronchus by 40 % [Fig. 2a]. No lymph node infiltrations were recognized with sonographic criteria. Biopsies were taken with common forceps and because of moderate hemorrhage with hot forceps [Fig. 2b]. There were no major complications during bronchoscopy and patient discharged 2 hours after the procedure.

Pathology examination of the specimen was difficult because the cells exhibited high degree of un-differentiation, necrosis and mucosa infiltration (ulceration). The viable malignant cells forming the solid lesion [Fig. 3a] were small - medium sized with irregular nuclei under several stages of mitosis. Almost 70 % of the cells expressed S-100 and MITF (nuclear staining) [Fig. 3b]. The main differential diagnoses of this lesion were at first poorly differentiated sarcoma and melanoma. BRAF and V600E of exon 15 mutations were also detected. Pathology report indicated that the lesion was a malignant metastatic melanoma with necrosis and ulceration.

## 3. Discussion

The lungs are rarely affected by primary melanoma with 0.01 % incidence of all primary tumors [8]. Some series reported that melanoma metastasis to the respiratory system, could reach 5–6 % of all tumors malignant metastasis and usually presented as various sized bilateral pulmonary nodules [9]. Concurrently, metachronous endobronchial metastases were identified rarely reaching 2,4 to 6, 7 % incidence [11,12] whilst late endobronchial recurrences (after 10 years) are extremely sparse documented only as case reports [7–10]. It becomes clear that the natural history of malignant melanomas is highly variable [5]. Spontaneous regression, widespread early metastasis or even late recurrences 10 years or more after the discovery of the primary tumor are well documented [5]. Late metastasis mechanism is currently based on the theory of dormancy [13]. The aforementioned theory proposed by Willis (1934) [15], although highly debated, stated that at the time the primary tumor is discovered it is already disseminated. The ectopic melanoma cells entering a mitotic pause called dormant state [14]. Factors regulating the above phenomenon are still unknown but temporal inability of tumor cells for neoangiogenesis, active resistance by host immune-surveillance mechanisms and hostile environment formed by interactions between tumor cells and extracellular matrix were previously proposed [15].

Our case is unique for many reasons. It became evident that it was impossible to distinguish if the tumor was a very late recurrence as there was no access to the primary lesion pathology. On the other hand a second primary melanoma of unknown origin could not be ruled out as it was detected 20 years after the primary site. Despite the latter no other melanoma seedings, nor lymphadenopathy discovered, making the above hypothesis rather problematic. Finally, we could not differentiate if the tumor started endobronchially or as a lung metastatic nodule that spread locoregionaly and broke into the bronchial mucosa. So the hypothesis that this lesion could be regarded as a very late endobronchial metastasis remained valid and extremely rare.

In any of the two above cases, prognosis still remains poor. Median survival estimated about 6–10 months for patients with metastatic melanomas [16] whilst 5 year survival for patients with second primary tumors was only 10 % [17]. Endobronchial melanomas patients had a median survival of only 6 months as well [6]. Therapeutic options were the same as treating cutaneous melanomas. Surgical removal of the melanoma site, radiotherapy, chemotherapy and bronchoscopic debulking of the endobronchial

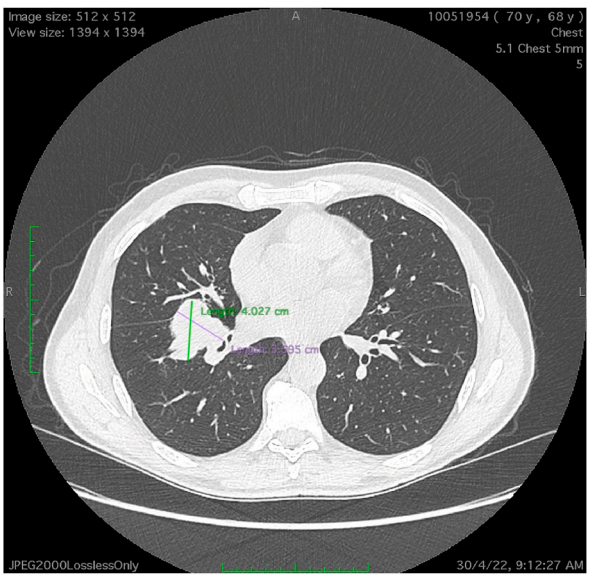


**Fig. 1a.** CT scan depicting right lower lobe mass measured spacing the right major fissure.

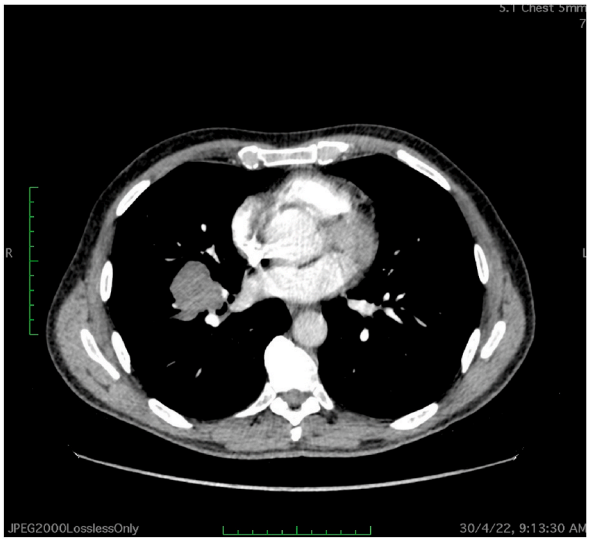


**Fig. 1b.** CT scan depicting right lower lobe mass and no mediastinal lymph nodes.

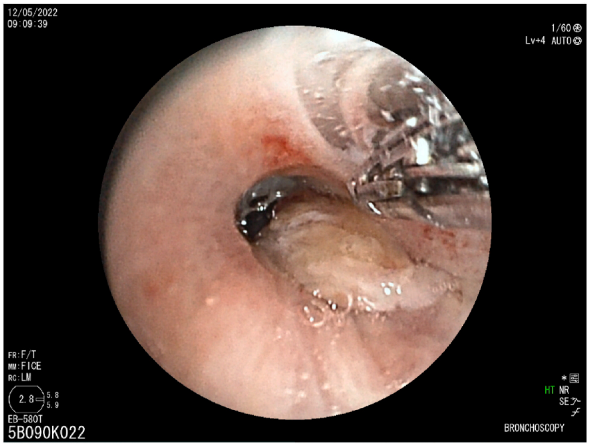


**Fig. 2a.** Grayish Endobronchial mass occluding the right lower lobe by 40 %. Tool in lesion.

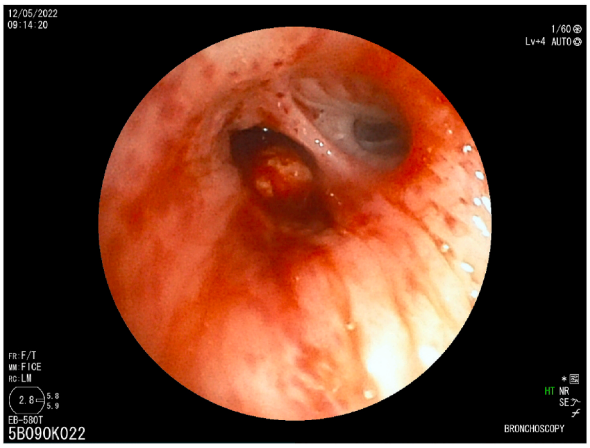


**Fig. 2b.** Mass hemorrhage after sampling.

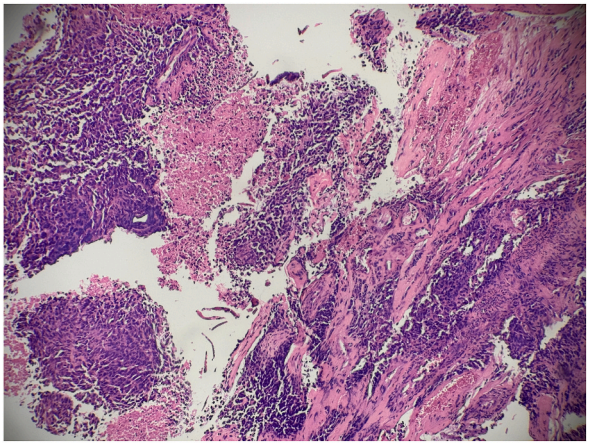

**Fig. 3a.** Viable malignant cells forming a solid lesion, small - medium sized with irregular nuclei under several stages of mitosis.

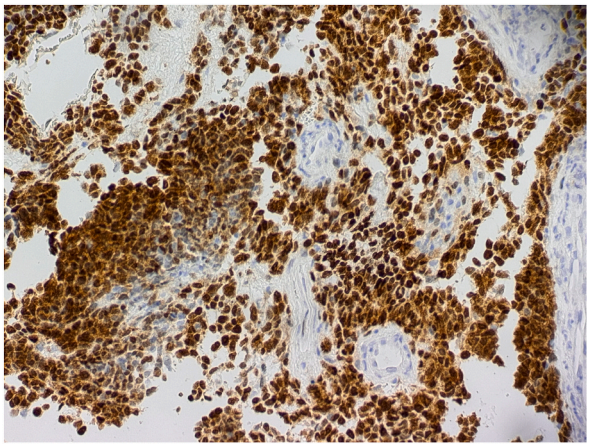

**Fig. 3b.** Nuclear staining 70 % of the cells expressed S-100 and MITF depicting a melanoma tumor.

component could apply but studies demonstrated that they couldn't impact the prognosis [6]. Simultaneously, it was advocated that 80 % of the patients that underwent metastectomy frequently relapsed [18]. Novel treatments had dramatically improved survival in advanced melanoma. The first-line therapeutic options for treating metastatic melanoma currently include immunotherapy (PD1 inhibitors) either as monotherapy or in combination with a CTLA-4 inhibitor or targeted therapy with BRAF and MEK inhibitors [19]. These therapies also demonstrated good results combined with surgical or bronchoscopic modalities [20]. Our patient underwent a combination of immunotherapy and targeted therapy due to BRAF V600E mutation. The lesion as showed on the CT scan (Fig. 1a) spanned the right major fissure so a right pneumonectomy was proposed, that the patient couldn't perform due to high risk of operative complications and poor lung function. He remains stable on follow up after 6 months of the initiation of immunotherapy and targeted therapy.

## 4. Conclusions

In conclusion, melanomas are rare tumors exhibiting long time to progression and to variable organs even inside the bronchi after 20 years. Bronchoscopy is a valuable invasive technique aiming diagnosis and even offering treatment options with minimal side effects. New immunotherapies and targeted therapies are game changers impacting the patients survival together with other modalities when they can be applied. Patients should be on follow up many years after treatment of the primary site and should be cautious when new symptoms arise. More data are needed and up to date pathology archives should be kept thoroughly, for comprehending the progression of the disease and developing more sufficient treatment options.

## CRediT authorship contribution statement

**Anastasios Palamidas:** Writing – original draft. **Bouros Dimosthenis:** Methodology, Resources, Supervision, Writing – review &

editing.

## 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.

## References


[1] T. Das Gupta, R. Brainsfield, Metastatic melanoma. A clinicopathological study, Cancer 7 (1964) 1323–3139.
[2] Heung Tae Kim, Young Whan Kim, Si Young Kim, Yung Jue Bang, Sung Koo Han, Noe Kyeong Kim, Keon Youl Kim, Yong Chol Han, Hyung Geun Song, Hyun Soon Lee, Sang Kook Lee, Endobronchial metastasis of malignant melanoma, diagnosed by bronchoscopy–report of a case, Kor. J. Intern. Med. 3 (1988) 77–80.
[3] M.P. Shepherd, Endobronchial metastatic disease, Thorax 37 (1982) 362–365.
[4] A. Marchioni, A. Lasagni, A. Busca, A. Cavazza, L. Agostini, M. Migaldi, P. Corradini, G. Rossi, Endobronchial metastasis: an epidemiologic and clinicopathologic study of 174 con-secutive cases, Lung Cancer 84 (2014) 222–228.
[5] H. Koh, A.J. Sober, T.B. Fitzpatrick, Late recurrence (beyond ten years) of cutaneous malignant melanoma. Report of two cases and a review of the literature, JAMA 251 (14) (1984) 1859–1862.
[6] A. Chaussende, C. Hermant, R. Tazi-Mezalek, Endobronchial metastases from melanoma: a survival analysis, Clin Respir J 63 (2016) 181–182.
[7] E. Pescarini, G. Spanikova, Z. Mbaidjol, E. De Antoni, V. Vindigni, F. Bassetto, Late metastatic Melanoma after 25 years: a case report and a brief literature review, Case Rep Surg 20 (2020) 2938236.
[8] A. Dountsis, C. Zisis, E. Karagianni, Late metastatic Melanoma after 25 years: a case report and a brief literature review, World J. Surg. Oncol. 1 (2003) 26.
[9] K. Zhang, T. Pelleg, S. Campbell, C. Rubio, L. Loschner, S. Ie, Pulmonary metastatic melanoma: current state of diagnostic imaging and treatments, Melanoma Manag 8 (3) (2021) 58.
[10] G. Karpathiou, M. Froudarakis, V. Da Cruz, F. Forest, M. Sauvage, J.M. Vergnon, M. Peoch, Endobronchial melanoma metastasis 40 years after the excision of the primary cutaneous tumor, Medicine 96 (2017) 34(e7931.
[11] N.J. Crowley, H.F. Seigler, Late recurrence of malignant melanoma. Analysis of 168 patients, Ann. Surg. 212 (1990) 173–177.
[12] H.M. Shaw, C.W. Beattie, W.H. McCarthy, G.W. Milton, Late relapse from cutaneous stage I malignant melanoma, Arch. Surg. 120 (1985) 1155–1159.
[13] M. Rocken, Early tumor dissemination, but late metastasis: insights into tumor dormancy, J. Clin. Investig. 120 (2010) 1800–1803.
[14] S. Friberg, A. Nystrom, Cancer metastases: early dissemination and late recurrences, Cancer Growth Metastasis 8 (2015) 31249.
[15] S. Osella-Abate, S. Ribero, M. Sanlorenzo, Risk factors related to late metastases in 1,372 melanoma patients disease free more than 10 years, Int. J. Cancer 136 (2015) 2453–2457.
[16] P. Rutkowski, P. Wysocki, Z. Nowecki, L. Rudnicka, A. Nasierwoska-Guttmejer, J. Fijuth, E. Kalinka-Warzocha, T. Świtaj, M. Wojtukiewicz, W. Zegarski, A. Jezior- ski, K. Krzemieniecki, R. Zaucha, E. Filipczyk-CisarÄ, K. Herman, M. Krzakowski, Cutaneous melanoma – diagnostic and therapeutic guidelines in 2013, Dermatol. 100 (2013) 1–15.
[17] L. Gong, X.Y. Liu, W.D. Zhang, S.J. Zhu, L. Yao, X.J. Han, M. Lan, Y.H. Li, W. Zhang, Primary pulmonary malignant melanoma: a clinicopathologic study of two cases, Diagn. Pathol. 7 (2012) 123.
[18] J.W. Smithy, M.A. Postow, Adjuvant checkpoint blockade following complete local therapy for melanoma metastases, Lancet 400 (2022) 1082–1083.
[19] B.C. Kim, H.K. Kang, Y.S. Kim, S. Haw, H.S. Kim, J. Kang, A rare case of endobronchial melanoma of unknown primary, Respiratory Medicine Case Reports 42 (2023) 101811.
[20] L. Zimmer, E. Livingstone, J.C. Hassel, M. Fluck, T. Eigentler, C. Loquai, S. Haferkamp, R. Gutzmer, F. Meier, P. Mohr, A. Hauschild, B. Schilling, C. Menzer, F. Kieker, E. Dippel, A. Rösch, J.C. Simon, B. Conrad, S. Körner, C. Windemuth-Kieselbac, J. Utikal, Adjuvant nivolumab plus ipilimumab or nivolumab monotherapy versus placebo in patients with resected stage IV melanoma with no evidence of disease (IMMUNED): a randomised, double-blind, placebo-controlled, phase 2 trial, Lancet 395 (2020) 1558–1568.