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Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (FDG PET/CT) Monitoring of Rapidly Progressive Low-Risk Cutaneous Melanoma: A Case Report of Durable Response to Combined Stereotactic Body Radiotherapy (SBRT) and Immunotherapy

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Abstract

We present a case of metastatic cutaneous melanoma without a BRAF mutation that showed an unusually aggressive disease course despite favorable initial histopathological features. The patient was initially diagnosed with superficial spreading melanoma with a negative sentinel node. After resection of the subcutaneous metastasis, rapid and extensive systemic dissemination occurred within two months. Metastases affected the liver, lungs, bone, soft tissue structures, and a large parailiac tumor. Therapy included combined immunotherapy (pembrolizumab + ipilimumab) and multiple series of stereotactic body radiotherapy (SBRT) for oligometastatic lesions. After an initial mixed response, secondary SBRT resulted in complete metabolic regression of most lesions on fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT). The remaining parailiac remnant showed a gradual decrease in size and metabolic activity during follow-up. Continuous pembrolizumab monotherapy and targeted SBRT provided long-term disease control, with no evidence of active disease on the last FDG PET/CT. This case highlights the heterogeneity of melanoma, the possible limitations of prognostic factors, and the potential role of earlier initiation of systemic therapy and a combined approach of SBRT and immunotherapy in selected patients.

Categories: Nuclear Medicine, Radiology, Oncology

Keywords: braf mutation, fdg pet/ct, immunotherapy, sbrt, superficial spreading melanoma, unusually aggressive disease

Introduction

Cutaneous melanoma represents a significant clinical challenge, particularly regarding thin or low-risk tumors that can, in certain cases, exhibit unexpected aggressive behavior and early metastatic progression [1,2]. While traditional clinicopathological features such as increased Breslow thickness, ulceration, high mitotic rate, and lymphovascular invasion are well-established predictors of poor outcomes, a distinct subset of patients with ostensibly low-risk primary tumors still experience early metastasis [3,4].

Despite substantial advances in immunotherapy and targeted therapy, metastatic melanoma remains associated with significant morbidity and mortality [5]. Approximately 50% of cases harbor BRAF mutations, most commonly V600E [6], which enables the use of targeted therapies that significantly improve survival outcomes [7].

Historically, melanoma has been considered a radioresistant tumor, partly due to enhanced DNA repair mechanisms and intrinsic cellular resistance to conventional fractionation [8,9]. However, the development of stereotactic body radiotherapy (SBRT), which allows highly precise delivery of ablative radiation doses, has challenged this paradigm. In advanced melanoma, SBRT has demonstrated significant efficacy in two clinically important settings. The first is oligometastatic disease, where SBRT provides excellent local control of a limited number of metastatic lesions. The second is oligoprogressive disease, in which SBRT can be used to ablate isolated, resistant lesions while the remaining disease remains controlled by ongoing systemic therapy [1,10].

We report a case of BRAF wild-type metastatic melanoma with an unusually aggressive clinical course. Despite favorable initial histopathological features and a period of disease stability, the patient developed rapid systemic dissemination within a short time interval. Management followed current National

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Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology for Melanoma: Cutaneous (Version 2.2025) for stage IV disease after resection of a solitary metastasis [11].

This case highlights two key points: first, the effectiveness of a multimodal approach combining immunotherapy and SBRT, which resulted in a durable complete metabolic response; and second, the potential need to reconsider current treatment strategies in selected patients, particularly regarding the timing of systemic therapy after the first metastatic event.

Case Presentation

Initial diagnosis

In December 2019, a 37-year-old man underwent excisional biopsy of a pigmented lesion in the left scapular region. According to the patient's medical history, the lesion had been present for approximately 15 years, with rapid progression characterized by a sudden increase in size, as well as noticeable changes in shape, observed seven days prior to the intervention (Figures 1, 2). Histopathology confirmed superficial spreading melanoma (Breslow 0.6 mm, Clark III), without ulceration or mitotic activity (Table 1, Figure 3) [12]. Sentinel lymph node biopsy was negative. Molecular testing was performed using the cobas® BRAF Mutation Test (Roche Diagnostics, Basel, Switzerland; real-time polymerase chain reaction) to detect the V600E (T1799A) mutation, which was not detected. Additional molecular profiling, such as NRAS, KIT, or Next-Generation Sequencing, was not performed.



FIGURE 1: Pigmented lesion of the left scapular region



FIGURE 2: Pigmented lesion of the left scapular region photographed during surgical resection

Parameter	Finding
Histological type	Superficial spreading melanoma
Breslow thickness	0.6 mm
Clark level	III
Ulceration	Absent
Mitotic activity	Not detected
Lymphovascular invasion	Absent
Microsatellites	Absent
Tumor-infiltrating lymphocytes	"Brisk"
Resection margins (lateral)	17 mm
Resection margins (deep)	23 mm
Sentinel lymph node	Negative

TABLE 1: Histopathological characteristics of the primary melanoma from initial excision

Discussion

This case highlights the limitations of standard prognostic factors, demonstrating that aggressive disease may occur despite low-risk features, and generates the hypothesis that the role of early systemic therapy in such atypical presentations warrants further investigation. Established prognostic factors for metastatic progression in melanoma include increased Breslow thickness, ulceration, high mitotic rate, lymphovascular invasion, sentinel lymph node involvement, nodular subtype, and primary tumor location on the trunk, head, or neck [13,14]. In the present case, the only identified risk factor was the localization of the primary tumor on the trunk. Despite otherwise favorable histopathological features, the disease demonstrated an aggressive clinical course with rapid dissemination to multiple organs.

Such rapid progression is uncommon, particularly in superficial spreading melanoma. While rare cases of fulminant metastatic spread have been reported, they are more frequently associated with nodular melanoma [3]. This case highlights the biological heterogeneity of melanoma and underscores the limitations of currently established prognostic models in predicting individual disease behavior [4].

A particularly notable aspect is the extremely short interval between a negative CT scan and the development of widespread metastatic disease. Within only two months, the disease progressed from no radiologically detectable lesions to extensive systemic dissemination involving the liver, lung, bone, and soft tissues. This observation raises important questions regarding the reliability of imaging-based surveillance and the adequacy of current risk stratification approaches.

Another key consideration relates to the therapeutic strategy following resection of a solitary distant metastasis. According to current recommendations, systemic therapy may be considered but is not mandatory in patients without evidence of residual disease [11]. In this case, the decision to pursue active surveillance was consistent with existing guidelines. However, the rapid progression observed shortly thereafter suggests that this approach may not be optimal in all patients.

This case supports the hypothesis that earlier initiation of systemic therapy after the first metastatic event could potentially prevent rapid disease dissemination in selected patients, even in the absence of traditional high-risk features [6,15]. Ultimately, these findings emphasize the importance of an individualized treatment approach and raise an important clinical question regarding the optimal management of such atypical cases, which should be explored in future studies.

The introduction of immune checkpoint inhibitors has significantly improved outcomes in advanced melanoma, with durable responses observed in a subset of patients [16,17]. In the present case, combined immunotherapy with pembrolizumab and ipilimumab resulted in sustained disease control, despite initial aggressive progression.

In addition, this case illustrates the potential role of SBRT as an effective local treatment modality in the setting of oligoprogressive disease. SBRT enabled precise targeting of resistant lesions while allowing continuation of systemic therapy.

Emerging literature suggests a theoretical synergistic interaction between SBRT and immunotherapy. While SBRT may hypothetically enhance antitumor immune responses through modulation of the tumor microenvironment, a mechanism often discussed as the abscopal effect, the exact contribution of this phenomenon in the present case remains speculative and cannot be definitively confirmed [1,18].

The durable complete metabolic response observed in this patient highlights the potential benefit of this multimodal approach. The combination of immunotherapy and SBRT may represent a valuable strategy in selected patients with metastatic melanoma, particularly in the setting of oligoprogression [1]. This mechanism is thought to involve SBRT-induced release of tumor-associated antigens, which promotes T-lymphocyte activation and generates a systemic antitumor immune response [19].

Conclusions

This case highlights several important clinical implications. First, metastatic progression may occur rapidly even in patients with apparently low-risk primary melanoma and favorable histopathological features. Clinicians should remain cautious when relying solely on traditional prognostic factors. Second, a negative imaging study does not exclude the possibility of imminent systemic dissemination. Short-interval follow-up may be warranted in selected patients, particularly after the detection and resection of the first metastatic lesion. Third, current treatment strategies that allow observation after complete resection of a solitary metastasis may not be optimal for all patients. Consequently, it could be hypothesized that earlier initiation of systemic therapy in selected cases warrants further investigation to evaluate its potential role in mitigating the risk of rapid disease progression. Finally, the combination of immunotherapy and SBRT represents an effective multimodal approach. SBRT may provide local control of resistant lesions while enhancing systemic immune response, contributing to durable disease control.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

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