

Case Study: The Dangers of Melanoma Recurrence

— Before falling into a coma, this 41-year-old woman had been free of melanoma for 16 years

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Melanoma: Epidemiology, Diagnosis, and Treatment

Key Points

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"Medical Journeys" is a set of clinical resources reviewed by doctors, meant for physicians and other healthcare professionals as well as the patients they serve. Each episode of this 12-part journey through a disease state contains both a physician guide and a downloadable/printable patient resource. "Medical Journeys" chart a path each step of the way for physicians and patients and provide continual resources and support, as the caregiver team navigates the course of a disease.

This month: A noteworthy case study.

A 41-year-old woman arrived at an emergency department (ED) after falling into an acute coma 6 hours earlier. Clinicians learned that over the past 6 weeks, she had progressively worsening impaired consciousness. Her medical history included malignant melanoma diagnosed 16 years previously, after a biopsy of a "dish-pattern" tumor on her back returned positive results. She had received five cycles of chemotherapy (the specifics about the therapeutic regimen and medications were not available), and no further diagnoses in the time since.

The patient's records showed that 5 years before she presented to the ED, she developed a persistent dry cough and chest pain; a CT scan at that time revealed a mass in her right lung that clinicians suspected was a metastasis. The patient received chemotherapy with paclitaxel, caspofungin, and sorafenib, but continued to have weakness, loss of appetite, and nausea; after three separate trials, clinicians determined that the treatment was ineffective.

Persistent Coma

On the day the patient presented to the ED, she had vomiting after eating, along with drowsiness -- she had taken mannitol, with some relief. She then became incontinent and suddenly fell into a coma. Six hours later she was sent to the ED with suspected cerebral apoplexy.

The coma was graded as 5 on the Glasgow Coma Scale (which has a range of 1-15). Clinicians palpated a soft mass measuring 2×2 cm in diameter in the right frontal scalp. Her right pupil dilated to 4 mm and showed no direct or indirect light reflection. She had subcutaneous nodules scattered throughout her body; the left limb yielded a positive Babinski sign, but the right limb did not move.

Clinicians ordered CT scans of the patient's head, which revealed multiple intracranial masses located at the right frontal and temporal lobes. Severe brain compression caused the tumoral hemorrhage to shift the midline over 1 cm, which led to acute cerebral herniation. Meanwhile, clinicians also detected a scalp tumor in the frontal region.

A CT scan of the lungs showed a foliated mass measuring 3.7×2.6×3.3 cm in the lower lobe of the right lung. Comparison of the current scan to one taken 5 years earlier showed that the small nodules in the upper lobe of the left lung had disappeared, but that new round nodules had developed in both lungs and that there was an area of low density at the 12th vertebra, which clinicians suspected was a metastasis.

The tumor was resected with a transfrontal approach. When the skull flap was removed, clinicians discovered that the tumor had invaded the dura mater.

Late cerebral metastasis of melanoma presents widespread dissemination in dural matter and adjacent temporal bone, temporalis, and hypodermis. (A) The extradural part grew infiltratively through the skull to subcutaneous tissue. Small melanic dots were disseminated in adjacent temporal bone, temporalis, and hypodermis (white arrows indicate the tumor). (B) Postoperative head CT scan revealed a recurrent intracranial hemorrhage in the right frontal lobe. (C) Immunohistopathology confirmed melanoma dural metastasis. The tumor cells were distinctly heterogeneous, arranged in a sheet pattern; nuclei of tumor cells were represented by visible pigments, and nuclear division could be observed easily.

Surgeons excised the tumor, hematoma, and dura, achieving a clear boundary between the tumor and the surrounding brain tissue. On day two after surgery, the patient began to have recurrent bleeding in the right frontal lobe, causing another decline in her level of consciousness. Even after intracranial hematoma evacuation and craniectomy, the patient was not restored to consciousness.

The family requested supportive treatment, and the patient received palliative care. Histopathology results confirmed the presumed diagnosis of metastatic malignant melanoma. For the next 3 months, the patient survived with hemiplegia of the left limb and a persistent state of drowsiness. She died 5 months after craniectomy.

Discussion

Clinicians reporting this [case](#) of a patient who presented with a cerebral metastasis of primary cutaneous melanoma after 16 disease-free years following her initial diagnosis said the case highlights the importance of regular, long-term clinical follow-up of

melanoma patients.

The authors noted that the most recent National Comprehensive Cancer Network guidelines for melanoma call for "wide excision, sentinel lymph node biopsy, and additional treatment of regional or distant metastatic disease."

Although late recurrence of melanoma, defined as developing after 10 disease-free years after the initial diagnosis, is rare, researchers have begun to focus on this scenario, which can require life-long follow-up, the case authors explained. They cited nine reports of late cerebral metastasis that occurred in patients with cutaneous melanoma, suggesting that this represents a significant decrease from earlier years and is likely due to the development and refinement of radiological techniques, as well as updates to melanoma management guidelines.

AAD Guidelines for Follow-up

For example, the American Academy of Dermatology (AAD) [guidelines](#) recommend specific timing for "surveillance intervals and follow-up tests, physical examination with emphasis on assessment of local recurrence, particularly for the lentigo maligna subtype, and a full skin check to evaluate for new primary cutaneous melanoma at least every 6 to 12 months for 1 to 2 years and annually thereafter for patients with stage 0 (melanoma in situ)."

Recommended follow-up procedures for cutaneous melanoma include the following:

- Comprehensive history
- Review of systems
- Physical examination with special attention to the skin and regional lymph nodes

Recommended minimum follow-up frequency by disease stage is every 6-12 months for 2 years and at least yearly for patients with stages IA to IIA melanoma; and every 3-6 months for 2 years and at least yearly for those with stages IIB to IIC melanoma.

How Common Are Such Late Recurrences?

The case authors note that although disease-free status 10 years after diagnosis is considered to be "nearly synonymous with cure," with no further follow-up required, reports suggest incidences of late recurrences after that in the range of 1.01% to 12.75%.

The relative rarity of late-recurring melanoma and lack of extensive long-term follow-up makes it "difficult to estimate the frequency, predisposing factors, and prognostic implications of late recurrence of melanoma," and there are only a few published descriptions of late recurrences involving the brain, the case authors wrote.

In addition, "of 1,372 patients with stage I-II melanoma who were disease-free 10 years after diagnosis, only 10 patients were found to have distant [metastases](#) involving the brain," while another analysis of 1,881 stage I/II melanoma patients identified only one who developed late cerebral metastasis.

Are There Predictive/Prognostic Factors?

"Established knowledge has indicated tumor thickness, ulceration, mitosis rate, invasion level, patient age, localization, and type of recurrence as the prognostic factors of melanoma, but there are no clear data about predictive and prognostic factors for late recurrence," the case authors continued.

They noted that characteristics of late metastasis of melanoma to the brain are distinct from other sites of late recurrence, explaining that "most lesions in the cerebral parenchyma are cystic."

The metastasis in their patient was solitary because it involved the dura mater. As well, the authors said, very few metastases involved only brain tissue, pointing to this and previous cases in which patients presented with accompanying metastatic lesions in the lung. Theoretically, regular imaging follow-up of the lungs "may help detect early metastases to the brain," but confirmation will require more data.

Role of PET-CT

"PET-CT is [recommended](#) in the detection of cerebral metastases of melanoma and is helpful in diagnosis and staging of melanoma recurrence, particularly if surgery is being considered," the team noted. These brain metastases are often complicated by intracranial hemorrhage, which is a major contributor to a poor prognosis that should be considered in patients with neurological deficits.

"Patients with distant recurrence of melanoma have a poor prognosis, with a 5-year survival rate of only 6.5% to 11%," and a median survival of less than a year when the brain is involved, even with treatment. "The treatment has not been standardized until now, and surgical resection is the best treatment when the lesion is unique, accessible, and circumscribed," the authors explained, adding that evacuating an intracranial hematoma immediately can be life-saving.

Some surgeons favor [resection](#) "even in the progressive cases in which the metastases cause severe neurological symptoms." Conversely, radiation and stereotactic radiosurgery are good options in cases where the lesion is widespread or can't be accessed.

Prognosis

Progression of the systemic diseases means that life expectancy is limited to a few months, although favorable survival and prognosis have also been achieved in patients using novel targeted treatments such as BRAF inhibitors, and immunotherapy (anti-CTLA antibody), the case authors stated.

Conclusion

They conclude that this report of a rare occurrence of a late cerebral metastasis after initial diagnosis of a primary cutaneous melanoma emphasizes that need for long-term follow-up.

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Part 1: [Melanoma: Epidemiology, Diagnosis, and Treatment](#)

Part 2: [Recognizing Melanoma: What It Is, What It Isn't](#)

Part 3: *Basics of Melanoma Diagnosis*

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Disclosures

The case report authors noted no conflicts of interest.

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