American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2022; 23: e935728
DOI: 10.12659/AJCR.935728

Received: 2021.12.06
Accepted: 2022.02.02
Available online: 2022.02.08
Published: 2022.03.08

A 41-Year-Old Woman with a Late Cerebral Metastasis 16 Years After an Initial Diagnosis of Cutaneous Melanoma

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF Qi Yu
BC Yawen Ma
AFG Tianda Feng

Department of Neurosurgery, Shengjing Hospital of China Medical University, Shenyang, Liaoning, PR China

Corresponding Author: Tianda Feng, e-mail: fengtd@sj-hospital.org
Financial support: None declared
Conflict of interest: None declared

Patient: Female, 41-year-old
Final Diagnosis: Melanoma brain metastasis
Symptoms: Intrercranial hemorraghe
Medication: —
Clinical Procedure: —
Specialty: Neurosurgery

Objective: Rare disease

Background: Late cerebral metastasis more than 10 years after the diagnosis of cutaneous melanoma is very rare. This report is of a woman with late cerebral metastasis 16 years after an initial diagnosis of cutaneous melanoma.

Case Report: A 41-year-old woman had been diagnosed with malignant melanoma 16 years prior from a biopsy of a dish-pattern tumor on the back, for which she received chemotherapy for 5 times (therapeutic regimen and medications were not available). She had not had a diagnosis of skin melanoma in the past 16 years. Before presentation to the Emergency Department, she had a progressive disturbance of consciousness for 6 weeks and sudden coma for 6 h. A head computed tomography scan indicated intracranial masses located at the right frontal and temporal lobes. The patient underwent surgery for tumor and hematoma removal. During surgery, dural metastasis with widespread dissemination in adjacent temporal bone, temporalis, and hypodermis was confirmed. Postoperative histopathology analysis confirmed the diagnosis of malignant melanoma metastasis. On the second day after surgery, the patient developed recurrent bleeding in the right frontal lobe, which led to deteriorated consciousness. She received hematoma evacuation and craniectomy and lived in a poor condition with drowsiness and hemiplegia of the left limb for 3 months and died 5 months after craniectomy.

Conclusions: This report has presented a rare occurrence of late cerebral metastasis 16 years after the initial diagnosis of a primary cutaneous melanoma. More recent primary melanoma of the skin was not identified, which supports the need for long-term follow-up of patients with a history of primary cutaneous melanoma.

Keywords: Intracranial Hemorrhages • Melanoma • Neoplasm Metastasis • Coma

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/935728

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

Background

Melanoma is the third most common source of brain metastases, following lung and breast cancers [1], and has one of the highest tendencies to develop brain metastases, with a prevalence of nearly 45% in patients with stage IV melanoma and 75% upon autopsy [2-5]. For most patients newly diagnosed with melanomas, wide excision, sentinel lymph node biopsy, and additional treatment of regional or distant metastatic disease are essential procedures according to the updated National Comprehensive Cancer Network (NCCN) guidelines for melanoma [6]. Regular clinical follow-up is recommended as the most important means of detecting cutaneous melanoma recurrence. The American Academy of Dermatology guidelines recommend 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). For stages IA to IIA cutaneous melanoma, comprehensive history, review of systems, and physical examination with specific emphasis on the skin and regional lymph nodes are recommended at least every 6 to 12 months for 2 years and at least yearly thereafter. For stages IIB to IIC, the recommended follow-up interval is every 3 to 6 months for 2 years, then at least annually thereafter [7]. Generally, patients who are disease-free 10 years after diagnosis are considered nearly synonymous with cure and are discharged from follow-up. However, late recurrences, defined as occurrences 10 years or more after diagnosis, have been reported in several studies, with incidence rates ranging from 1.01% to 12.75% [8-11]. Owing to the limited population of patients and lack of extensive longitudinal follow-up, it is difficult to estimate the frequency, predisposing factors, and prognostic implications of late recurrence of melanoma. Among all the recurrent locations, very few publications have described late cerebral metastasis (late recurrences involving the brain) [12, 13]. In a cohort of 1372 patients with stage I-II melanoma who were disease-free 10 years after diagnosis, only 10 patients (7.3%) were found to have distant metastases involving the brain [8]. In another collection of 1881 patients with stage I or II melanoma, only 1 patient (0.5%) was identified as having late cerebral metastasis [11].

Late cerebral metastasis that occurs more than 10 years after the diagnosis of cutaneous melanoma is very rare. This report is of a 41-year-old woman with a diagnosis of late cerebral metastasis 16 years after an initial diagnosis of cutaneous melanoma.

Case Report

A 41-year-old woman was sent to the Emergency Department (ED) because of progressive disturbance of consciousness for 6 weeks and sudden coma for 6 h. The patient was diagnosed with malignant melanoma 16 years before from the biopsy of a dish-pattern tumor on the back, for which she received chemotherapy for 5 times (therapeutic regimen and medications were not available). She had not had any other diagnoses of skin melanoma in the past 16 years. Five years before presentation, the patient had persistent dry cough and discomfort in the chest; a suspected metastatic mass was then detected in the right lung by computed tomography (CT) scan. The patient received chemotherapy (paclitaxel, caspofungin, and sorafenib) but failed treatment after 3 times, presenting with weakness, loss of appetite, and nausea. Then, 6 weeks ago, the patient had vomiting after eating accompanied by drowsiness, which was relieved with mannitol. After a sudden coma as well as incontinence for 6 h, she was sent to the ED with suspicion of cerebral apoplexy.

On physical examination, the patient was in a deep coma, with a Glasgow Coma Scale score of 5 points. A soft mass measuring 2×2 cm in diameter was palpated in the right frontal scalp. The right pupil dilated to 4 mm without any direct and indirect light reflection. The whole body was scattered with subcutaneous nodules. There was a positive Babinski sign in the left limb, but no movement in the right limb.

Head CT scans revealed multiple intracranial masses located at the right frontal and temporal lobes (**Figure 1A, 1B**). With severe brain compression, tumoral hemorrhage shifted the midline over 1 cm, resulting in acute cerebral herniation. Meanwhile, a scalp tumor was also found in the frontal region (**Figure 1C**). A lung CT scan indicated a foliated mass measuring 3.7×2.6×3.3 cm in the lower lobe of the right lung (**Figure 1D**). Compared with the CT scan taken 5 years earlier (**Figure 1E**), small nodules in the upper lobe of left lung had disappeared, but new round nodules were found in both lungs this time. In addition, a metastasis of the 12th vertebra was suspected according to the low density detected in the CT scan (**Figure 1F**).

The patient underwent tumor resection surgery through a trans-frontal approach. After the skull flap was removed, the dura mater was found to be invaded extensively by the tumor (**Figure 2A**). The extradural part grew infiltratively through the skull to the subcutaneous tissue. Small melanic dots were disseminated in a widespread fashion in adjacent temporal bone, temporalis, and hypodermis (**Figure 2A**). The intradural part was about 4.3×4.1×5.2 cm in size with abundant blood supply. Total removal of the tumor, hematoma, and dura was performed. The boundary between the tumor and surrounding brain tissue was clear. On the second day after surgery, the patient developed recurrent bleeding in the right frontal lobe, which led to deteriorated consciousness again (**Figure 2B**). Intracranial hematoma evacuation and craniectomy were performed, but the patient's consciousness did not improve after surgery. Palliative

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

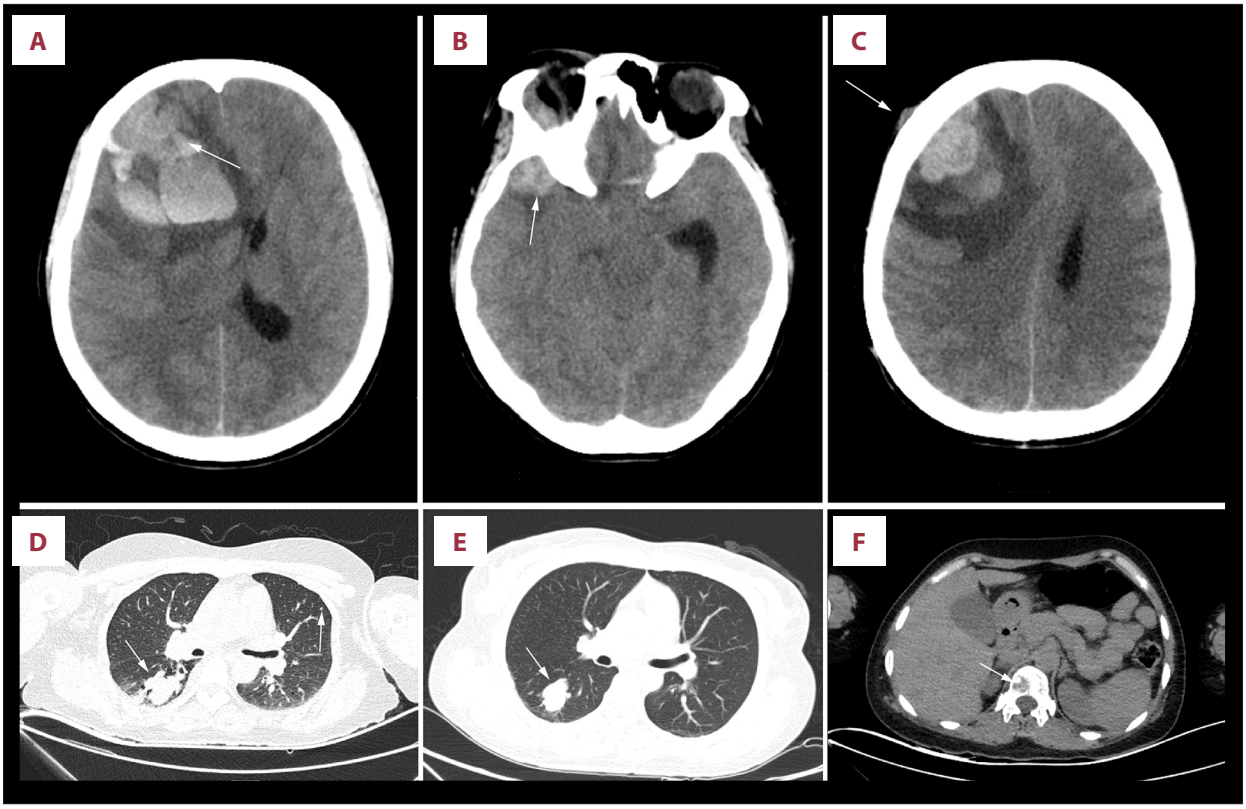

Figure 1. Preoperative head and lung computed tomography (CT) showed late cerebral metastasis of melanoma. (**A**) Right frontal melanoma brain metastasis with intracranial hemorrhage compressing the brain severely to the contralateral hemisphere (white arrow indicates the tumor). (**B**) Another metastasis located at the right temporal lobe (white arrow indicates the tumor). (**C**) Cutaneous tumor at right frontal scalp (white arrow indicates the tumor). (**D**) Foliate mass measuring 3.7×2.6×3.3 cm in the lower lobe of right lung. Small round nodules scattered in both lungs (see white arrows). (**E**) Lung CT scan taken 5 years earlier indicated an isolated mass in the lower lobe of right lung (see white arrow). (**F**) Suspected metastasis in the 12th vertebra (see white arrow).

care was provided at the request of the family for supportive treatment. Histopathology confirmed diagnosis of malignant melanoma metastasis (**Figure 2C**). The patient lived in a poor condition with drowsiness and hemiplegia of the left limb for 3 months and died 5 months after craniectomy.

Discussion

Although late recurrence of melanoma (disease-free 10 years after initial diagnosis) is rare, researchers have begun to focus on this scenario, which can require life-long follow-up. To date, there are 9 cases reported in the literature of late cerebral metastasis occurring in patients with cutaneous melanoma [12-17]. The number of reported cases of late recurrence of melanoma involving the brain has significantly decreased owing to the development of radiological techniques and updates to the melanoma management guidelines in recent years. 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 [18-23]. Possible factors associated with late recurrence of melanoma include thinner primary melanomas, non-ulceration, non-head/neck location, younger patient age, and female sex [9,11,24], but these are still debated [25].

In contrast to other late recurrent sites of melanoma, brain metastasis presents unique characteristics. Most lesions in the cerebral parenchyma are cystic, as seen in past cases [12-17]. However, the metastasis in our present case was solitary because of the involvement of the dura matter. Another interesting finding is that there were few metastases involving only brain tissue. In previous cases as well as in the current case, it was found that patients presented with accompanying metastatic lesions in the lung. It is suggested that regular radiological follow-up of the lungs can help detect early metastases to the brain [26], but a large number of cases and controlled trials are still needed to verify this hypothesis. PET-CT is recommended in the detection of cerebral metastases

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

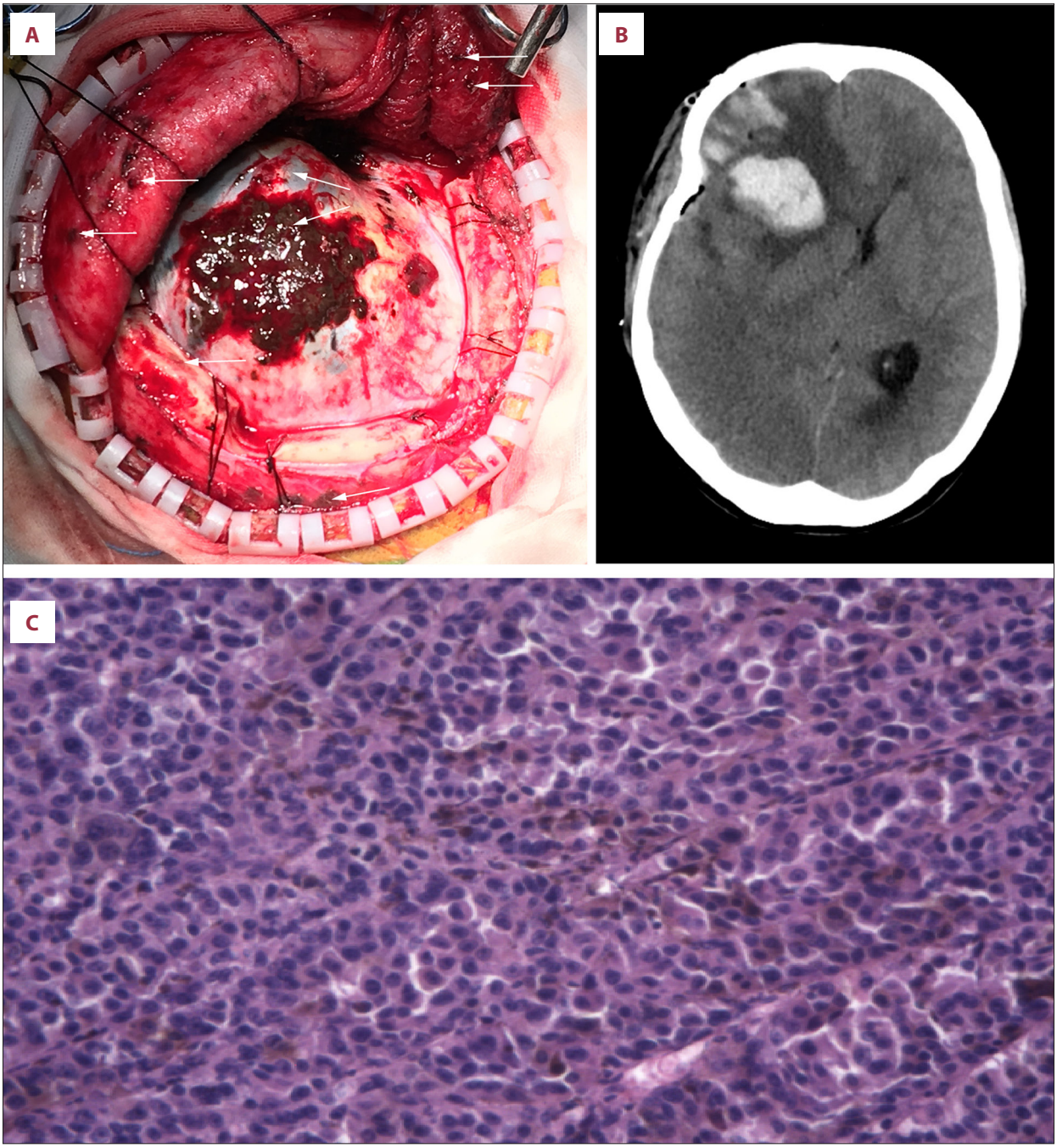

Figure 2. Late cerebral metastasis of melanoma presents widespread dissemination in dural matter and adjacent temporal bone, temporalis and hypodermis. (**A**) The extradural part grew infiltratively through the skull to subcutaneous tissue. Small melanic dots were disseminated in adjacent temporal bone, 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; nuclear division could be observed easily.

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

of melanoma and is helpful in diagnosis and staging of melanoma recurrence [27], particularly if surgery is being considered. Intracranial hemorrhage is a common complication of melanoma brain metastases and a major factor resulting in poor prognosis [28]. Intracranial hemorrhage should be noted in patients with neurological deficits.

The prognosis for patients presenting with distant recurrence of melanoma is poor, with a 5-year survival of 6.5% to 11% [29]. The median survival in patients with brain metastases is less than 1 year despite treatment [30]. The treatment has not been standardized till now, and surgical resection is the best treatment when the lesion is unique, accessible, and circumscribed. Immediate evacuation of the intracranial hematoma can be a life-saving procedure. Some surgeons have suggested that resections should be performed even in the progressive cases in which the metastases cause severe neurological symptoms [31]. Radiation therapy and stereotactic radiosurgery are feasible for patients in which the lesion is inaccessible or widespread [32]. Life expectancy does not exceed a few months owing to the progression of the systemic diseases. Novel targeted therapy (BRAF inhibitors) [33] and immunotherapy (anti-CTLA antibody) [34] have also shown favorable responses on survival and prognosis.

Conclusions

This report has presented a rare occurrence of a late cerebral metastasis at 16 years after the initial diagnosis of a primary cutaneous melanoma. More recent primary melanoma of the skin was not identified, which supports the need for long-term follow-up of patients with a history of primary cutaneous melanoma.

Department and Institution Where Work Was Done

Department of Neurosurgery, Shengjing Hospital of China Medical University, Shenyang, China.

Acknowledgements

We would like to thank Editage (www.editage.com) for providing their English language editing service.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

References:

1. Eroglu Z, Holmen SL, Chen Q, et al. Melanoma central nervous system metastases: An update to approaches, challenges, and opportunities. Pigment Cell Melanoma Res. 2019;32:458-69
2. Berghoff AS, Preusser M. Targeted therapies for melanoma brain metastases. Curr Treat Options Neurol. 2017;19:13
3. Glitza Oliva I, Tawbi H, Davies MA. Melanoma brain metastases: Current areas of investigation and future directions. Cancer J. 2017;23:68-74
4. Margolin K, Ernstoff MS, Hamid O, et al. Ipilimumab in patients with melanoma and brain metastases: an open-label, phase 2 trial. Lancet Oncol. 2012;13:459-65
5. Westphal D, Glitza Oliva IC, Niessner H. Molecular insights into melanoma brain metastases. Cancer. 2017;123:2163-75
6. Swetter SM, Thompson JA, Albertini MR, et al. NCCN Guidelines(R) Insights: Melanoma: cutaneous, Version 2.2021. J Natl Compr Canc Netw. 2021;19:364-76
7. Swetter SM, Tsao H, Bichakjian CK, et al. Guidelines of care for the management of primary cutaneous melanoma. J Am Acad Dermatol. 2019;80:208-50
8. Osella-Abate S, Ribero S, Sanlorenzo M, et al. Risk factors related to late metastases in 1,372 melanoma patients disease free more than 10 years. Int J Cancer. 2015;136:2453-57
9. Faries MB, Steen S, Ye X, Sim M, Morton DL. Late recurrence in melanoma: Clinical implications of lost dormancy. J Am Coll Surg. 2013;217:27-34; discussion 34-36
10. Brauer JA, Wriston CC, Troxel AB, et al. Characteristics associated with early and late melanoma metastases. Cancer. 2010;116:415-23
11. Hansel G, Schonlebe J, Haroske G, Wollina U. Late recurrence (10 years or more) of malignant melanoma in south-east Germany (Saxony). A single-centre analysis of 1881 patients with a follow-up of 10 years or more. J Eur Acad Dermatol Venereol. 2010;24:833-36
12. Mansour D, Kejariwal D. It is never too late: ultra-late recurrence of melanoma with distant metastases. BMJ Case Rep. 2012;2012:bcr0120125474
13. Puca A, Vari R, Carbone A. Very late cerebral metastasis from malignant melanoma. Br J Neurosurg. 1998;12:63-65
14. Brega K, Robinson WA, Winston K, Wittenberg W. Surgical treatment of brain metastases in malignant melanoma. Cancer. 1990;66:2105-10
15. Crowley NJ, Seigler HF. Late recurrence of malignant melanoma. Analysis of 168 patients. Ann Surg. 1990;212:173-77
16. Miller TR, Pack GT. The familial aspect of malignant melanoma. Arch Dermatol. 1962;86:35-39
17. Gawenda M, Franzen D, Lorenzen J, Muller U. [Brain and gallbladder metastases 10 years after local excision of a cutaneous malignant melanoma]. Dtsch Med Wochenschr. 1995;120:289-92 [in German]
18. Balch CM, Gershenwald JE, Soong SJ, et al. Final version of 2009 AJCC melanoma staging and classification. J Clin Oncol. 2009;27:6199-206
19. Reintgen DS, Cox C, Slingluff CL Jr., Seigler HF. Recurrent malignant melanoma: The identification of prognostic factors to predict survival. Ann Plast Surg. 1992;28:45-49
20. Leiter U, Meier F, Schittek B, Garbe C. The natural course of cutaneous melanoma. J Surg Oncol. 2004;86:172-78
21. Balch CM. Cutaneous melanoma: Prognosis and treatment results worldwide. Semin Surg Oncol. 1992;8:400-14
22. Garbe C, Buttner P, Bertz J, et al. Primary cutaneous melanoma. Prognostic classification of anatomic location. Cancer. 1995;75:2492-98
23. Meier F, Will S, Ellwanger U, et al. Metastatic pathways and time courses in the orderly progression of cutaneous melanoma. Br J Dermatol. 2002;147:62-70
24. Levy E, Silverman MK, Vossaert KA, et al. Late recurrence of malignant melanoma: A report of five cases, a review of the literature and a study of associated factors. Melanoma Res. 1991;1:63-67
25. Sarac E, Wilhelmi J, Thomas I, et al. Late recurrence of melanoma after 10 years – is the course of the disease different from early recurrences? J Eur Acad Dermatol Venereol. 2020;34:977-83
26. Singh C, Raypattanaik NM, Sharma I, Kaman L. Primary retroperitoneal teratoma in a young male: A case report. Cureus. 2021;13:e15376
27. Deroose CM, De A, Loening AM, et al. Multimodality imaging of tumor xenografts and metastases in mice with combined small-animal PET, small-animal CT, and bioluminescence imaging. J Nucl Med. 2007;48:295-303

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

28. Schrag M, Kirshner H. Management of intracerebral hemorrhage: JACC Focus Seminar. J Am Coll Cardiol. 2020;75:1819-31
29. Hafstrom L, Jonsson PE, Stromblad LG. Intracranial metastases of malignant melanoma treated by surgery. Cancer. 1980;46:2088-90
30. Sloan AE, Nock CJ, Einstein DB. Diagnosis and treatment of melanoma brain metastasis: A literature review. Cancer Control. 2009;16:248-55
31. Tonomura S, Kitaichi T, Onishi R, et al. A dural metastatic small cell carcinoma of the gallbladder as the first manifestation: A case report. World J Surg Oncol. 2018;16:57
32. Redmond AJ, Diluna ML, Hebert R, et al. Gamma Knife surgery for the treatment of melanoma metastases: The effect of intratumoral hemorrhage on survival. J Neurosurg. 2008;109(Suppl.):99-105
33. Chapman PB, Hauschild A, Robert C, et al. Improved survival with vemurafenib in melanoma with BRAF V600E mutation. N Engl J Med. 2011;364:2507-16
34. Nardin C, Mateus C, Texier M, et al. Tolerance and outcomes of stereotactic radiosurgery combined with anti-programmed cell death-1 (pembrolizumab) for melanoma brain metastases. Melanoma Res. 2018;28:111-19

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]