Radiology Case Reports 16 (2021) 119–122

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journal homepage: www.elsevier.com/locate/radcr

Case Report

Metastatic melanoma of unknown origin mimicking neurofibromatosis ☆

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ARTICLE INFO

Article history:
Received 26 June 2020
Revised 15 August 2020
Accepted 16 August 2020

Keywords:
Melanoma of unknown primary
Metastatic melanoma
CNS metastasis
Schwannoma
Neurofibromatosis

ABSTRACT

We present an unusual case of metastatic melanoma in a young patient with imaging appearance resembling neurofibromatosis. A 36-year-old-man with a history of cervical radiculopathy presented with cauda equina syndrome. An MRI was performed for further evaluation demonstrating multiple intradural, extramedullary enhancing lesions in the thoracic and lumbar spine, as well as extra-axial enhancing lesions with involvement of the lateral ventricles and posterior fossa. Bilateral pulmonary masses were found on chest CT. Lung lesions were biopsied and positive for metastatic melanoma. Melanoma is the third most common primary neoplasm to produce brain metastasis and should be considered on the differential as a cause of newly detected intracranial and intraspinal masses in young patients.

Introduction

Metastatic melanoma of unknown primary (MUP) is the presence of metastatic melanoma without evidence of a primary skin lesion. At least 8% of patients who present with melanoma metastases are diagnosed with MUP. Often times melanoma metastasis to the central nervous system (CNS) presents with intracerebral lesions that are hyperintense in T1 weighted MRI due to variable content of melanin. In this case report we present the unusual MRI appearance of pathology proven melanoma metastasis, and a review of MUP with its prognostic factors.

Case report

A 36-year-old male patient with a medical history of cervical radiculopathy presented to the emergency department complaining of lower back pain, saddle anesthesia, and incontinence for 2 months. The patient's family history was positive

☆ Competing interests: The authors have declared that no competing interests exist.

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https://doi.org/10.1016/j.radcr.2020.08.034

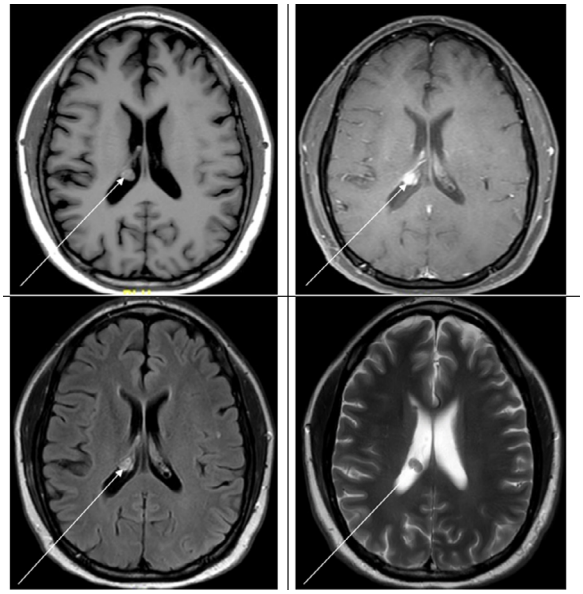

Fig. 1 – Axial T1 MRI of the brain without (A) and with (B) contrast, FLAIR (C) and T2 (D) weighted image demonstrate a focal lesion in the right lateral ventricle with isointense signal intensity to grey matter, and diffuse enhancement (white arrows).

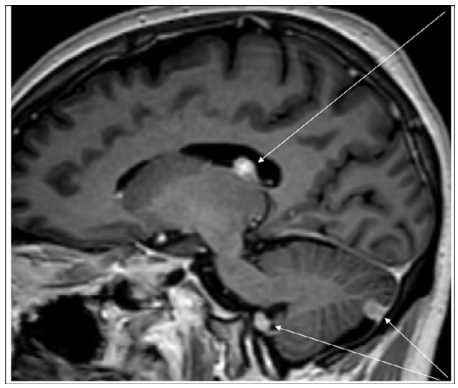

Fig. 2 – Sagittal T1 MRI of the brain with contrast demonstrates the focal lesion in the right lateral ventricle and 2 small focal extra-axial lesions in the posterior fossa, with diffuse enhancement (white arrows), with the posterior lesion in the posterior fossa associated with a dural tail.

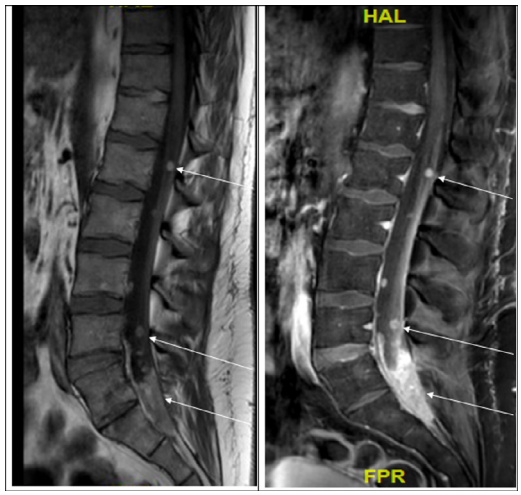

Fig. 3 – Sagittal T1 MRI without (A) and fat saturated post contrast (B) demonstrate multiple small focal intradural extramedullary enhancing lesions with involvement of the cauda equina and an enhancing lesion in the sacral spinal canal (arrows).

for multiple cancers, but no specific information was available. Vital signs at triage were notable for increased blood pressure (170/115 mm Hg) secondary to pain. Patient was awake and alert, with no cranial nerve deficits. Paresthesia in the left ulnar distribution and tenderness to palpation of the lumbar spine were noted on exam. An MRI of the head was performed, revealing extra-axial enhancing lesions with involvement of the lateral ventricles and posterior fossa, with 1 lesion demonstrating a dural tail reminiscent of meningioma (Figs. 1 and 2). MR imaging of the spine demonstrated multiple intradural, extramedullary enhancing lesions in the thoracic and lumbar spine, suggestive of multiple schwannomas (Fig. 3). Initial tumor biomarkers of carcinoembryonic antigen (CEA), human chorionic gonadotropin (beta-hCG), alpha fetoprotein (AFP), and beta-2 microglobulin were negative. A biopsy was performed, with pathology results consistent with metastatic melanoma (Fig. 4). Upon additional review of patient's history, he denied ever having had a concerning skin lesion and a primary melanoma lesion was not found on clinical examination. The patient was referred to radiation oncology for emergent palliative cranial spinal radiation and genetic studies were sent out for possible systemic treatment options. Neurosurgery evaluation did not indicate a surgical intervention for his neurological symptoms at that time. Medical treatment was given using corticosteroids.

Discussion

MUP is the presence of metastatic melanoma without evidence of a primary skin lesion. The incidence of MUP is 2-3% of all diagnosed melanomas, and typically presents in the fourth to fifth decades of life [1]. 40% to 50% of patients diagnosed with stage IV metastatic melanoma have brain metastases [2]. At least 8% of patients who present with distant melanoma metastases are diagnosed with MUP [3]. Risk factors for developing CNS metastasis include presence of visceral tumor and lung metastasis, MUP, depth of tumor invasion, and male gender [4]. Good prognostic indicators include single brain lesion, good performance status, absence of neurologic symptoms, younger age, and longer disease-free interval [4]. The incidence of stage IV MUP has increased over the last thirty years, especially among patients younger than 30 years old [5]. As the incidence of MUP is on the rise, it is

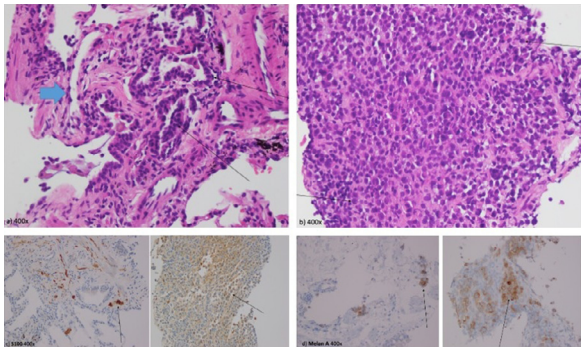

Fig. 4 – Histopathology shows hematoxylin and eosin stained epithelioid cells with rounded and hyperchromatic nuclei (A) causing thickening and a desmoplastic response in the alveolar lung wall (black arrow) with small benign epithelial cells lining the alveoli (blue arrow). High power view (B) shows the diffuse, solid malignant growth with the cells characterized by high nuclear/cytoplasmic ratio, hyperchromasia with eosinophilic cytoplasm and focal prominent nucleoli (arrows). Immunohistochemical stain is positive for S100 in malignant cells (C) as demonstrated by brown cytoplasmic and nuclear staining (arrows). MelanA, which is a specific marker for metastatic melanoma (D), is positive as demonstrated by brown cytoplasmic staining (arrows). Staining in any percentage of tumor cells is interpreted as positive. (Color version of figure is available online.)

important not to discount this disease in the younger adult patient with multiple lesion imaging.

Metastatic melanoma requires a multidisciplinary approach for management with consideration of quality of life. For patients with symptomatic brain metastasis, steroids are often used to decrease cerebral swelling and to improve symptoms. Historically, stereotactic radiosurgery and whole-brain radiotherapy, with or without chemotherapy, is used to control metastases [6]. More recently, systemic treatment such as ipilimumab, an anti-CTLA-4 monoclonal antibody, and vemurafenib, an inhibitor of $BRAF^{V600E}$ positive melanoma, have provided an alternative for patients [6]. Patients with brain metastases remain at risk of CNS progression even after treatment, and should have MRI imaging surveillance every 3 months [7].

Prior to biopsy, our radiologists and neurologists also considered a diagnosis of neurofibromatosis type 2 given our patient's age, imaging appearance and reported negative personal history of cancer. The most commonly encountered enhancing intradural-extramedullary spinal lesions are schwannomas and the presence of multiple schwannomas is suggestive of neurofibromatosis type 2 [8], with the differential including meningioma. Their imaging appearance on non-contrast CT and T1 weighted MR images is similar to attenuation and signal intensity of spinal cord. Extradural spinal cord compression by metastases is a far more common presentation, with up to 20% of new epidural spinal cord compression by neoplasm as the initial presentation of metastatic malignancy [9]. Melanocytic tumors are typically visualized by hyperintensity on T1 weighted and T2 weighted signal intensity loss [10] with 7% of melanoma lesions detected principally on T2 weighted sequences [11]. Brain metastases of patients containing a significant amount of melanin are more likely to demonstrate increased T1 signal intensity than those with amelanotic or lightly melanotic tumors [11]. In the presented case, the extra-axial lesions are isointense to minimally increased in signal intensity to grey matter on T1 weighted sequences which can be seen with the presence of melanin or metabolic products, isointense signal intensity on T2 weighted sequences, and avid diffuse enhancement on postcontrast images which can be seen with schwannoma or metastatic disease. Metastatic disease to the choroid plexus and extra-axial location as seen in our patient, is an uncommon location. Despite its relative rarity as a systemic neoplasm, melanoma is the third most common primary to produce brain metastasis and thus must be considered as the cause of newly detected intracranial masses in patients with no known primary [12], in either intra-axial or extra-axial location.

Consent

We are using entirely anonymized images from pathology slides, CT scans, and MRI. These do not contain any identifying marks and are not accompanied by text that might identify the individual concerned.

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