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An Unusual Case of Malignant Melanoma with Metastasis to the Placenta During Pregnancy

Kenny Garcia-Ramiu[1], Ibrahim Mohsin[1], Alexandra Ikeguchi[2], Brian Newberry[1]

[1] Internal Medicine Residency Program, Norton Community Hospital, Norton, Virginia, USA

[2] Department of Hematology/Oncology, Oklahoma University Stephenson Cancer Center, Oklahoma City, Oklahoma, USA

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ABSTRACT

Introduction: We describe an unusual case of metastatic melanoma of the brain with an unknown primary site during pregnancy.
Case Description: A 35-year-old woman in the third trimester of pregnancy presented with ataxia, nausea, vomiting, headaches and diplopia. CT of the brain revealed a hyper-attenuating 2.1 cm mass in the fourth ventricle with mild obstructive hydrocephalus. A healthy newborn was delivered by urgent caesarean section. Craniotomy and resection of the brain lesion confirmed melanoma. Pathology of the placenta reported a 'focal nest of melanocytes identified in intervillous space'.
Discussion: Brain and maternal placenta pathology findings were consistent with melanoma, making this case relevant because of the possibility of metastatic melanoma in a fetus.
Conclusion: Epidemiological data on congenital and infantile melanoma are scarce. Also, there is no database for long-term follow-up of children born to pregnant mothers with metastatic melanoma. Delayed presentation of melanoma in the child cannot be ruled out.

LEARNING POINTS

- Melanoma brain metastasis is an uncommon initial presentation during pregnancy.
- During pregnancy, vague symptoms such as headaches and nausea can easily be attributed to the pregnancy itself rather than more serious conditions like cancer.
- Metastatic melanoma diagnosed during pregnancy with disease in the placenta is a rare occurrence and should trigger close follow-up of the neonate secondary to concerns of transplacental metastasis.

KEYWORDS

Melanoma, metastasis, placenta

INTRODUCTION

After primary lung and breast cancer, melanoma is the third most frequent type of cancer associated with brain metastasis [1]. Melanoma brain metastasis is considered an aggressive disease with less than 10% of cases originating from an unknown primary tumour location. The primary site for melanoma is usually the skin, but in rare situations melanoma will initially present in a metastatic location, for example the brain, with an unknown primary or in the absence of a previous melanoma diagnosis [2]. Here, we describe an unusual occurrence of metastatic melanoma of the brain with an unknown primary site during pregnancy. Brain and maternal placenta pathology findings were consistent with melanoma, making this case relevant because of the possibility of an initial presentation of metastatic melanoma in a fetus.

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CASE DESCRIPTION

A 35-year-old woman in the third trimester of pregnancy presented to the emergency department with complaints of ataxia for several weeks and severe nausea and vomiting during the previous week. She also reported dizziness, headaches and diplopia. The patient had no pertinent history except the use of tanning beds on a routine basis in her teens and twenties. She denied alcohol, tobacco or illicit drug use. There was a family history of 'skin cancers' in her father and sister. She reported previous skin lesions that were treated with cryotherapy, but no skin cancer diagnosis in the past. The full body skin examination was significant for macules with variations in colour scattered all over her body. She was described as a 'Fitzpatrick type 2' phototype with fair skin and blue eyes. Fitzpatrick skin type (or phototype) is used to classify skin according to its reaction to exposure to sunlight. The patient was in the category of people who sunburn easily and tan poorly [3]. Initial work-up with CT of the brain revealed a 'hyper attenuating mass along the floor of the fourth ventricle measuring 2.1 cm with mild obstructive hydrocephalus'. The characteristics of the mass were suggestive of medulloblastoma. Imaging of the chest, abdomen and pelvis was completed with contrast but no further sites of disease were observed. Neurosurgery was consulted and reported that this primary brain tumour would likely be slow growing and would not require immediate intervention unless the symptoms of hydrocephalus (nausea and vomiting) worsened. Therefore, expectant management was appropriate at that time. Corticosteroids were continued for antenatal preparation and maturation of the fetal lungs. Magnetic resonance imaging of the brain revealed 'T1 hyperintensity of the lesion, somewhat atypical for medulloblastoma but can be seen with hemorrhagic or melanotic metastasis'. Given these results, the possibility of a slow growing/benign lesion was less likely due to the oedema surrounding the lesion. A caesarean delivery was planned and a healthy newborn was delivered.

The placenta was sent for cytology and analysis. Pathology of the placenta reported a 'focal nest of melanocytes identified in intervillous space (mother side), confirmed by sox10 immunostaining. No definitive intravillous (fetal side) lesions are identified'. Within 2 days of the caesarean section, a sub-occipital craniotomy and resection of the posterior fossa tumour was carried out. Pathology of the tumour was consistent with metastatic melanoma with a BRAF V600 mutation. Imagining with PET/CT revealed no other sites of cancer. Further management with Gamma Knife radiation was administered for consolidation and was followed by combination immunotherapy with ipilimumab and nivolumab. Regular follow-up is being carried out to track this patient for disease outcome and relapse-free survival data.

DISCUSSION

Malignant melanoma often affects women of childbearing age. Additionally, cases of melanoma have continued to increase in this patient population as women are waiting longer to become pregnant [4]. The incidence in pregnancy has been estimated to range from 0.14 to 2.8 per 1,000 live births and melanoma accounts for about 8% of all tumours arising during pregnancy. A study from Sweden found that their national registry reported that melanoma was the most common cancer in women who were or had been pregnant within the last 2 years [5]. In our case, cytology of the maternal side of the placenta was consistent with sox100 positive melanoma. The pathophysiology of transplacental spread of melanoma is not well understood but may be influenced by the high vascularity of the placenta, placental production of angiogenic and growth factors, and impaired fetal immune response [6]. A review of the literature found that the majority of cases are due to haematogenous malignant spread. One study reported the most common culprit was melanoma metastasis: 31% of 87 cases of placental or fetal metastasis were attributed to melanoma. Furthermore, 22% of the cases of melanoma placental metastasis affected the fetus, with five out of the six fetuses dying from this disease [7].

The newborn in our case was considered to be at high risk due to the placental pathology findings. However, initial pathology results showed no melanoma involvement in the fetus side of the placenta. It is understood that maternal leukaemia/melanoma cells have a higher rate of infiltration of the placenta than the fetus. This phenomenon is presumed to be secondary to migratory cancer cells including an age-related deletion mutant with decreased stem cell function [8].

Given the rarity of congenital and infantile melanoma, specific epidemiologic data are limited. In addition, there is no database for the long-term follow-up of children born to pregnant mothers with metastatic melanoma. Also, the possibility of delayed presentation of melanoma cannot be ruled out, but currently there are no established protocols for genetic testing and imaging. Close monitoring and clinical evaluation during the first few years of life is recommended. The newborn described in this report will be closely monitored for any signs and symptoms of respiratory distress, masses or lumps, and jaundice, with a low threshold for imaging. Routine skin examinations will also be conducted by a paediatrician. It would be of special interest to follow the newborn for the possibility of congenital or infantile melanoma. The child is living and well the time of the writing.

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