

# Maternal melanoma with placental metastasis

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## ABSTRACT

**A 40-year-old woman, a grand multipara with uncertain gestation, presented with severe, prolonged diarrhoea. She was previously diagnosed to have melanoma. Examination revealed gross ascites with hepatosplenomegaly and uterus corresponding to 29 weeks gestation. An emergency caesarean section confirmed widespread metastases to the ovaries, mesentery and placenta. A viable male foetus was delivered with features of intrauterine growth restriction. The baby survived, but the mother died a week later. This case highlights the importance of thoroughly assessing placentas and babies of patients with melanoma for metastases.**

**Keywords: maternal melanoma, maternal mortality, melanoma, placental metastasis**

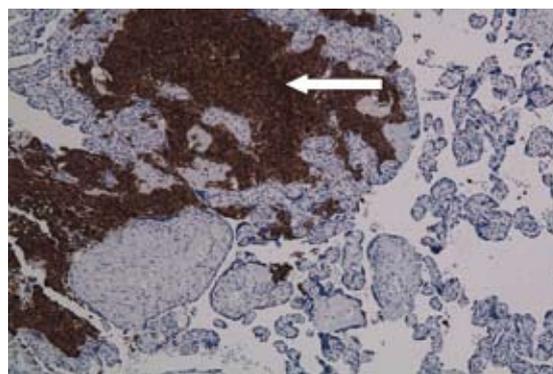
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## INTRODUCTION

Malignancy is rare in pregnancy, with an observed occurrence of one per 1,000 births.<sup>(1)</sup> Breast cancer is the commonest cause, whereas melanoma reportedly constitutes approximately 8% of all malignancies in pregnancy.<sup>(1)</sup> We present a patient with melanoma with developed metastasis to the placenta, causing intrauterine foetal growth restriction. The effect of pregnancy on melanoma is reviewed.

## CASE REPORT

A 40-year-old woman (G7P6) of uncertain gestation presented with a cauliflower-like lesion (4 cm × 4 cm × 1.5 cm) on her left buttock 18 months ago. Diagnosis of melanoma was made by biopsy. The histological examination showed thick sheets of polygonal malignant melanocytes with vesicular nuclei and prominent nucleoli. The tumour cells were seen in the epidermis and were deep in the dermis, but not involving the lines of resection. She declined further treatment and defaulted follow-up. Upon admission to the hospital, following a fortnight of diarrhoea, she was moribund with dehydration and compensated metabolic acidosis. Examination revealed gross hepatosplenomegaly with ascites. Ultrasonography (US) revealed a foetus corresponding to 29 weeks gestation



**Fig. 1** Photomicrograph shows immature villi corresponding to gestational age. Nests of malignant melanocytes are seen in the intervillous spaces (arrow). Tumour cells stained positive for HMB-45 (Immunoperoxidase × 100)

with severe oligohydramnios. Cardiotocography showed recurrent late decelerations, and an emergency caesarean section was carried out to salvage the foetus.

Intraoperatively, the gross hepatosplenomegaly and ascites were confirmed. There were metastases on the mesentery, ovaries and placenta; biopsies were taken from these sites. Postoperatively, the patient's condition deteriorated. The patient died a week postpartum. A male foetus was born weighing 1:405 kg with evidence of intrauterine growth restriction. He recovered well and was declared free of the metastatic tumour after 18 months of follow-up. Histological examination of the biopsies revealed nests of malignant melanocytes exhibiting round to oval nuclei, with finely granular cytoplasm in the ovaries, mesentery and placental villi. There was no foetal vessel infiltration. Immunohistochemistry staining with HMB-45 was positive.

## DISCUSSION

There is much misunderstanding regarding the survival of the patients with melanoma. The risk of death due to melanoma was not shown to be significantly higher in pregnant women when compared to non-pregnant women.<sup>(2)</sup> Furthermore, there was no evidence to support that pregnancy worsens a preexisting melanoma or reactivates a previous melanoma. However, the thickness of the tumour was significantly higher in the third trimester as compared to an earlier trimester. This could be due to the tendency of the naevi to darken and enlarge

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during pregnancy, thus delaying the possible diagnosis of melanoma in changing naevus. However, several studies do not support this theory of such changes in the naevi.<sup>(3-5)</sup> Axial tumours tend to carry a poorer prognosis, and are associated with a higher risk of death, as has been demonstrated by this patient, who had a primary tumour in the buttock.<sup>(2)</sup> Women are known to have a higher incidence of melanoma compared to men, but the survival rate in women is better.<sup>(6,7)</sup> In view of this, termination of pregnancy is not justified for cases of malignant melanoma during pregnancy, as it would not improve the maternal outcome.<sup>(2)</sup>

Placental metastasis from maternal cancers is very rare. There have been 87 reported cases of placental and/or foetal metastasis since 1866.<sup>(8)</sup> The majority of these cases were secondary to melanoma (31%), although it is not the commonest malignancy in pregnancy. It is highly possible that higher production of many growth factors during pregnancy, and the increased vascularity of a placenta, promotes metastasis. A literature review by Altman et al demonstrated that all the patients with placental metastasis also had metastasis to other viscera; this was suggestive of the advanced stage of the disease (stage IV).<sup>(1)</sup> Maternal outcome at such an advanced stage of the disease is fatal, with no reported case of maternal survival so far.<sup>(1,8)</sup>

Prematurity is a common complication of infants born with placental disease.<sup>(8)</sup> The premature growth-restricted foetus in this case did not demonstrate evidence of metastasis, despite proximity to the placental metastasis. Although the majority of placental metastasis is melanoma-related, foetal metastasis is very uncommon. Alexander et al suggested that neither tumour burden nor the extent of placental invasion correlates with foetal metastasis.<sup>(8)</sup> Foetal metastasis may occur before the immune system is well-developed, whereby the foetus develops tolerance towards the tumour and is subsequently unable to eliminate it. Other unfavourable factors postulated to affect foetal outcome, such as primiparity, maternal age less than 30 years, primary metastatic site at the leg, onset of disease more than three years prior to current pregnancy, lymph node involvement prior to pregnancy, visceral or distant metastases in the third trimester, and birth at more than 36 weeks gestation,<sup>(9)</sup> were not supported by a recent review by Alexander et al.<sup>(8)</sup>

Foetal metastasis occurs more commonly in male foetuses compared with their female counterparts.<sup>(1,8,9)</sup> Male foetuses are also more likely to succumb to the

disease once foetal metastasis occurs.<sup>(8,9)</sup> It is possible that male foetuses are more immunotolerant than female foetuses. This is further supported by a report of spontaneous regression of disease in an affected female foetus with a biopsy-proven metastatic melanoma.<sup>(8)</sup> The common sites of foetal metastasis are the skin and liver.<sup>(1,8)</sup> However, the majority of affected babies do not survive despite past attempts of experimental immunotherapy.<sup>(8)</sup>

Pregnancy has no proven adverse effect on malignant melanoma, and vice-versa. Termination of pregnancy is not recommended in order to improve outcome. Physicians should be more vigilant of any changes in the naevi of pregnant women. All pregnant patients with malignant melanoma should have their placentas thoroughly examined, both grossly and histologically. The paediatrician should be alerted when there is evidence of placental metastasis, so that the child could be followed-up for 24 months, to exclude the possibility of foetal metastasis. Several recommendations have been suggested for foetal surveillance; these include inspection of the skin, examination and US scan of the abdomen,<sup>(1)</sup> baseline chest radiograph and liver enzyme analysis, including lactate dehydrogenase.<sup>(8)</sup> At the moment, there is no recommendation for adjuvant therapy for infants who are at risk of metastasis.<sup>(8)</sup>

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