Development of melanoma throughout two close pregnancies

Case report

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Summary: Primary melanoma is the most malignant and the least frequent of all cutaneous tumors. Its incidence in pregnancy varies from 0.1 to 2.8‰. Up to today, impact of pregnancy on melanoma's course is still a much debated question in the literature. Some earlier reports suggested a particularly serious prognosis for melanoma associated with pregnancy, while more recent studies show that pregnancy may influence relapses without significantly altering survival.

This paper reports the case of a woman affected by melanoma, whose clinical conditions became more and more serious during her second pregnancy and the following puerperal period. The progressive impairment of her clinical condition has suggested a correlation between the two close pregnancies and the unfavourable course of her disease.

Key words: Melanoma; Pregnancy; Newborn.

INTRODUCTION

Primary melanoma is the most malignant and the least frequent of all cutaneous tumors (3%). Its incidence is 4 cases/100,000 people every year. The American Cancer Society in 1990 estimated 12,800 cases of malignant melanoma (MM) developed in the US in female patients: of these, 25% (3,100) died ([15, 21]). In the same year mortality due to all the other cutaneous tumors reached 1,500 cases, this means that more than 2/3 of patients who die of cutaneous cancers are affected by malignant melanoma.

Thirty to 35% of female patients are in the reproductive age, so that melanoma's incidence in pregnancy ranges between 0.1 and 2.8‰ ([1, 16, 21]).

Melanoma seldom arises on covered zones. It more frequently grows on lower rather than upper extremities. Although the mechanism inducing melanocytes malignant transformation is still unknown both in normal skin and in precancerous lesions (neoplastic nevus, xeroderma pigmentosum), almost certainly repeated trau-

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mas, ionizing and actinic radiations play a major epidemiologic role ([9, 10]).

Melanoma of the skin and mucous membranes arises at the interface between the epidermis and dermis.

A possible hereditary disposition linked to an autosomic gene with incomplete penetrance has been recently hypothesized ([8, 17, 19]).

Some reports in the fifties and sixties revealed a particularly aggressive prognosis of MM in pregnancy ([6, 11]).

CASE REPORT

Case and familiar history of a female patient affected by malignant melanoma who came under our observation in January 1993 was analysed. The woman, D.G., 37 years of age has been a carrier of a cutaneous proliferous neoplasia on the right forearm vola since 1988.

During a first pregnancy in 1990, and the following puerperal period, this neoplasia underwent colour and consistency changes, growth, and superficial alterations, such as exfoliation, erosions, scabs and bleeding ulcerations.

In March 1991, our patient underwent a biopsy with malignant melanoma histology diagnosis but refused any treatment. As late as January 1992, she consented to undergo emaculation, which detected a level IV, nodular melanoma, 2.24 mm thick (Table 1, 2, 3), (Fig. 1).

In April 1992 the woman began a second pregnancy, and in November of the same year she noted the appearance of an axillary fossa tumefaction homolateral to the neoplastic lesion, which, by ultrasound and clinical analysis revealed to be a malignant melanoma axillary metastasis.

In December 1992, during the 35th week of gestation, our patient underwent an axillary fossa lymphadenectomy of I and II level: histologic tests showed massive metastases in two lymph nodes and permeation of lymph spaces of several I level lymph nodes while II level lymph nodes were free from neoplasia.

In January 1993 the woman spontaneously delivered, during the 39th week of gestation, a living and viable 3,400 g male newborn who did not show either inborn nevi or other skin lesions.

Abdominal bimanual palpation did not reveal any anomalous formation; hypochondrial organs were palpable: spleen at arcus costarum and liver at 2 cm from arcus costarum. Placenta histology was free from neoplastic lesions. After a 200 g physiologic loss of weight, the newborn, who was breastfed, showed a normal ponderal increase.

Bilirubin value, for the entire hospital stay was never over 7.5 mg %. Morphologic study of pheripheral blood did not reveal any abnormal cellular element. After discharge, a three months' check-up showed normal antropometric and clinic values.

Haemochrome, reticulocytes count, erythrocyte sedimentation rate (ESR), lactic dehydrogenase

Table 1. – *Clinic-histopatologic classification (Clark, 1967).*

	5 year survival
1) Lentigo maligna melanoma	55.2%
2) Superficial spreading melanoma (SSM)	46.5%
3) Nodular Melanoma (NM)	27.3%
4) Acral Lentigenous melanoma	
5) Blue malignant nevi	

Table 2. – *M. M. prognosis correlated to level of invasion (Clark, Mc Govern, Mihm 1969).*

	5 year survival
Level 1: Confinement of the malignant melanoma cells to the epidermis	99%
Level 2: Extension of the cells into the papillary dermis	85%
Level 3: Tumor extending through the papillary dermis and reaching the reticular dermis without invading it	65%
Level 4: Tumor invading the reticular dermis	50%
Level 5: Tumor invading the subcutaneous fat	30%

Table 3. – *Classification correlating lesion thickness and survival ([3]).*

	5 year survival
1) Thickness less than 0.76 mm	99%
2) Thickness between 0.76 and 1.5 mm	95%
3) Thickness between 1.51 and 2.25 mm	85%
4) Thickness between 2.26 and 3.0 mm	75%
5) Thickness more than 3 mm	50%

(LDH) and free erythrocyte protopirphyrin (FEP) test resulted normal for the age; and a peripheral blood morphologic study did not detect abnormal circulating elements.

Melanoma cell research by GD2 and GD3 monoclonal antibodies was negative. Abdominal ultrasonography did not detect invading space formations, and showed normal hypocondrial organs.

Our patient, whose general condition became more and more serious, was subjected after delivery to chemotherapeutic cycles.

Now, after about 8 months, she has diffuse metastases.

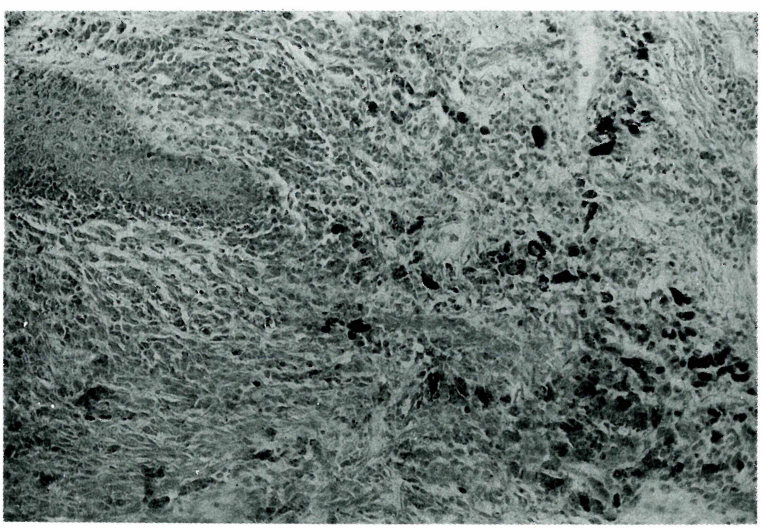

Fig. 1. — Nodular melanoma, level IV, 2.24 mm thick.

DISCUSSION

During pregnancy hyperpigmentation is especially localized at nipples, the areolae, the vulva, the linea alba, and internal thigh faces.

Hyperpigmentation is likely to express an increased melanocyte stimulating hormone (MSH) production, whose levels go up after the second month of pregnancy.

Studies on animals have shown that estrogens stimulate MSH production ([7, 14]). However, impact of pregnancy on melanoma's development is still debated in the literature.

In the 1950s, Pack and Scharnagel ([11]), after observing 32 cases of malignant melanoma associated with pregnancy, concluded that pregnancy hastened the tumor's growth and facilitated possible following metastases, so that they recommended that women already treated for melanoma did not begin new pregnancies.

On the other hand, in 1960 George *et al.* ([6]) stated that 5 and 10 year survival of their 115 patients affected by melanoma was not significantly different from that of the group control of 330 women.

More recently, Reintgen *et al.* ([12]) did a retrospective study in order to assess the importance of pregnancy on melanoma. In their study three groups of patients with Stage I disease were considered: group 1 consisted of patients diagnosed with melanoma during pregnancy: group 2 consisted of women who became pregnant within five years of their disease; group 3 was a group control. Survival was not different in the three groups. Furthermore, a significant difference among the disease-free intervals in the

course of the illness was noticed: pregnancy, though making relapses easier, did not alter global survival.

Wong *et al.* ([20]) compared clinical course of Stage I disease during pregnancy with a non-pregnant control population. Five-year survival for women diagnosed with melanoma during pregnancy and for the group control was almost the same (86% and 87% respectively).

Several authors observed that pregnancy influenced growth and expansion of melanoma ([2]). They therefore recommended abortion before neoplastic progression; with metastases abortion would be worthless.

To sum up, although earlier studies implied a dangerous effect of pregnancy on melanoma, the latest research concludes that pregnancy may support relapses, but cannot interfere with a long-distance prognosis.

Of all tumors, melanoma is the most likely to give placental and fetal metastases. There are, in fact, examples of fetal metastatic localizations involving the liver, lungs, lower extremities, and generalized metastases ([4, 5, 13]).

In the literature there are only three cases of primary congenital melanoma of the fetus. The mothers, multiparous, had previously delivered healthy infants ([18]): a careful exam of the placenta and fetus is always expedient.

According to us, in our case report the short interval between the two pregnancies has probably played a particularly unfavourable role both for prognosis and appearance of relapses.

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