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Eruptive Acral Lentigines – A New Paraneoplastic Sign?

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SUMMARY Cutaneous signs may be the first indications of an internal disease. Any definitive sign of a neoplastic disease is of special importance since early diagnosis and early treatment may make a telling difference in improving prognosis. Presented is a 68-year-old patient with advanced stage melanoma that was associated with the appearance of multiple acral lentigines. The exact time-course of onset of the lentigines in relation to the formation of the melanoma could not be established. However, from the information we could take out of our patient, it is clear that the lentigines had appeared either shortly before or after the appearance of the melanoma. In conclusion we suggest that the present case represents a new paraneoplastic sign.

KEY WORDS: eruptive acral lentigines, paraneoplastic dermatosis, paraneoplastic sign

INTRODUCTION

"What you see on the outside can provide valuable clues that all is not well on the inside" (http://www.contemporarypediatrics.com/contpeds/article/articleDetail.jsp?id=148523) (1).

We describe a patient with what we suggest might be a new paraneoplastic sign consisting of the appearance of eruptive acral lentigines.

CASE REPORT

A 68-year-old female of Ethiopian origin presented with a chronic painful ulcer of a few month duration on the sole of her right foot. She seemed to be otherwise healthy except for mild hypertension that was well controlled by Enaladex 10 mg *per* day. Physical examination revealed a 4-cm soft ulcerated tumor on the plantar side of her right foot. Additional findings were multiple asymptomatic symmetric well-demarcated brown macules, averaging 1-3 mm in diameter on the soles of both her feet (Fig. 1). According to the patient, these macules had appeared fairly suddenly about one year before. Unfortunately, this is the maximum of information we could fish out of our patient, who had not been very minded to changes in her skin and body. There was no inguinal lymphadenopathy. Vascular work-up including duplex and Doppler ultrasonography of her lower legs was unremarkable as was her right sole x-ray. A wide excision of the right plantar tumor was performed and the wound was covered with a skin graft taken from her thigh (Fig. 1). The pathology

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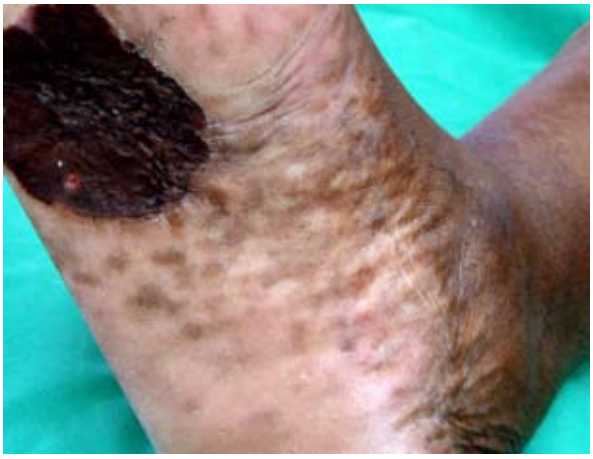

Figure 1. The patient's soles after surgery to remove the melanoma on her right foot. The darker area is the skin graft that had been taken from her thigh. Note multiple lentigines.

report described a polypoid malignant melanoma 3 cm in diameter and a depth of invasion of approximately 5 mm (Clark V). Further investigations were performed but only three months following surgery due to the patient's poor compliance. She underwent abdominal ultrasound, which was normal, computerized tomography (CT) of the thorax, which revealed multiple metastases in the lungs, and brain CT that demonstrated multiple metastases on both hemispheres. A biopsy performed on one macule showed minimal changes consisting of increased melanin in the melanocytes in the basal cells, slight elongation of the epidermal rete ridges and no melanin in histiocytes or macrophages of the dermis. These findings were compatible with simple lentigo. Due to the advanced state of her metastatic disease, she received only palliative treatment with radiation to the brain and medication (dexamethasone and phenytoin) to prevent convulsions. She received no chemotherapy.

DISCUSSION

An "outbreak of pigmented moles" was first described in 1868 by Hutchinson in a 22-year-old otherwise healthy woman (2), and a few more cases of eruptive nevi (some of them of acral distribution; (3)) have since been described (4). This rare phenomenon has been associated with dermatological diseases and immunosuppression, either disease-related or following the administration of immunosuppressive medication (reviewed in ref. 2). Our patient presented with eruptive acral lentigines (as opposed to nevi) and despite the similarities between them, such as sharing the sudden appearance of melanocytic lesions, we propose that acral lentigines represent a separate pathological entity the occurrence of which is associated with the development of malignancy. The sudden occurrence of acral lentigines appears to be a paraneoplastic sign, and not an immunosuppressive one. We are aware of only one report of eruptive acral lentigines occurring in two patients with acquired immune deficiency syndrome (AIDS) (immunodeficiency in one and neoplastic disease in the other) (5). We recently diagnosed four patients as having acral lentigines associated with malignant diseases: three of them received chemotherapy and the fourth received hormonal therapy (tamoxifen) and was not immunosuppressed (6).

A major limitation of our report is the lack of our ability to describe the exact time-course of the onset of lentigines in relation to the formation of the melanoma. However, from the information we could take out of our patient, it is clear that the lentigines had appeared at old age, either shortly before or after the appearance of the melanoma. Multiple acral nevi and lentigines are not uncommon in blacks, the incidence being higher in the dark brown than in the fair or light brown individuals (7). The usual histologic pattern seen in plantar-palmar lesions was that of lentigo simplex. Clinical differentiation of a lentigo from a junctional nevus is usually impossible (7). The differentiation of lentigines of the palms and soles from early expression of acral lentiginous melanomas may be difficult. In our patient we had a histologic diagnosis of lentigo for the multiple pigmented acral lesions. It is highly unlikely that the melanoma of our patient arose from a benign acral lentigo, as the time-span between the development of these lesions seemed to be too short.

The most plausible theory that may account for the formation of eruptive nevi and/or lentigines postulates that an intact immune state normally inhibits the proliferation of melanocytic lesions. Immune suppression or even a change in T cells might induce melanocyte-stimulating hormone (MSH), which is an endogenous growth factor for normal melanocytes. Eruptive nevi or lentigines with a propensity for the palms and soles represent an interesting and poorly understood subset of multiple eruptive nevi. A combination of altered immune surveillance and certain anatomic trophic factors present in the skin of the palms and soles must be at play. One such factor might be melanocortin receptors that bind MSH, and are present on abundant palmoplantar eccrine glands. Another possible factor is the lack of a MSH antagonist,

the agouti signaling protein that is produced in the dermal papillae of hair follicles, which are absent on the palms and soles (3,4).

Does one swallow (a case report) make a summer (a sign)? Only time will tell. Most diseases, variants, phenomena, and etiologies, however, started with single case reports (8-10). We believe that the association between a neoplasia and acral lentigines is not coincidental. The fact that our herein described patient as well as our other four patients developed a unique, rare, and very well-defined dermatosis in close temporal relationship with a malignancy adds more credence to a possible connection between the two events. The fact that we saw several such patients within less than one year indicates that this phenomenon is not very rare, and suggests that this association may well have been overlooked until now.

CONCLUSIONS

We suggest that our reported case of a 68-year-old patient with advanced stage melanoma that was associated with the appearance of multiple acral lentigines represents a new paraneoplastic sign.

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