Trauma and foreign bodies may favour the onset of melanoma metastases

DR VINCENZO DE GIORGI (Orcid ID : 0000-0001-6531-7998)

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Trauma and foreign bodies may favour the onset of melanoma metastases

V. De Giorgi,[1,3] P. Maida,[2] L. Salvati,[1] F. Scarfì,[1] L. Trane,[1] A. Gori,[3] F. Silvestri,[1] F. Venturi[1] and P. Covarelli[4]

1 Department of Dermatology, University of Florence, Florence, Italy;
2 Clinica Luganese Moncucco, Lugano, Switzerland
3 Cancer Research "AttiliaPofferi" Foundation, Pistoia, Italy
4 Department of Surgery, University of Perugia, Perugia, Italy

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Corresponding author:VINCENZO DE GIORGI, MD
e-mail: vincenzo.degiorgi@unifi.it

Metastasis is a common cause of morbidity and mortality in patients with cancer. Both experimental and clinical data support that trauma and inflammation augment the development of metastases (1-2).The mechanisms implicated in this process include excessive corticosteroid secretion, coagulopathy in the peripheral vasculature, immune suppression, and excessive production of reactive oxygen species (3).

However, cases in which inflammation seems to predispose the injured tissues to metastases for different types of tumour are described in the literature (3-4).This phenomenon is defined as “inflammatory oncotaxis”. Trauma creates a favourable environment for metastatic foci by inducing the expression of inflammatory mediators(i.e., cytokines, chemokines, and growth factors)(5-7). For example, lung tissue trauma preceded cancer metastasis in lung squamous cell carcinoma, thereby illustrating how inflammation and tissue injury could converge to create “fertile soil” for circulating metastatic cells or to accelerate the development of pre-existing metastasis (3).

Surgical stress after the diagnosis of a tumour may further contribute to the metastasis of the primary tumour due to the excessive secretion of corticosteroids, altered coagulation dynamics,and immunosuppression (4).

Regarding melanoma metastasis specifically, the activation of Notch1 in endothelial cells is involved in the development of secondary tumours. Notch1 receptor binding induces VCAM1 expression, which, in turn, attracts neutrophils whose infiltration facilitates metastatic cell adhesion (8). In their investigation of Notch1’s role in metastasis, Wieland et al. suggest that a targeted antibody-based therapy that specifically block the activation of Notch1 would reduce the incidence of metastasis (8).

Here, we describe the unusual case of a patient with metastatic melanoma whose tumour recurred in a finger that had experienced minor yet direct trauma.

A 77-year-old man presented with a swollen right fore finger, which he had injured while gardening a few months ago. Three years prior, the patient underwent treatment for melanoma on his left leg (1.1-mm-thick tumour, stage IIA) and had follow-up appointments every six months there after with no recurrence to date. Physical examination revealed circumferential swelling extending from the second right metacarpophalangeal joint to the proximal interphalangeal joint. On the dorsal side, a linear wound was evident (Fig. 1a) and, on the volarside, the lesion appeared to be

angiomatous (Fig. 1b). Scattered bluish areas were visible deep within the tissue. A contrast-enhanced computed tomography scan of his right hand illuminated a foreign body (Fig. 1c,arrow) and a solid irregular mass with scarce enhancement (Fig. 1d,asterisk). Pathological analysis of a skin biopsy revealed melanocytic proliferation and granulomatous inflammation characteristic of a foreign body response. The patient was diagnosed with metastatic melanoma and, four months later, succumbed to the progression of the disease.

Melanoma's propensity to metastasize into atypical sites is well documented, however, the factors and conditions that direct it towards developing in one area over another are unknown. Here we describe such a case in which the atypical metastasis'particular localization was almost certainly associated with a persistent immune response in that region. This inflammation-based oncotaxis event occurred in response to a latent foreign body in our patient's finger, and was then amplified and perpetuated by pro-inflammatory mediators and vasodilation. The Notch1 receptor was activated, inducing VCAM1 expression and eventually facilitating metastatic cell adhesion. As the first to describe melanocytic proliferation in response to a foreign body, this study provides a foundation for future investigations, and will hopefully increase the awareness and, therefore, detection and prevention of this nuanced form of cancer progression.

Tissue trauma and any ensuing chronic inflammation could facilitate metastases through two distinct but not mutually exclusive pathways. In the first, the primary insult induces local pro-inflammatory and wound-healing responses that enhance the seeding of metastatic cells from distant sites. In the second, dormant metastatic cells already present at the site at the time of trauma are stimulated to proliferate upon injury due to changes in the microenvironment (i.e., macrophage-induced pro-inflammatory milieu of cytokines, chemokines, and growth factors)(4). Future studies are warranted to determine which mechanism underlies. Such studies would greatly improve the outcome for patients with melanoma specifically over time. It would be extremely useful not to forget those phenomena when following patients with melanoma over time, considering the numerous cases prevalent in our population.

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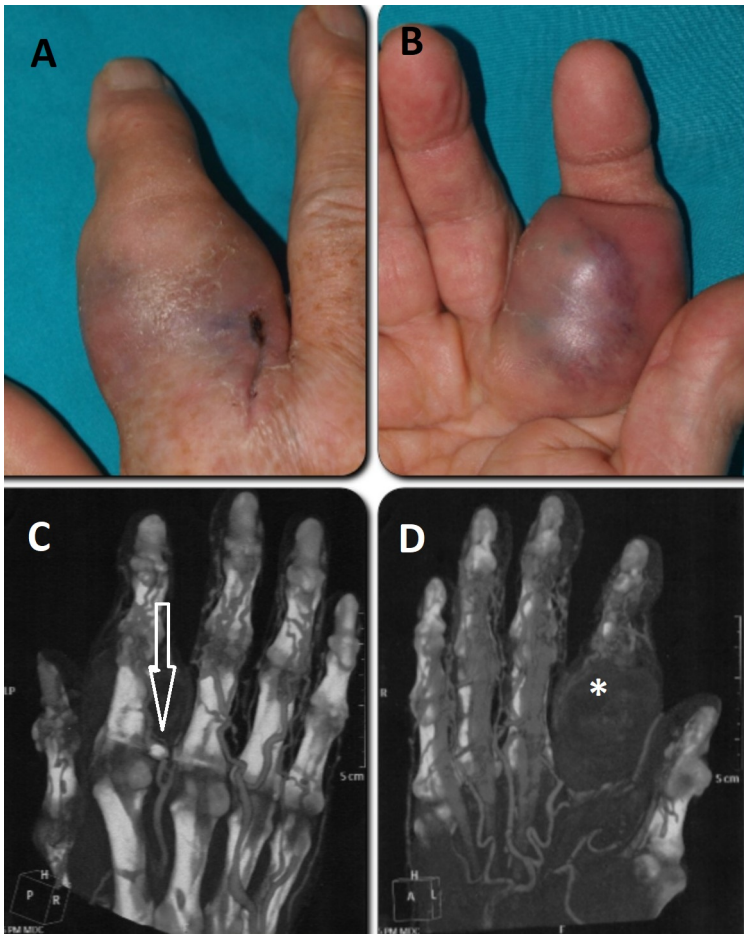
Figure Legend

Figure 1. Melanoma metastasis identified on the swollen right fore finger of a 77-year-old patient. (a) Linear wound present on the dorsal side of the finger. (b) Angiomatous lesion on the volar side.(c)Contrast-enhanced computed tomography image of a foreign body (arrow). (d) Solid,irregularly-shaped mass visualized with scarce enhancement (asterisk).



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