

A diagnostic trap for the dermatopathologist: granulomatous reactions from cutaneous microimplants for cosmetic purposes

We present a case of late granulomatous reactions from silicone that first appeared in a site different from that of the injection causing an incorrect diagnosis of liposarcoma in the beginning. The histological picture was a cystic-macrophagic granuloma in both the injection site (upper lip) and the migrating site (paranasal regions). We think that the foreign body has undergone an antigravity migration from the upper lip to the right paranasal region. To our knowledge, such a phenomenon has not been yet reported in literature.

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Over the past two decades, dermatologists and, especially, dermatopathologists have come into contact with a new diagnostic trap consisting of the granulomatous reactions from ‘inert’ materials injected intracutaneously for cosmetic purposes. The incidence of the granulomatous reactions against the ‘fillers’ depends, above all, on the type of substance used.

The case we are presenting is interesting due to the long time that elapsed between the cosmetic operation and the appearance of the clinical symptoms (which led initially to a misleading diagnostic picture); for the site of onset of the dermatopathy (which was different from the injection); and for the unusual histologic features (which, in the absence of the correct clinical picture, led to an erroneous diagnosis of liposarcoma).

Case description

A 53-year-old woman was sent by her attending physician to a surgery department for a unilateral swelling located in the right paranasal region. In her anamnesis, the patient reported that, in spite of the

fact that the lesion had appeared a few months earlier, she had gone to the doctor only once it became visible.

Clinical examination revealed presence of an ovoid plaque, mobile deeply, but fixed on the surface, and covered by clinically healthy skin. Surgical excision of the plaque was performed, and the histological diagnosis was liposarcoma. A year later, the sudden appearance of a new swelling in other parts of the face led the patient to consult our Division and so, during the compiling of her clinical history, the important information that emerged that 8 years earlier, she had received injections in her upper lip with a filler, the composition of which was uncertain. The patient had not connected the first paranasal lesion with the cutaneous microimplant, because the plaque had appeared in a region that had not been injected (Fig. 1). We performed a further biopsy of the injection site whose histological examination was characterized by an atrophic epidermis and a dermis occupied, through its entire thickness, by ‘cystic and macrophagic granulomas’ characterized by extracellular empty microcysts



Fig. 1. Diffuse indurated swelling at the implant site (upper lip and nasolabial folds). Migrating reactions at the paranasal regions.

surrounded by a mainly mononuclear infiltrate of vacuolated macrophages. At low magnification, these microcysts appeared as round holes of different sizes, sometimes confluent, reminiscent of a 'Swiss cheese pattern'. Giant cells were numerous,

and they had a floret-like appearance with numerous clear, peripherally situated vacuoles and central closely packed nuclei. Mononuclear cells were also vacuolated with peripheral hyperchromatic notched signet-ring type nuclei, conferring a lipoblast-like appearance. Lymphocytes were scanty (Fig. 2). The immunohistochemical examination showed negativity for S100 and positivity for CD68 of the above-said cellular elements, both mono- and multinuclear (Fig. 3).

Finally, we reviewed the first biopsy of the migrating site erroneously diagnosed as liposarcoma. Its histological examination has shown the same 'cystic and macrophagic granulomas' deep inside the muscular layer (Fig. 4).

Discussion

Various histological patterns of granulomatous reactions after the injection of fillers have been described. They vary from typical foreign body type granulomatous reactions to cystic-macrophagic granulomatous reactions.¹⁻³ The latter description characterizes our case in which, even though the physician was reluctant to name the substance he had injected, the histological appearance is extremely suggestive of a granuloma from silicone.^{6,8}

The patient, at the time of the first biopsy, neglected to mention the cosmetic treatment received 8 years earlier, since the granulomatous reaction was very much delayed and appeared in a site different from the initial injection. Thus, in the

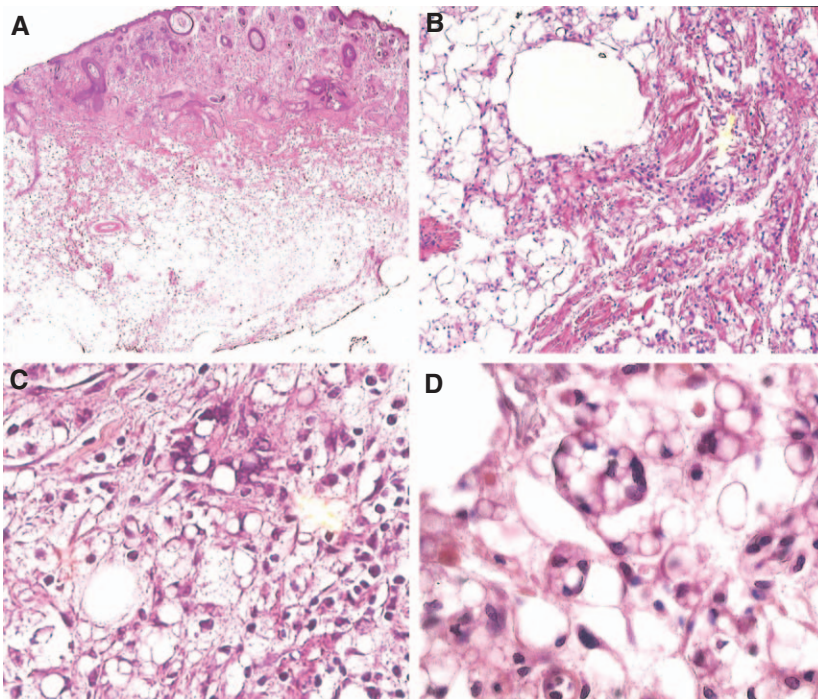


Fig. 2. Biopsy specimen from the upper lip, the region injected with an unknown filler (H&E): (A) At low magnification, an atrophic epidermis and a dermis occupied by 'cystic and macrophagic granulomas', characterized by round extracellular holes of different sizes, sometimes confluent, reminiscent of 'Swiss cheese pattern'. (B, C) The cystic and macrophagic granulomas surrounds and breaks up striated muscle bundles. A giant cell with numerous clear vacuoles and central closely packed nuclei (arrow). (D) At high magnification, mononuclear vacuolated macrophages with peripheral hyperchromatic notched nuclei conferring a lipoblast-like appearance.

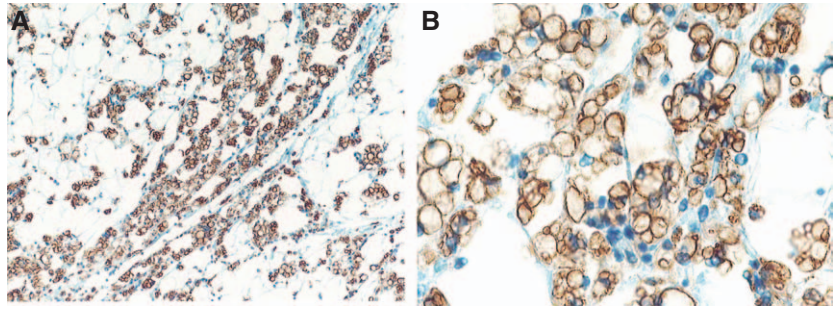


Fig. 3. (A, B) Positivity for CD68 of mono- and multinuclear cellular elements.

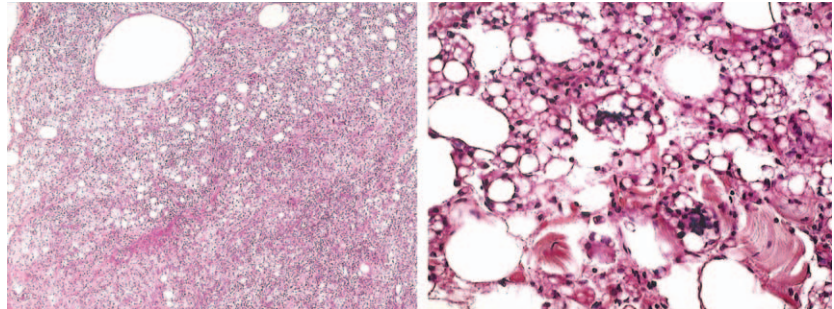


Fig. 4. Biopsy specimen from the right paranasal region, the migrating site (H&E). At low and high magnification, the histological picture has shown the same 'cystic and macrophagic granulomas'.

absence of a complete clinical history, the diagnosis of the first pathologist was that of a well-differentiated liposarcoma.

It should be remembered that the common morphological denominator of liposarcoma is the lipoblast, which appears as a mononuclear or multinuclear cell with one or more cytoplasmic vacuoles containing fat. Some cells have their nucleus pressed to the side by the presence of a single cytoplasmic vacuole with a 'signet ring' appearance. In some lipoblasts, the nucleus maintains a central position with peripheral indentations caused by numerous multiple small vacuoles.⁶

With conventional histology, it can be very difficult to distinguish the lipoblast of a liposarcoma from the vacuolated histiocyte of a granulomatous reaction to fillers, such as silicone. Therefore, without an exact clinical-histological correlation (past medical history, lesion site, multifocality) and in the absence of the support of immunohistochemistry, it could be difficult to distinguish between the two cases.

Awareness of this possible diagnostic pitfall may help physicians to classify correctly these facial lesions because of fillers that could be mistaken for liposarcomas or liposclerosis by conventional histology.^{6,8}

The etiopathogenesis of these reactions is still unknown, but the possibility of *gravity migration* and extremely late reactions does exist and it has already been reported in the medical literature.⁵⁻⁸ In our

case, the first biopsy was a cystic-macrophagic granulomas of the same type as the second one. So we think that the foreign body has undergone an anti-gravity migration from the upper lip to the right paranasal region. To our knowledge, such a phenomenon has not been yet reported in literature.

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