Eosinophilic Granulomatous Reaction after Intradermal Injection of Hyaluronic Acid

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Sir,

Hyaluronic acid, one of the components of the extracellular matrix of dermis and other tissues, has natural hydrating functions with an ability to bind a large volume of water. It can be modified to form an insoluble, cross-linked, high viscosity gel whose dermal injection is suitable for the correction of soft tissue defects and the improvement of facial contouring. Dermal injection is generally believed to be safe without causing any serious adverse reactions. Acute reactions, which include bruising, erythema, and oedema, disappear within a couple of days. Delayed hypersensitivity reactions are considered to be exceptional since hyaluronic acid is non-immunogenic. We recently encountered a rare case of a delayed hypersensitivity reaction that was histologically characterized by a granulomatous change in a woman after the injection of hyaluronic acid for the correction of facial wrinkling.

CASE REPORT

In October 2002, a 30-year-old woman received a dermal injection of hyaluronic acid gel (Rofilan Hylan Gel, Rofil Medical International NV, Breda, Netherlands) consisting of a stabilized 100% cross-linked hyaluronic acid biosynthetically produced by bacterial fermentation to her lower eyelids. She did not undergo any pre-treatment skin testing to check for skin hypersensitivity to the injected materials. Acute inflammatory changes consisting of redness and bruising disappeared within a few days. In June 2003, she received her second hyaluronic acid injection to her lower eyelids. Two weeks later, because she gradually developed indurated erythema at the injected sites, she was referred to our hospital. On examination, there were hard erythematous nodules, 2×3 cm in size, in the bilateral lower eyelids (Fig. 1a). A skin biopsy specimen taken from the lesion in the left lower eyelid revealed a foreign body granuloma composed of histocytes and multinucleated giant cells with a prominent eosinophil infiltration encircling basophilic materials of variable sizes and shapes existing in the deep dermis and subcutis (Figs 1b and c). She was treated orally with prednisolone 15 mg for 7 days, which improved the inflammation. However, recurrence occurred with smaller, tender nodules at the injection sites, which rapidly improved with daily oral intake of 10 mg prednisolone for 7 days. Two months later, most of the lesions resolved, leaving scars.

DISCUSSION

Hyaluronic acid represents an alternative treatment option for the aging face, particularly for facial lines, and for the treatment of distensible atrophic facial scarring. Its injection is considered safer than other materials, such as silicon and collagen, but it produces transient

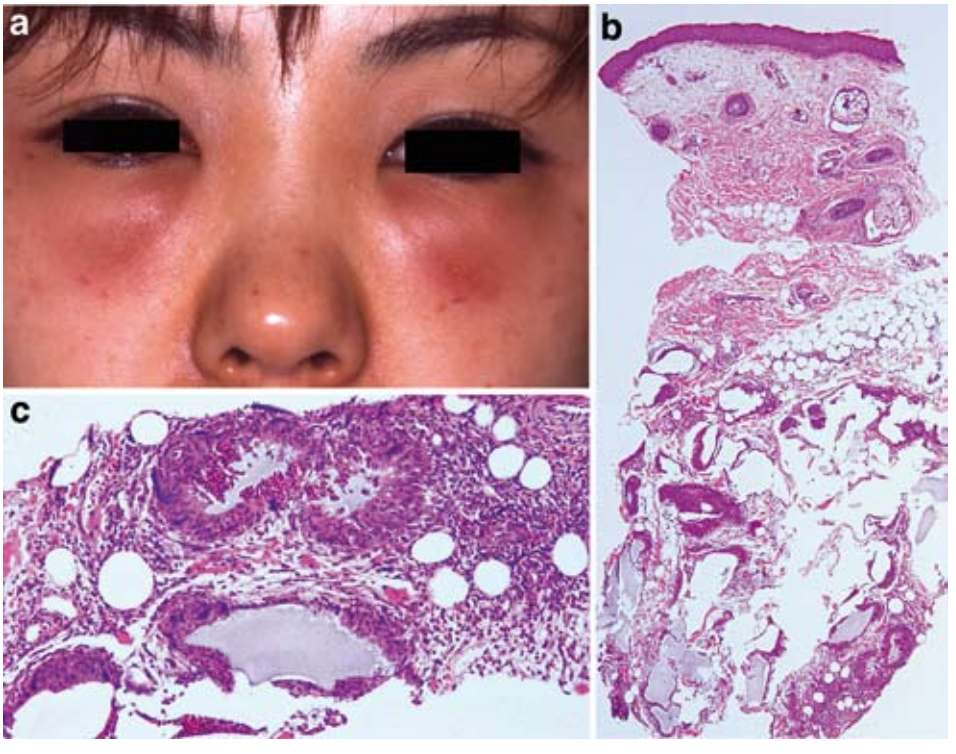

Fig. 1. (a) Clinical appearance showing erythematous nodules in the inferior eyelids. (b) Biopsy specimen from the lesion showing a nodular infiltration in the deep dermis and subcutaneous tissues. (c) An area consisting of bluish-stained hyaluronic acid gel surrounded by giant cells and a massive peripheral infiltrate of eosinophils. (H&E staining: b ×10; c ×200).

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inflammatory reactions, such as redness, bruising and pain in 3–5% of patients within 2 weeks (1, 2). In general, because it does not elicit clinically significant inflammatory, immunological, or foreign body reactions, no special skin testing for allergy is recommended. However, several reports have described undesirable side-effects consisting of granulomatous reactions (3–8). In our case, oral prednisolone was effective for suppressing the granulomatous reaction associated with massive infiltration of eosinophils. However, Honig et al. (4) reported a severely inflamed case, in which painful nodules evolving into abscesses required surgical treatment 3 months after hyaluronic acid injections. In addition to hyaluronic acid, numerous products are now available for tissue augmentation, such as polylactic acid microspheres. These products appear to be clinically safe, but they have been shown to cause foreign body granulomas and other adverse reactions in a small percentage of patients (9).

In our case, the patient was injected with Rofilan Hylan Gel (Rofil Medical International NV, Breda, The Netherlands), which is biosynthetically produced through a bacterial fermentation process. The cause of the observed inflammation after the second intradermal injection of hyaluronic acid was not determined, but we cannot rule out the possibility that it could be allergic in nature due to protein impurities (10). Histopathologically we found foreign-body type granuloma associated with an eosinophilic infiltration, which suggests an allergic reaction to the injected materials. Alternatively, the injected hyaluronic acid may stimulate phagocytic activity, as occurs in foreign body reaction. Although hyaluronic acid is one of the best materials used for dermal filler at present, patients should be informed about potential complications, including allergic reactions.

Conflicts of interest: The authors have no conflicting financial interests.

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