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Dermal filler complications: a clinicopathologic study with a spectrum of histologic reaction patterns

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ABSTRACT

Although dermal fillers are generally accepted as safe and well-tolerable cosmetic tools, adverse reaction still forms a prognostic problem. The aim of this study was to demonstrate the clinicopathologic patterns of dermal filler complications in our center. A 5-year single-center study that included patients complained from filler complications and referred to the dermatopathology unit in Al-Azhar University for histologic assessment. The study included 38 female patients with an average age of 47 years. The mean onset of complications was 14.6 ± 5.27 months after injection. The injected material included hyaluronic acid (18.4%), silicone (52.6%), bovine collagen (15.8%) and polyacrylamide hydrogel (13.2%). Most lesions were located on the face (55.3%), less commonly on the hands (18.4%), buttocks (21%), and rarely on the vulva (5.3%). The clinical spectrum included indurated plaque (23.7%), nodular lesion (31.6%), inflammatory mass (15.8%), atrophic lesion (10.5%), skin discoloration (13.1%) and ulceration (5.3%). Histologically, granulomatous reaction was the major finding, either a foreign body granuloma (34.2%) or infectious granuloma (13.2%). Other histologic reactions included dermal pseudocysts with chronic inflammation (26.3%), dermal fibrosis (15.8%), and eosinophilic panniculitis (10.5%). Our results confirmed that dermal fillers could be manifested with variable clinical presentations and show different histologic reactions. Because of long-standing duration until complications occur, history taking is crucial and should be emphasized in every suspected patient. It is hoped that this article will increase awareness for recognition of these variable complications and help select the appropriate therapy.

1. Introduction

Soft tissue augmentation (dermal fillers) becomes one of the most important cosmetic tolls that offer rejuvenation and aesthetic improvement previously only achievable with surgery. In comparison with cosmetic surgery, dermal fillers have the advantages of lower cost and limited-to-no recovery time [1]. The basic indications of dermal fillers were the filling of rhytides and folds, in addition to correction of soft tissue loss due to disease or age. In the present time, the most common uses of dermal fillers are cheek and chin augmentation, nose reshaping, lip enhancement, and hand rejuvenation [2].

The marked increase of filler procedures is associated with more liability of complications, and this could be related to the injection technique or the chemical composition of the fillers [3]. The complications associated with filler injection may be immediate, early onset (within days) or long duration (after weeks to years). Immediate complications included injection site reaction such as erythema, edema, pain, and bruising. Early complications included infection (mostly staphylococcal or streptococcal), hypersensitivity reaction, skin discoloration, vascular occlusion, and contour irregularities [4].

Delayed complications included infections (mostly mycobacterial), foreign body granulomatous reaction, migration of implanted material, persistent discoloration, and scarring [5]. It was observed that few reports are available about filler complications in developing countries. In this study, we reported the clinicopathologic spectrum of delayed filler complications among Egyptian patients aiming to increase awareness for recognition of these variable complications and help select the appropriate therapy.

2. Patients and methods

A single-center study included all patients complained from delayed filler complications along 5 years' duration (from March 2009 to February 2014). Patients were referred from private dermatology clinics for skin biopsy and histologic assessment in the dermatopathology unit, Al-Azhar University, Cairo, Egypt.

History of filler injection was proved in all patients at the same area of complicated lesion. History of trauma, skin diseases, and systemic illness was recorded. Clinical examination of the lesion was carefully

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performed. Clinical features of the lesion were recorded, most importantly the location, size, shape, induration, surface, and color changes. Routine laboratory investigations included complete blood count, blood glucose level, liver function tests, and kidney function tests.

Skin biopsy was performed from the lesion, either from the central part or from the edge. The determination of biopsy site was mostly selected after consideration of the location (facial or extrafacial) and morphology (ulcerative or nonulcerative) of the lesion. Punch (core) biopsy (4-6 mm in diameter) was the standard technique in most cases. However, in few cases, elliptical biopsy was preferred for a better assessment.

For each specimen, 2 slides were stained with hematoxylin and eosin. Special stains were required for better demonstration of deposited materials or identification of organisms. Examination with polarize light microscope was routinely performed in all cases with granulomatous reaction. The study was approved by the local ethical committee of Al-Azhar University. A written consent was obtained from each patient for skin biopsy and medical photography.

3. Results

We were able to collect 38 patients; all were females with an average age of 47 years. The mean onset of symptoms ranged was 14.6 ± 5.27 months. Most lesions were located on the face (55.3%). The most reported injected material was silicone (52.6%). Laboratory investigations revealed hyperglycemia in 3 patients (7.9%) and elevated liver enzymes in 2 patients (5.3%).

The clinical spectrum of the lesions ranged from discoloration of the skin into inflammatory mass as shown in the Table. The most common clinical presentation was nodular mass and indurated plaque, whereas ulcerative lesions were the least (Figs. 1 and 2). Histologic examination revealed 3 levels of tissue reaction: confined to the superficial dermis (23.7%), more located in the mid and deep dermis (60.5%), and markedly extended into the subcutis (15.8%).

Table
Demographic, clinical data, and histologic features of 38 female patients with filler complications

Demographic data	Total no. of patients (n = 38)
Age (y)	
Range	31-57
Mean ± SD	46.3 ± 4.52
Average	47
Onset of complications after injection (mo)	
Range	6-25
Mean ± SD	14.6 ± 5.27
Average	11
Site of the lesions	
Face	21 (55.3%)
Hands	7 (18.4%)
Vulva	2 (5.3%)
Buttock	8 (21%)
Injected material	
Hyaluronic acid	7 (18.4%)
Silicone	20 (52.6%)
Bovine collagen	6 (15.8%)
Polyacrylamide hydrogel	5 (13.2%)
Clinical morphology of the lesions	
Indurated plaque	9 (23.7%)
Atrophic lesion	4 (10.5%)
Nodular mass	12 (31.6%)
Inflammatory mass	6 (15.8%)
Ulcerative lesion	2 (5.3%)
Discoloration	5 (13.1%)
Histologic patterns	
Foreign body granuloma	13 (34.2%)
Infectious granuloma	5 (13.2%)
Dermal pseudocysts	10 (26.3%)
Dermal fibrosis	6 (15.8%)
Eosinophilic panniculitis	4 (10.5%)

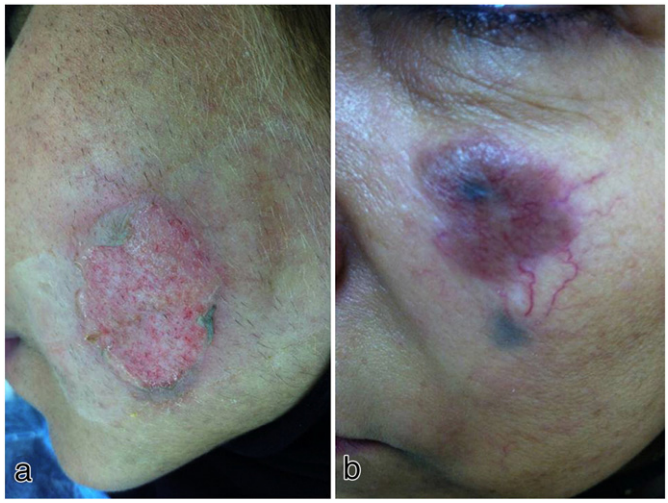

Fig. 1. Delayed filler complications in 2 female patients manifested as atrophic plaque (a) and nodular mass (b) on the left cheeks.

The most common tissue reaction was foreign body granuloma that was reported in 13 cases (5 hyaluronic acid, 7 silicone and one bovine collagen). The lesions were characterized by patchy distribution and nonsuppurative pattern. The infiltrate was composed mainly of epithelioid and foamy histiocytes admixed with inflammatory cells, mainly lymphocytes with scanty plasma cells, eosinophils and rarely neutrophils. In most cases, there were a considerable number of multinucleated giant cells surrounding the clear spaces of injected material, dermal vasculatures, and skin appendages (Fig. 3).

Infectious granuloma was reported in 5 cases (2 silicone, one hyaluronic acid, one bovine collagen and one hydrogel). The lesions were characterized by suppurative or caseating granuloma with central caseation necrosis and prominent neutrophilic infiltrate. The epidermis showed variable degree of acanthosis, hyperkeratosis, and follicular hyperkeratosis. The granuloma was more located in the upper and mid-dermis with marked presence of multinucleated giant cells (Fig. 4). Although no organisms could be identified by special stains, polymerase chain reaction confirmed the diagnosis of atypical mycobacterium (*Mycobacterium fortuitum* in 3 cases and *Mycobacterium marinum* in 2 cases).

In 10 cases (9 silicone and one hydrogel), the histologic reaction was formed of dermal pseudocysts with chronic inflammatory infiltrate but without granuloma formation. There were different sizes of cystic spaces distributed all over the dermis and in some cases, extended into the subcutis with mixed infiltrate (Fig. 5).

Dermal fibrosis was observed in 6 cases with 2 different patterns; 4 cases (one hyaluronic acid, one silicone, and 2 bovine collagen) showed pandermal fibrosis that was characterized by increased number of fibroblasts with scanty inflammatory infiltrate and marked fibrosis of collagen bundles (Fig. 6a and b). The second pattern was only observed in 2 cases (one bovine collagen and one hydrogel), and it showed thickened, homogenized collagen bundles in the deep dermis with scanty fibroblasts (Fig. 6c and d).

Eosinophilic panniculitis was reported in 4 cases (one silicone, one bovine collagen and 2 hydrogel), and it was characterized by dense eosinophilic infiltrate in the subcutis, mostly with septal distribution but partially extended into the fat lobules. Degranulation of eosinophils was prominent in all cases, but flame figures were not observed in any case (Fig. 7).

4. Discussion

All fillers are considered foreign bodies that may stimulate the immune system leading to varying degrees of tissue reactions. Although