Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Foreign-Body Reaction to Dermal Filler: Good Response to Treatment With Allopurinol☆

Respuesta favorable al tratamiento con alopurinol de reacción granulomatosa a relleno

Dear Editor:

Procedures involving dermal filler for cosmetic purposes are carried out every day. However, this practice is not risk-free. One reported complication is that of foreign-body granulomatous reaction to a component of the filler.[1,2] One of the initial treatment options is infiltration with corticosteroids, although the condition can also be managed with oral allopurinol.[3–5]

An 83-year-old woman was referred for a lesion on her left cheek that had been treated for 3 weeks with oral antibiotic therapy (amoxicillin clavulanate, 875/125 mg/8 h), surgical drainage, and a 2-week tapering course of oral corticosteroids (starting with prednisone 30 mg/d), albeit with minimal improvement. The patient's history was remarkable only for the fact that she reported undergoing surgery in this area some years previously. Similarly, she denied having received infiltrations or fillers. Physical examination revealed a fistulous tract with purulent discharge, depressed areas of scarring, and, adjacent to these areas, a reddish exudative papular lesion. The lesions were surrounded by an edematous area with a doughy consistency, occupying almost the whole cheek (Fig. 1A). Ultrasound revealed several nodular hypoechoic lesions that differed in size, the largest being 1 cm in diameter. These were mainly superficial, with vascularization in the interior and slightly increased echogenicity of the underlying subcutaneous tissue. A histopathology study was recommended. Biopsy revealed a foreign-body granulomatous reaction in the dermis and subcutaneous tissue, with the presence of 2 different materials in the histology sections: a superficial eosinophilic material with no associated granulomatous reaction and a deeper basophilic amorphous material accompanied by a moderate inflammatory infiltrate composed of macrophages with granular cytoplasm (Fig. 2). Given the diagnosis of a foreign-body granulomatous reaction and the uselessness of previous treatments, we offered the patient the possibility of treatment with allopurinol under a compassionate use regimen (300 mg/d, po) combined with mometasone furoate in blocks of 15 days every month. This treatment led to a slow but gradual improvement with fluctuations until the lesions were totally controlled 8 months later (Fig. 1B), with resolution of the initial soft tissue edema and atrophic scarring. Treatment was well tolerated, and no adverse effects were reported during follow-up.

Comment

While relatively harmless, infiltration of dermal filler is not free of complications, which can be classed as short-term, such as hematomas and infections, and long-term, such as migration of material or foreign-body granulomatous reactions, as in the present case. Granulomatous reactions are

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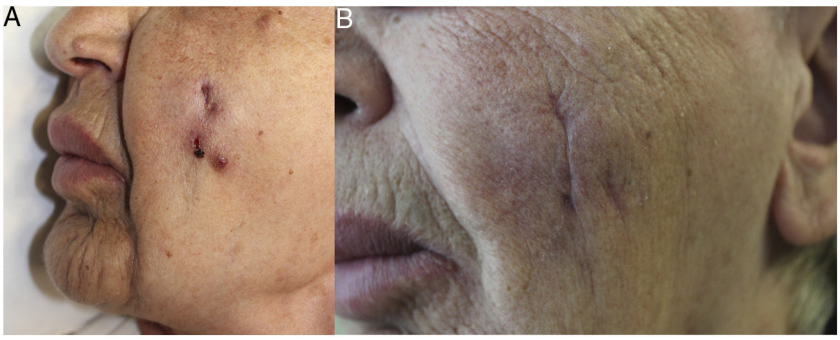

Figure 1 A, Edematous area with loss of expression wrinkles and external orifices of fistulous tracts. B, Reduced edema and scarring of the tracts.

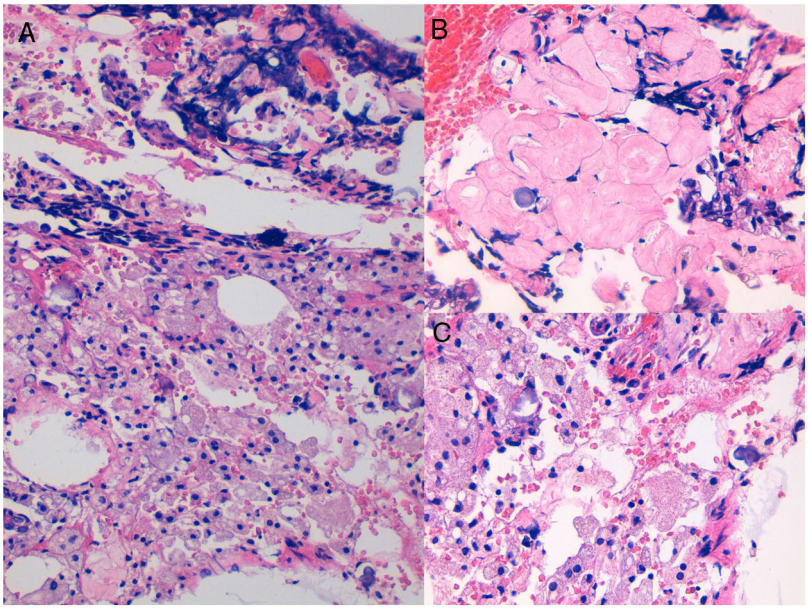

Figure 2 Hematoxylin-eosin. A, Intense foreign-body granulomatous reaction (original magnification, ×20). B, Eosinophilic material (original magnification, ×40). C, Basophilic material (original magnification, ×40).

more frequent with longer-term fillers, especially those that are permanent or semipermanent, such as silicone, polyacrylamide, and polymethyl methacrylate polymers. Once infection has been ruled out, the most common maintenance treatment reported in the literature is application of topical corticosteroids followed by infiltration of corticosteroids alone or combined with 5-fluorouracil.[1,2] If the product used is suspected of being hyaluronic acid, the infiltration can be with hyaluronidase.[5] In more refractory cases, oral corticosteroid regimens can be used. Nevertheless, in the long term, these treatments can lead to unaesthetic adverse effects, such as skin atrophy.[1,2]

Given the similarity between foreign-body granulomas and sarcoid granuloma,[6] Reisberger et al.[4] prescribed allopurinol (200 mg/d, increasing gradually to 600 mg/d). Subsequent studies revealed improvements in granulomatous reactions to silicone[3] and tattoo materials.[7,8] In these cases, daily doses range from 300 mg[3,7] to 600 mg.[8] Oral allopurinol can be combined with infiltrations of 5-fluorouracil and triamcinolone acetonide.[5]

Allopurinol has been associated with downregulation of intracellular adhesion molecule 1 and $P2X_7$, which are receptors of the monocyte and macrophage lineages. The reduction in intracellular adhesion molecule interferes with cellular adhesion, and $P2X_7$ receptors have been associated with the cell fusion process leading to multinucleated giant cells during granulomatous inflammation.[8]

A review of the literature shows that the more superficial material (eosinophilic, with no associated reaction) could correspond to substances such as silicone, paraffin, or polymethyl methacrylate microspheres. Polymethyl methacrylate seems to be the most likely option, since the remaining products usually produce cystic/lanceolate areas in histopathology, with a very characteristic pattern. In morphological terms, the deeper material (basophilic with an associated inflammatory reaction) could correspond to polyacrylamide hydrogel, polyalkylimide gel, polyvinyl hydroxide microspheres in polyacrylamide gel, alginate reticulation, or hyaluronic acid. Given that the patient had undergone surgery several years previously, we can

rule out hyaluronic acid, with a permanent filler seeming more likely. Polyacrylamide gel is more multivacuolated in appearance, whereas polyalkylimide is more granular; therefore, the substance involved in the present case could be polyalkylamide.[5,9]

In conclusion, we present a case of foreign-body granulomatous reaction with a good response to daily allopurinol 300 mg. This treatment could be a useful alternative in patients who do not respond to conventional therapy.

Conflicts of Interest

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Hair Changes During Treatment With Trametinib☆

Cambios en el pelo asociados a trametinib

Dear Editor:

The mitogen-activated protein kinase (MAPK) pathway is the therapeutic target in a large number of neoplasias. MEK inhibitors such as trametinib have been used to treat solid tumors and blood cancers in adults, whereas its use in children is extremely rare.[1] Cutaneous manifestations associated with these therapies are frequent, but little data exists on hair abnormalities. We present the case of a girl who developed trichoschisis and trichorrhexis nodosa during treatment with trametinib.

A 2-year-old Caucasian girl with a history of neurofibromatosis type 1 (NF1), which had been diagnosed at the age of 9 months, and carrier of a de novo heterozygous mutation in c.7006G>T presented optic glioma and cervical plexiform neurofibroma with

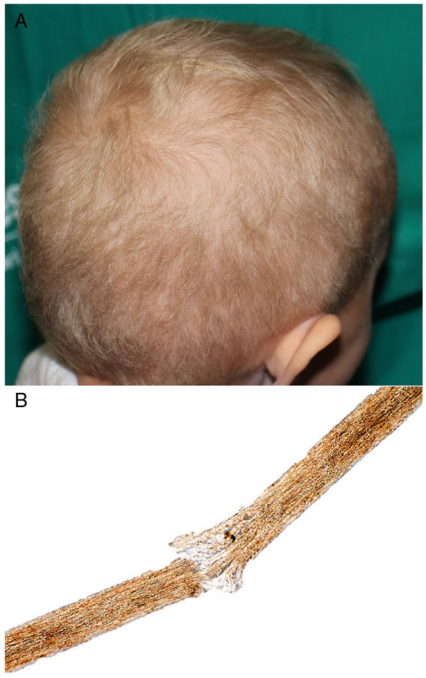

Figure 1 A, Sparse blond hair with a dry and dull appearance. B, Focus of transverse fracture with unraveled edges in the hair of a girl after 10 months of treatment with trametinib.

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