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CASE REPORT

Successful Treatment of Delayed Onset Nodules After Dermal Fillers Injection with Abrocitinib: A Case Report

Zhen Li[1,*], Jiejie Lu[1,*], Miaoting Wu[1], Bo Yu[2,3], Zhili Yang[1]

[1]Plastic and Cosmetic Center, The Fifth People's Hospital of Hainan Province, Haikou, Hainan, People's Republic of China; [2]Department of Dermatology, Peking University Shenzhen Hospital, Shenzhen, Guangdong, People's Republic of China; [3]Shenzhen Key Laboratory for Translational Medicine of Dermatology, Biomedical Research Institute, Shenzhen Peking University - The Hong Kong University of Science and Technology Medical Center, Shenzhen, Guangdong, People's Republic of China

*These authors contributed equally to this work

Correspondence: Zhili Yang; Bo Yu, Email 316940160@qq.com; Drboyu_derm@126.com

Abstract: Delayed-onset nodules (DONs) are masses that occurs primarily at or near the injection site stemmed from the injection of dermal fillers. This term is descriptive and encompasses a range of potential underlying diagnoses, including product redistribution, delayed hypersensitivity reaction, biofilm, granuloma, among others. Addressing DONs can pose significant challenges, varying tremendously grounded in multiple factors such as whether the nodule is inflammatory, its timing of emergence, and the specific filler material utilized. In this context, we present the case of a 32-year-old woman who presented to the hospital with facial nodules persisting for one month. The patient was diagnosed with DONs (suspected foreign body granulomas) on the basis of her clinical presentation and laboratory test results. She was treated with abrocitinib, a Janus kinase (JAK) inhibitor, for four weeks, which resulted in the complete resolution of her rash. Subsequent follow-up visits confirmed no adverse effects or relapses.

Keywords: filler, delayed-onset nodules, granuloma, abrocitinib, treatment

Introduction

Over the past two decades, dermal fillers have surged in popularity for use in cosmetic procedures. Nonetheless, the occurrence of complications increasingly augments as their usage increases. These include contusions, swelling, edema, infections, lumps and bumps, skin discoloration, biofilm formation, and blood vessel damage.[1] It has been reported that the occurrence of complications of injection filler in oral and maxillofacial region was 17.1%.[2]

The term delayed-onset nodules (DONs) refers to a visible or palpable mass that typically occurs at or near the injection site at least two weeks after dermal filler administration. This descriptive term encompasses a range of potential underlying diagnoses, including product redistribution, delayed hypersensitivity reaction, biofilm, granuloma, among others. The underlying pathologies and their incidences remain poorly understood due to the lack of specificity in clinical signs, challenges in accessing diagnostic tests, cost constraints, and patient reluctance to undergo such procedures.[3]

Any filler is considered first as a foreign material by the body, which attempts to eliminate it. While foreign body granulomas is reckoned as a form of chronic inflammation that occurs in response to foreign material that cannot be phagocytosed by macrophages. Histopathological analysis typically shows a collection of foreign bodies, inside or outside inflammatory cells, surrounded and embedded in a connective and fibrotic tissue.[4] Despite the fact that treatments for foreign body granuloma are currently available, they pose conspicuous challenges as a consequence of adverse effects, high recurrence rates, and uncertain treatment outcomes.

In this context, we report a case of a 32-year-old woman diagnosed with DONs (suspected foreign body granuloma), who was successfully treated with abrocitinib.

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Case Report

A 32-year-old woman with facial papules and nodules persisting for one month was presented to the dermatology department of The Fifth People's Hospital of Hainan Province in September 2024. Two months prior, she received a 10 mL dermal filler injection, consisting of an unknown brand of collagen and small-molecule hyaluronic acid (HA), at a cosmetic institution. A month and a half ago, the patient underwent hair transplant surgery at the forehead hairline at a local clinic without experiencing any discomfort. One month ago, she underwent facial High-Intensity Focused Ultrasound (HIFU) therapy. Three days after the HIFU therapy, she developed multiple red papules the size of mung beans and nodules arranged neatly on the face, accompanied by mild pruritus. She sought treatment at a local clinic and was prescribed oral prednisone tablets 5 mg daily for three weeks, but the rash showed no improvement. The patient felt that the papules and nodules significantly impacted her social and professional life, as well as her sleep quality.

Specialist examination revealed multiple dark red papules and nodules, approximately the size of mung beans, distributed on the patient's face. These lesions exhibited a regular arrangement, infiltration, a firm texture, and were non-tender (Figure 1). The patient declined to undergo histopathological examination of the facial skin. Routine blood tests, tumor markers, T-spot testing, myocardial enzyme assays, electrocardiography, and chest CT scans showed no significant abnormalities. Serological tests for syphilis, hepatitis C antibodies, and HIV antibodies returned negative results.

Based on the patient's history, the clinical consideration was DONs (suspected foreign body granuloma). After thorough communication with the patient, active infectious diseases were ruled out, and the patient was prescribed oral axitinib tablets 100 mg daily for one month, along with methylprednisolone tablets 16 mg daily for seven days. After two weeks of treatment, the rash showed significant improvement, and the itching resolved completely. During a follow-up two months after treatment, the patient reported that she did not touch the rash and still had pigmentation spots on his face (Figure 2). No recurrence of symptoms and adverse reactions were observed during follow-up.

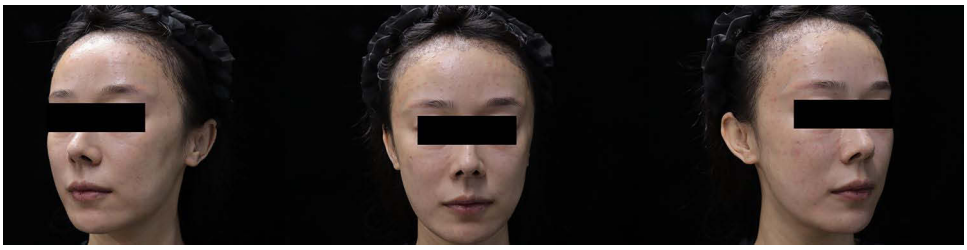

Figure 1 Clinical photographs exhibit the pre-treatment of the patient's condition.

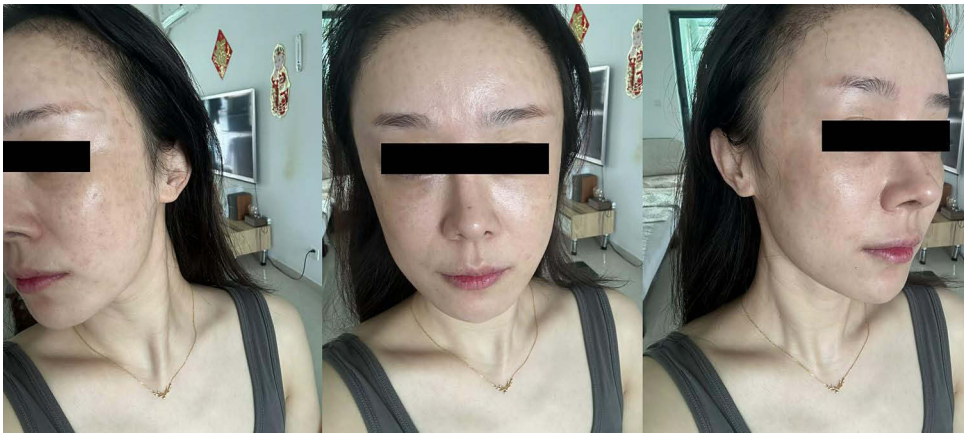

Figure 2 Clinical photographs displayed the abrocitinib was given 100 mg daily for 4 weeks and followed up for 2 months after completion of treatment.

Discussion

As a delayed onset reactions subsequent to dermal filling, the etiology of DONs is unknown. Nevertheless, relevant experts hold a standpoint that three hypotheses may contribute to the occurrence of delayed onset reactions: (1) the physicochemical properties of the filler material; (2) infection due to inoculation; and (3) the host immune response.[5] In contrast to the anti-inflammatory effects of high molecular weight HA, low molecular weight HA is deemed to conduct a paramount role in the advancement of late-onset nodules by activating toll-like receptors and stimulating the development of reactive oxygen species.[6] Nodules must be categorized as inflammatory or noninflammatory. Therapeutically, There is expert consensus recommends HA filler dissolution in cases of inactive infection. Adjunct therapy with low-dose triamcinolone acetonide combined with 5-fluorouracil (5-FU) is advised for intralesional injections until nodular resolution.[1,7] For antibiotic treatment, there are consensus guidelines for HA related complications that recommend oral clarithromycin plus moxifloxacin, or minocycline.[8]

Additionally, the precise mechanism of interaction between low molecular weight HA and collagen during intradermal injection remains unclear. To minimize potential complications, it is generally advised to avoid mixing injectable substances.[9] Furthermore, the alteration or degradation of injectable fillers may occur following treatment of the overlying skin with lasers, light-based devices, or other energy-based technologies.[10]

Nonetheless, the term DONs is descriptive rather than diagnostic. Potential underlying diagnoses encompass product redistribution, delayed hypersensitivity reaction, biofilm, granulomas, and others. Research indicates that when bacterial infection is ruled out, DONs appearing within three months after intradermal injection are primarily attributed to foreign body granulomas, it belongs to delayed hypersensitivity reaction, which is principally mediated by T lymphocytes.[11,12]

Despite the availability of treatments for foreign body granuloma, they present challenges due to adverse effects, high recurrence rates, and unpredictable treatment outcomes. In various cases, the use of corticosteroids or local injections of 5-fluorouracil has shown considerable efficacy in reducing the inflammatory response. However, it is essential to rule out infection before initiating treatment. Additionally, rebound effects must be anticipated once their anti-inflammatory effects cease, as these treatments may potentially activate biofilms. If a hyaluronic acid product has been used, it can be degraded by injecting hyaluronidase to hydrolyze the hyaluronic acid glycosaminoglycan polysaccharide complex. It is important to note that an allergic reaction can occur at any time. If the granuloma persists despite conservative treatments, surgical resection should be considered. However, these surgeries may have significant complications and long-term after-effects.[10] Alternatively, JAK inhibitors may offer a safer and more tolerable profile compared to conventional treatment options. Recent case reports also support for JAK inhibitors as a novel therapeutic approach.[13,14]

The JAK-STAT pathway is intricately linked to cell proliferation, differentiation, and immune regulation. Upon binding to cytokine receptors, JAK activates the translocation of STAT proteins to the nucleus by transmitting cytokine signals, thus regulating the transcription of effector genes. Practically, over 50 cytokines, including IFN-γ, IL-2, IL-6, IL-12, and IL-23, depend on the JAK-STAT pathway for their function. JAK inhibitors can effectively block the pathway at the JAK level, preventing the activation of STATs and simultaneously inhibiting the activity of these cytokines.[15] Abrocitinib, a highly selective JAK-1 inhibitor that is orally administered, was approved by the Food and Drug Administration in 2022 for the treatment of moderate to severe atopic dermatitis.[16]

The current study suggested that in granuloma-associated inflammatory diseases, cytokines are produced by both macrophages and T cells, collectively amplifying the inflammatory response. Specifically, T cell secretion of IFN-γ brings about activation of STAT1 in macrophages, and activated macrophages produce IL-6, which further activates STAT3 in T cells.[17,18] In the presence of pathogenic antigens, these mutually reinforcing cytokine programs may have created a self-sustaining cycle, thus perpetuating granulomatous inflammation. Drugs that disrupt the cytokine-based JAK-STAT pathway between the above two aspects. Afterwards, they could be an effective approach to treat the disease. As a highly selective JAK-1 inhibitor, the rapid onset of action, safety, and tolerability of abrocitinib may heighten patient adherence to the treatment regimen. Consequently, we elected to administer abrocitinib to our patients, ultimately achieving satisfactory therapeutic outcomes.

This study has several limitations that should be ameliorated in the near future. First and foremost, as this report is based on a single case, the results are not generalizable to all patients with DONs. On top of that, the mechanism of abrocitinib's

treatment of DONs is unclear, and the use of drugs is not standardized. Last but not least, assessing the long-term efficacy and safety of abrocitinib necessitates long-term follow-up studies.

Conclusion

It is said that the best way to deal with complications after injections of skin fillers is to avoid them. Given the massive popularity of such products, plastic surgeons and dermatologists will be increasingly confronted with associated complications, such as DONs. Despite the availability of treatments, they present challenges due to adverse effects, high recurrence rates, and unpredictable treatment outcomes. In this case, abrocitinib quickly and effectively relieved the patient's symptoms such as rash and improved the patient's quality of life. However, larger observational studies are recommended to fully understand the potential benefits of abrocitinib in actual clinical practice.

Consent Statement

The patient had given written informed consent for the publication of her clinical details and accompanying images. The Hospital Ethics Committees of the Fifth People's Hospital of Hainan Province approved to publish the case details.

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Disclosure

The authors declare no conflicts of interest in this work.

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