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Opt for Methotrexate Before Biologics in the Treatment of Recalcitrant Delayed-Onset Reactions to Dermal Fillers

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To the Editor:

We read with interest the case of a post-hyaluronic acid (HA) filler reaction treated with abrocitinib, a JAK inhibitor (JAKi), by Lopez and colleagues.[1] The article brings to light a crucial issue in aesthetics: the treatment of challenging delayed-onset reactions (DIRs) that show an unsatisfactory response to established therapies, including oral antibiotics, intralesional and oral steroids, and hyaluronidase injection.[2-4] Such reactions commonly present with granuloma formation.[5] Lopez et al. elaborate that the satisfactory response to abrocitinib in their case mirrors the reported response of sarcoidosis, granuloma annulare, and ulcerative colitis to tofacitinib, another JAKi.[1] While the case of Lopez et al. is a significant development, it is limited by the description of partial response ('improvement'), lack of histopathology and short follow-up (2 months) that does not ensure that the DIR would not recur, given the short half-life of abrocitinib.

JAKis can cause serious and life-threatening adverse effects and should be avoided in patients with a history of active malignancies, thromboembolic phenomenon, and cardiovascular disease.[6] The long-term safety data of JAKis are limited. JAKis can decrease immune surveillance and increase the susceptibility to cancer in patients with rheumatoid arthritis.[7] However, there are limited data on the nonmelanoma skin cancer risk among patients taking abrocitinib.[7] We recently saw a case of an aggressive, metastatic squamous cell carcinoma that developed and progressed fast after the patient was started on abrocitinib.

Low-dose oral methotrexate (MTX) is a safe and effective treatment option for challenging DIRs and has more available data than abrocitinib.[8-11] Also, MTX has a much longer use history in inflammatory skin conditions. MTX treatment was demonstrated to be beneficial in the management of delayed inflammatory reactions induced by HA,[11] liquid injectable silicone (LIS),[8,9,11] polymethylmethacrylate (PMMA),[9] hydroxyethylmethacrylate,[9] and polycaprolactone.[10]

We recently published a series of 13 patients that developed recalcitrant DIRs to dermal filler injection.[11] Eight reactions were triggered by injection of HA fillers, 4 by LIS, and 1 by PMMA. The average starting dosage of MTX was 12.1 mg/week (range, 7.5-12.5 mg/week). Patients were treated for 2-3 months in most cases. The average follow-up post-MTX therapy was 11.8 months. Complete response to MTX treatment was observed in 10 patients (6 HA and 4 LIS cases), partial response in 1 (HA case), and unsatisfactory response in 2 (HA and PMMA cases). No DIR recurrences in cases that showed a complete response were observed in the follow-up period.

MTX treatment was tolerated well in our series, with mild, temporary transaminase elevation in 1 patient.[11] Oral folic acid supplementation (FAS) minimized other adverse effects, and the only case of nausea was observed in a patient that did not receive FAS. Low-dose (ie, up to 15 mg per week) short-term oral MTX treatment is considered safe.[11] While laboratory monitoring during low-dose MTX therapy is recommended, liver function abnormalities from low-dose MTX are mild and deemed reversible upon discontinuation of the drug. Lipid abnormalities may occur with abrocitinib; laboratory monitoring of complete blood cell counts and lipid panels is recommended.

The body of literature described above favors low-dose oral MTX as second-line therapy for DIRs to fillers that have not responded to conventional therapies, such as oral antibiotics, intralesional and oral steroids, and hyaluronidase. Its rapid efficacy and good safety profile support its use in managing challenging DIRs.[11] As there are no clear advantages to JAKis, MTX should be used as the first treatment option in cases of resistant HA-induced DIRs. A cost-benefit analysis overwhelmingly supports using MTX over JAKis, as MTX is significantly less expensive.

DISCLOSURES

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