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LETTER

# Neoadjuvant intralesional methotrexate for juvenile xanthogranuloma in an adult

Dear Editor,

Juvenile xanthogranuloma (JXG) is a non-Langerhans cell histiocytosis usually occurring in infants and typically located in the head or neck.[1] Clinically, solitary skin lesions are found in 60%–82% of patients and the most common variant is characterized by one yellowish nodule. Adult onset is rare, and although JXG is usually self-limiting in children, spontaneous resolution is uncommon at older ages. In addition, up to 50% of patients with spontaneous regression develop an atrophy or anetodermal area.[2] Thus, complete excision is frequently performed in this population subgroup to achieve better cosmetic results. In disseminated forms, different chemotherapy regimens, corticosteroids and other systemic therapies are used. Herein, we report a case of adult JXG treated with intralesional methotrexate (MTX) resulting in a rapid reduction in size.

A 20-year-old man presented with a 2-month history of a well-demarcated and rapidly enlarging nasal pink nodule with recent ulceration, measuring 0.8 cm (Figure 1A). No lymphadenopathies or analytical abnormalities were noted. Since cutaneous biopsy could not be performed owing to patient's refusal and in view of the rapid growth and the keratotic surface of the tumor (a scale was removed before the Figure 1A was taken), he was misdiagnosed of keratoacanthoma (KA). Taking into account the cosmetic importance of the area affected, a single intralesional injection with 0.6 ml of MTX (25 mg/ml) was administered. One month after infiltration, a substantial reduction in tumor size was observed, with no adverse events (Figure 1B). Finally, the residual tumor was surgically removed and submitted for histopathological examination. Results showed a histiocytic proliferation in the dermis with Touton giant cells presenting few mitoses but no significant cytologic atypia (Figure 1C,D). Immunohistochemically, cells were positive for CD68 and negative for S100. According to these histopathological findings, the lesion was diagnosed as adult JXG. After 24 months of follow-up, no recurrence has occurred.

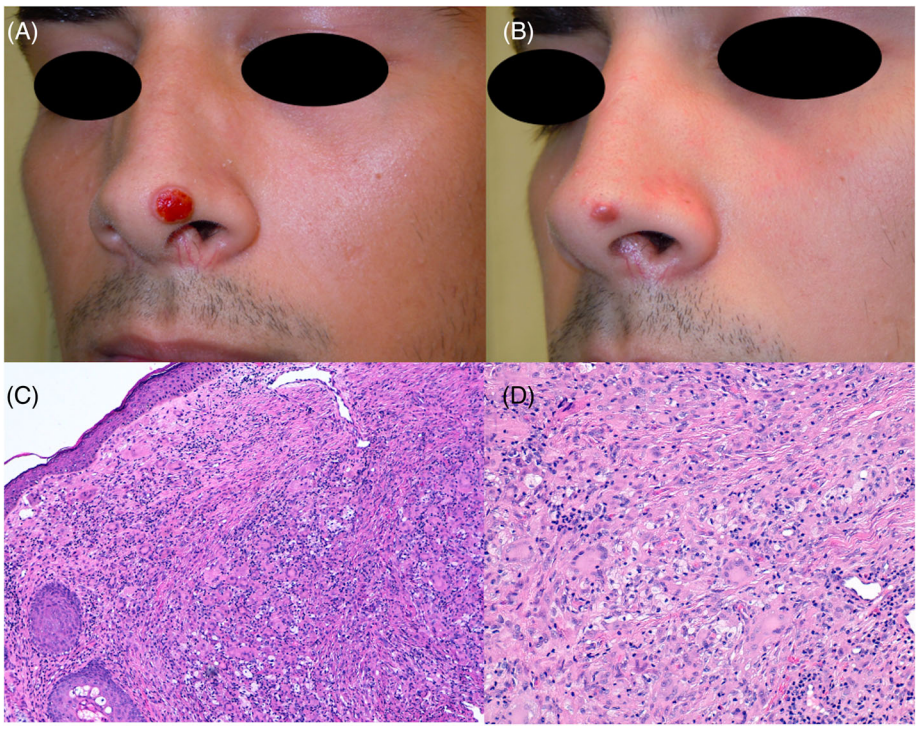


**FIGURE 1** (A) Well-demarcated nasal nodule with crateriform ulceration in the nose before treatment. (B) Tumor reduction 1-month after methotrexate injection. (C) Histiocytic proliferation limited to the dermis (×10). (D) Cells with abundant and focally foamy eosinophilic cytoplasm, regular vesicular nuclei, and Touton-giant-cells with a *wreath-like* arrangement of nuclei (×20)

MTX is a well-known folic acid antagonist widely used in inflammatory diseases and neoplasms.[3] Regarding skin tumors, its use in KA[4] and squamous cell carcinoma (SCC)[5] has been reported. Rarely, cutaneous histiocytic proliferations can show an unusual morphology and, when presenting as keratotic and rapidly enlarged forms specially in sun-exposed areas in adults, they could resemble KA or SCC.[6] In this way, our misdiagnosis before administering MTX led to the fortuitous finding that intralesional MTX may be effective in JXG. MTX has been successfully employed in combination with other chemotherapy agents in systemic JXG treatment[7] and orbital xanthogranuloma,[8] supporting its potential efficacy against this entity. However, we have not found reports about its intralesional use to treat solitary JXG. Nevertheless, other intratumoral injections such as triamcinolone acetonide for limbal xanthogranuloma, have been described with successful results.[9]

Recently, histological changes after intralesional MTX treatment in cutaneous SCC have been described. A chronic inflammatory reaction composed of lymphocytes, histiocytes and plasma cells was reported in all treated cases with frequent presence of necrosis areas, local fibrosis, and remaining dysplastic cells. In this respect, it is worthy of mention that characteristic histopathological clues of JXG as presence of xanthomatous/foamy histiocytes or Touton cells were not observed in any case.[10]

As noted above, spontaneous resolution of adult onset JXG is uncommon, and an area of atrophy frequently develops. Therefore, we propose intralesional MTX, especially in JXG located in important cosmetic areas, in monotherapy or as a neoadjuvant option. Further studies are needed to help determine the efficacy and safety of this treatment in non-spontaneously resolved JXG and in other non-Langerhans cell histiocytoses limited to the skin, in which it could also be an alternative.

We report a case of adult onset JXG successfully treated with intralesional MTX followed by surgical removal, a novel therapeutic option.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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