ANGIOLYMPHOID HYPERPLASIA WITH EOSINOPHILIA TREATED WITH LOW-DOSE METHOTREXATE

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INTRODUCTION

Angiolymphoid hyperplasia with eosinophilia (ALHE) is an uncommon, benign disorder that presents as solitary or multiple papulonodules, located predominantly in the head and neck region. The pathogenesis of ALHE remains controversial. It has occurred following various forms of trauma or infection. The disorder is commonly regarded as an angioproliferative process accompanied by an inflammatory infiltrate that is thought to be a reactive component. ALHE may represent a T-cell lymphoproliferative disorder of a benign or low-grade malignant nature. Other reported cases have shown damaged arteries and veins at the base of the lesion, suggesting that an underlying arteriovenous malformation may play a role in the pathogenesis. Additionally, some evidence suggests that ALHE may be related to traumatic pseudoaneurysm, supporting a vascular origin.

Multiple treatments are proposed in the dermatologic literature for ALHE. We report a case of multiple lesions on the neck treated with low-dose methotrexate.

CASE REPORT

A 31-year-old woman presented in 2006 with a single erythematous nodule with overlying fine scales located on the right side of the neck. Three months later, she returned to the clinic with additional new lesions on the same side of the neck. Ultrasound scan and cutaneous magnetic resonance imaging showed proliferation of subcutaneous blood vessels without arteriovenous malformation. The histopathology findings showed vascular hyperplasia lined by enlarged endothelial cells that have ovoid nuclei and intracytoplasmic vacuoles accompanied by mixed inflammatory infiltrate of lymphocytes and eosinophils (Fig 1). Peripheral hypereosinophilia (900 g/L) was also seen. The patient was treated initially with oral prednisone, 30 mg daily for 1 month, resulting in complete regression of the lesions. She gained 6 kg during the treatment period but showed no other adverse effects. However, despite slowly tapering the prednisone, the lesions recurred 48 hours after stopping treatment. Remarkable long-lasting improvement was observed after initiation of pulsed dye laser therapy. A total of 6 complete sessions at a rate of one session per month led to resolution of symptoms for 6 years. After 6 years,
she had another relapse that was resistant to 4
sessions of pulsed dye laser therapy (Fig 2, A).
The patient refused to take systemic steroids because of
their adverse side effects. While reviewing the
dermatologic literature, we found a case of orbital
ALHE resistant to corticosteroid therapy in which
the patient was treated successfully with low-dose
methotrexate and remained symptom free 1 year
after discontinuation of the treatment. After
an extensive discussion of the different treatment
modalities and their potential risks and benefits
with our patient, we opted for the initiation of
methotrexate. The patient was started on metho-
trexate, 15 mg/wk for 12 months, after which we
observed that the lesions were significantly
improved (Fig 2, B). The dose was subsequently
reduced to 10 mg/wk for 7 months and then to
5 mg/wk for 3 months, after which methotrexate
was stopped. The patient remained free of recur-
rence with a 4-month follow-up.

DISCUSSION

Treatment is usually required for ALHE, as
spontaneous regression is rare. Many treatments
are proposed in the dermatologic literature.
Complete surgical excision is the preferred choice,
but recurrence may happen if excision is incomplete.
Other alternative treatments have been reported
with variable levels of success. These treatments
include laser therapy (pulsed dye, CO2, copper
vapor), systemic or intralesional corticosteroid
injection, cryotherapy, imiquimod, tacrolimus,
isotretinoin, radiotherapy, interferon alfa 2a, anti-
interleukin-5 antibody, photodynamic therapy, and
methotrexate. The surgical excision was not applicable in our
case because of the multiplicity and the infiltrative
nature of the lesions. This infiltrative nature could
also explain the inefficacy of laser therapy at this
stage.

Methotrexate is a potent competitive antagonist
of the enzyme dihydrofolate reductase that is essential
in DNA synthesis process. Methotrexate has anti-
flammatory, immunosuppressive, and antiprolifer-
ative effects and has been used successfully in the
treatment of various skin diseases either with or
without a vascular component. Examples of these
cutaneous lesions with vascular components include
various vasculitides such as polyarteritis nodosa,
Takayasu arteritis, and Wegener granulomatosis. The
advantages of methotrexate include the
once-weekly administration, the well-established
side-effect profile, and the low cost.

The treatment regimen was well tolerated in our
case, and the patient had a positive response. This
response can be attributed to methotrexate’s dual
mechanism of action: anti-inflammatory and
antiangiogenic. The patient underwent periodic
check-ups with no adverse effects observed either
clinically or from laboratory markers that included
complete blood count with differentiation,
creatinine, and liver transaminases. We continue
following up with her and observing the efficacy of
the treatment. Although there are no studies to
confirm the most effective management regimen,
we believe that methotrexate could have a promising
role in the treatment of ALHE.

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