

第 5 4 号

出典：皮膚科学専門誌 1992 年 10 月論文

「Journal of the American Academy of Dermatology」

メトロニダゾール単剤外用剤の抗炎症作用及び免疫抑制作用

Title : [Treatment of recalcitrant cheilitis granulomatosa with metronidazole.](#)

表題 : 難治性肉芽腫口唇炎をメトロニダゾールで治療。

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論文掲載誌 : Journal of the American Academy of Dermatology 1992 Oct;27(4):629-30.

同誌 1992年10月(4)629~630頁

要旨掲載なし : No abstract available.

PubMed の ID : PMID: 1401320 [PubMed - indexed for MEDLINE]

630頁の上から18行目から21行目(添付ファイルの2/2を参照)に次のように記載あり。(以下、原文のまま)

The mechanism of action of MNZ is unknown but may be related to its anti-inflammatory properties. MNZ suppress granuloma formations around parasite eggs and inhibits cell-mediated immunity.

MNZ(メトロニダゾール)の作用機序は知られていないが、この薬剤の特質である抗炎症作用が関連していると考えられる。MNZは(メトロニダゾール)は、寄生虫卵の周辺の肉芽腫形成を抑制し、細胞媒介性免疫を抑制する。

Treatment of recalcitrant cheilitis granulomatosa with metronidazole

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Cheilitis granulomatosa (CG), a rare disorder of unknown origin, is characterized by swelling of one or both lips with typical granulomatous findings on histologic examination. The condition usually follows a refractory course of swelling progressing to permanent distortion of the normal anatomic architecture of the face with resulting functional problems. Antibiotics, antifungal drugs, antiinflammatory drugs, oral or intralesional corticosteroids, x-ray therapy, and surgery have been used in treatment with little therapeutic effect.¹

We previously described a patient with CG who also had an early stage of Crohn's disease.² This patient failed to improve with intralesional corticosteroids but responded dramatically to metronidazole (MNZ), which has often been used to treat intestinal Crohn's disease. The response of this patient to MNZ emphasizes the association of CG with Crohn's disease.

CASE REPORT

A 56-year-old woman was seen in September 1988, with a 2-month history of swelling of the left side of her lower lip. The swelling extended slowly around the mouth. Examination revealed that the lower lip on the left side was indurated, erythematous, and swollen. The adjacent perioral skin was also involved (Fig. 1). A biopsy specimen showed multiple noncaseating granulomas throughout the dermis.

Although the patient had no gastrointestinal symptoms, sigmoidoscopy revealed multiple ulcers in the sigmoid colon and upper rectum. A biopsy specimen showed noncaseating granulomatous inflammation compatible with Crohn's disease. She was initially treated with ketotifen, 400 mg daily, for 4 months, but this treatment did not relieve the lip swelling. Intralesional triamcinolone acetonide (10 mg/ml) was administered 10 times in 5 months. Her lip swelling decreased slightly; there was a

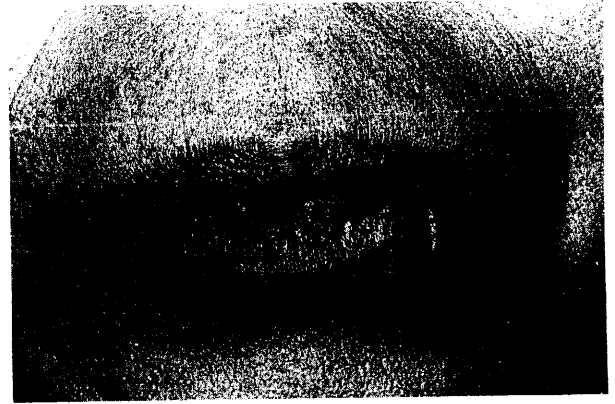


Fig. 1. Swelling of left side of lower lip before treatment with MNZ.



Fig. 2. After 3 months, complete healing of lesion was achieved.

tendency to relapse. In 1989, oral MNZ, 500 mg twice daily, was given. After 1 month the lip was much improved, and after 3 months complete healing was achieved (Fig. 2). Her condition was successfully maintained with that dosage for 2 months without intralesional corticosteroids. After discontinuation of this drug, there was no relapse for 2 years. Her ulcers in the colon and rectum also cleared.

DISCUSSION

A few treatments of CG have had some success. Podmore and Burrows³ used clofazimine to treat four patients with CG and were able to induce the

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16/54/37816

histologic disappearance of granulomas. However, in these patients, facial edema persisted. Kato and Tagami⁴ found a mast cell stabilizer (Tranilast) to be effective in one patient. Chiba et al.⁵ also reported that two of three CG patients treated with mast cell stabilizers, ketotifen and/or Tranilast, showed complete resolution. Our patient was unresponsive to these treatments.

MNZ, one of a group of nitroimidazole compounds, was originally shown to be effective in the therapy for human trichomonal infections.⁶ Bernstein et al.,⁷ Brandt et al.,⁸ and Duhra and Paul⁹ used MNZ in the treatment of Crohn's disease and found complete or significant healing in most patients. MNZ has also proved to be effective in the treatment of perioral dermatitis and papulopustular rosacea. These results prompted us to use MNZ in our patient.

The mechanism of action of MNZ is unknown but may be related to its antiinflammatory properties. MNZ suppresses granuloma formations around parasite eggs and inhibits cell-mediated immunity.¹⁰ MNZ is well tolerated by most patients. Adverse effects caused by a prolonged or high-dose regimen are most commonly gastrointestinal symptoms such as nausea and vomiting and a metallic taste. The

most serious toxicity occurs in the central nervous system, but this is reversible.⁶

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Alopecia universalis in a patient seropositive for the human immunodeficiency virus

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Immunologic processes probably are important in the pathogenesis of alopecia universalis although the exact mechanism remains unclear. Human immunodeficiency virus (HIV) infection results in immune dysregulation that may manifest as autoimmune phenomena.¹ We report a case of alopecia universalis that developed 2 years after HIV antibody was detected. To our knowledge this is the first report of HIV seropositivity associated with alopecia universalis.

CASE REPORT

A 37-year-old homosexual man was found to be HIV antibody positive in January 1986. He started to lose scalp hair in 1988 and eyelashes in 1989. He was otherwise without symptoms and had no HIV-related diseases. There was no significant personal or family history and he was not taking any medications. Examination demonstrated loss of all scalp hair, eyelashes, eyebrows, and all body hair (Fig. 1). Pitting of the fingernails was evident. His CD4 count was 810 (normal >400), immunoglobulin concentrations were normal, and the VDRL was negative.

DISCUSSION

Various humoral and cellular immunologic abnormalities have been described in patients with

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No reprints available.

16/54/38322