

ovoid-shaped *Giardia* cysts. A one-day oral treatment with ornidazole (Tiberal<sup>®</sup>, Roche) at dosage of 1,500 mg, then repeated after 2 weeks, was given. The cutaneous lesions gradually improved after the first dose of the drug. After one month, however, new papules on elbows appeared and a coproparasitological control revealed the persistence of the parasitic infection. A new cycle of ornidazole (1,500 mg/day for 3 days) was prescribed. One month later both cutaneous lesions and *Giardia* cysts in stools were still present. An alternative treatment with oral paromomycin (Humatin<sup>®</sup>, Parke-Davis), 500 mg q.i.d for 5 days was prescribed. The parasitological follow-up at 1, 3 and 6 months was negative and cutaneous signs and symptoms completely resolved.

## DISCUSSION

The strict relationship between cutaneous lesions and giardiasis was confirmed by the response to specific therapy (12–14). Probably, as in helminth infestations, a T-cell-mediated delayed hypersensitivity reaction may recall eosinophils (15, 16), but induction of cutaneous lesions remains unclear.

Recently, Wells' syndrome associated with recurrent giardiasis has been reported, underlying, again, the presence of eosinophils (17). The histopathologic findings of our patient were characterized mainly by lymphocytes, with many eosinophils, which, however, were not the predominant component of the infiltrate, with no evidence of the so-called flame figures. On the basis of these findings, a diagnosis of eosinophilic cellulitis could be excluded. Clinically, the papules and some excoriated lesions could also suggest lichenified atopic dermatitis; however their localization (dorsum) and their distribution (crops of brownish papules) were not characteristic of atopic dermatitis and the histopathologic findings were not consistent with lichen simplex chronicus. This lichen-planus-like clinical presentation without histopathology of lichenoid dermatitis, should be considered in the spectrum of clinical and histopathologic cutaneous findings during *Giardia intestinalis* infection, more frequently characterized by urticaria or atopic dermatitis lesions.

## REFERENCES

- Smith LA. Still around and still dangerous: *Giardia lamblia* and *Entamoeba histolytica*. Clin Lab Sci 1997; 10: 279–286.
- Ridley MJ, Ridley DS. Serum antibodies and jejunal histology in giardiasis associated with malabsorption. J Clin Pathol 1976; 29: 30–34.
- Luján HD, Mowatt MR, Byrd LG, Nash TE. Cholesterol starvation induces differentiation of the intestinal parasite *Giardia lamblia*. Proc Natl Acad Sci USA 1996; 93: 7628–7633.
- Geller M, Geller M, Flaherty DK, Black P, Madruga M. Serum levels in giardiasis. Clin Allergy 1978; 8: 69–71.
- Nash TE, Herrington DA, Losonsky GA, Levine MM. Experimental infections with *Giardia lamblia*. J Infect Dis 1987; 156: 974–984.
- Di Prisco MC, Hagel I, Lynch NR, Jimenez JC, Rojas R, Gil M, et al. Association between giardiasis and allergy. Ann Allergy Asthma Immunol 1998; 81: 261–265.
- Kennou MF. Skin manifestations of giardiasis. Some clinical cases. Arch Inst Pasteur Tunis 1980; 57: 257–260.
- Sánchez-Carpintero I, Vázquez-Doval FJ. Cutaneous lesions in giardiasis. Report of two cases. Br J Dermatol 1998; 139: 152–169.
- Farthing MJG, Chong SKF, Walker-Smith JA. Acute allergic phenomena in giardiasis. Lancet 1983; 17: 1428.
- Veronesi S, Palmerio B, Negosanti M, Tosti A. Urticaria and giardiasis. Dermatologica 1983; 166: 42–43.
- Spaulding HS Jr. Pruritus without urticaria in acute giardiasis. Ann Allergy 1990; 65: 161.
- Werkman HP, Meuwissen JH. Single-dose treatment of giardiasis with ornidazole in children. Lancet 1979; 2: 1373.
- Bulut BU, Gulnar SB, Aysev D. Alternative treatment protocols in giardiasis: a pilot study. Scand J Infect Dis 1996; 28: 493–495.
- Nash T. Efficacies of zinc-finger-active drugs against *Giardia lamblia*. Antimicrob Agents Chemother 1998; 42: 1488–1492.
- Smith PD, Gillin FD, SpiraWM, Nash TE. Chronic giardiasis: studies on drug sensitivity, toxin production, and host immune response. Gastroenterol 1982; 83: 797–803.
- Singer SM, Nash TE. T-cell dependent control of acute *Giardia lamblia* infections in mice. Infect Immun 2000; 68: 170–175.
- Canonne D, Dubost-Brama A, Segardr M, Piette F, Delaporte E. Wells' syndrome associated with recurrent giardiasis. Br J Dermatol 2000; 143: 425.

## A Patient with a Muco-cutaneous Eruption and Intestinal Giardiasis

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Sir,

Acute neutrophilic dermatoses are a diagnostic challenge to clinicians and can sometimes mimic erythema nodosum (EN). Overlapping of the clinical dermatoses and their histopathology exists and the relationship between skin manifestations and potential etiologic factors may be indefinite. We describe here a case where the diagnosis of EN was established by biopsy and where intestinal giardiasis was recognized as a potential etiopathogenetic agent.

## CASE REPORT

A 44-year-old woman presented with intermittent fever, up to 40°C, lasting 5 days and followed by painful skin nodules and

pustules in association with stomatitis, painful vaginal erosions and arthralgia. The patient had been using contraceptive pills for about 3 years but was taking no other permanent medication. Neither had she any remarkable health problems, apart from a history of recurrent aphthous stomatitis, which recidivated one week before the present illness.

On examination, the patient appeared tired and sick. She complained about arthralgia in her knees. The lower legs were painful and swollen, with several inflamed, bright red, slightly raised nodules. The nodules (2 to 5 cm in diameter) also occurred on the arms, in the upper part of the body and in the genital mucosa. A central pustule was seen in some nodules and pustular lesions occurred diffusely in the skin. In the

buccal mucosa, the patient had a couple of slightly red lesions after the healing aphthous stomatitis, and in the vaginal mucosa, 3 aphthae-like, 1–2 cm-wide painful erosions. Otherwise, the gynecological status was normal.

On admission, the serum C-reactive protein (CRP) was 280 mg/l (normal < 10 mg/l) and the erythrocyte sedimentation rate (ESR) was 26 mm/h. Peripheral blood white cell count was  $19.7 \times 10^9/l$  (normal  $3.4-9 \times 10^9/l$ ) with  $13.6 \times 10^9/l$  (79%) polymorphonuclear and  $0.03 \times 10^9/l$  (0%) eosinophilic cells. The serum creatinine value was normal. Urinalysis showed microscopic hematuria and proteinuria; the daily protein excretion in the urine was 0.6 g. Liver function tests were normal as well as an X-ray examination of the lungs. On admission, the patient had intermittent fever, and because of suspected septic bacterial infection, intravenous ceftriaxone (2 g daily) was started. When the fever persisted, 4 days later, Behçet's disease was then suspected. The clinical examination by the neuro-ophthalmologist was normal and no parherygia was observed. Owing to the strong suspicion of a reactive state, oral prednisolone (60 mg daily) was started. One day later the temperature of the patient had normalized, her general condition remarkably improved, the CRP had decreased to 70 mg/l and ESR was 32 mm/h. Oral prednisolone medication continued for 2 weeks, at decreasing doses. The patient was then symptom free and the CRP was 2 mg/l.

A skin biopsy, taken 2 days after admission and before commencement of corticosteroid treatment, revealed a mild perivascular infiltrate of lymphocytes in the upper dermis. Deeper in the dermis there was dense infiltration of mainly neutrophilic granulocytes with some histiocytes, which also infiltrated the adipose tissue septa corresponding to histopathology of lobular panniculitis. A diagnosis of EN was made.

Detailed serological tests for viruses, bacteria and other infectious agents were performed to reveal a potential infectious etiology of the patient's disease. No remarkable increase in antibodies to the *Streptococcus*, *Staphylococcus*, *Borrelia*, *Salmonella*, *Campylobacter*, *Yersinia*, *Mycoplasma* or *Chlamydia* species was detected. Neither was there any evidence of acute or recent infection caused by cytomegalovirus or *Herpes simplex* virus. No remarkable findings were detected in the bacterial cultures taken from the blood, skin swabs, urine and feces or in the *Herpes simplex* culture taken from the genital erosions. However, when the fecal parasites were examined, fecal carriage of *Giardia lamblia* was detected. The patient had visited Egypt 4 months earlier, and suffered from diarrhea at that time. She was now given a one-week course of metronidazole (800 mg 3 times a day) orally, simultaneously with the prednisolone medication.

Two weeks later, in a visit to our outpatient clinic, it was found that the patient was completely healed.

## DISCUSSION

We consider that the hidden giardiasis could have been the triggering agent of the mucocutaneous manifestations in our patient. This concept is conceivable, since different gastrointestinal pathogens have been mentioned as etiologic agents for EN (1, 2) and other immune-complex mediated phenomena (3). Review of the literature revealed two previous reports, where giardiasis was suspected as an etiologic agent for EN (4, 5). Previously, giardiasis has been associated with various other reactive skin manifestations, such as chronic urticaria, Quincke's oedema, urticaria vasculitis and Well's syndrome (6, 7).

Systemic diseases associated with EN include sarcoidosis, inflammatory bowel diseases, and malignant diseases. Our patient did not show any signs of these diseases. The panniculitis, the pustular lesions, aphthous mucosa and arthralgia as well as the clinical and the histopathological findings were reminiscent of Behçet's disease (8). There were no neuro-ophthalmologic symptoms, but their occurrence is known to be variable (9). Although the patient recovered completely during corticosteroid therapy followed by oral metronidazole, the possibility of Behçet's disease must be reconsidered, if similar symptoms recur.

The clinical features of our patient also resembled those of Sweet's syndrome. Unfortunately the apparently pustular skin lesions, which occasionally were deep and nodular, were not biopsied. Overlapping cases of Sweet's syndrome and EN have been reported earlier (10). Simultaneous occurrence of Behçet's disease and Sweet's syndrome has also been suspected in occasional cases (11–13), reflecting the difficulty in making definite differential diagnoses in some cases.

Several drugs, including contraceptive pills, have been described as causing EN, although the association tends to be uncertain (1, 2, 14). Our patient had used contraceptive pills for years and afterwards she continued with the same type of contraception. Thus, it could only have had some co-influence on other simultaneous triggering factors.

This case provides further data on the potential association between EN-like lesions, neutrophilic dermatoses and intestinal giardiasis. It is recommended that the possibility of intestinal giardiasis should be considered in patients with a reactive panniculitis corresponding to EN.

## REFERENCES

- Cribrier B, Caille A, Heid E, Grosshans E. Erythema nodosum and associated diseases. A study of 129 cases. *Int J Dermatol* 1998; 37: 667–672.
- Garcia-Porrúa C, Gonzalez-Gay MA, Vazquez-Caruncho M, Lopez-Lazaro L, Lueiro M, Fernandez ML, et al. Erythema nodosum: etiologic and predictive factors in a defined population. *Arthritis Rheum* 2000; 43: 584–592.
- Baldock NE, Catterall MD. Erythema nodosum form yersinia enterocolitica. *Br J Dermatol* 1975; 93: 719–720.
- Giordano N, Fioravanti A, Mariani A, Marcolongo R. Erythema nodosum and *Giardia intestinalis*. *Clin Rheumatol* 1985; 4: 481–483.
- Harries AD, Taylor J. Erythema nodosum associated with invasive amoebiasis and giardiasis. *Br J Dermatol* 1986; 114: 394.
- Cdirila M, Panaitescu D, Capraru T. Frequency of *Giardia lamblia* in certain allergic syndromes. *Med Intern* 1981; 19: 367–372.
- Canonne D, Aubost-Brama A, Segard, Piette F, Delaporte E. Well's syndrome associated with recurrent giardiasis. *Br J Dermatol* 2000; 143: 425–427.
- Jorizzo JL, Abernethy JL, White WL, Mangelsdorf HC, Zouboulis CC, Sarica R, et al. Mucocutaneous criteria for the diagnosis of Behçet's disease: an analysis of clinicopathologic data from multiple international centers. *J Am Acad Dermatol* 1995; 32: 968–976.
- Zouboulis CC. Epidemiology of Adamantoides-Behçet's disease. *Ann Int Med (Paris)* 1999; 150: 488–498.
- Cohen PR, Holder WR, Rapinai RP. Concurrent Sweet's syndrome and erythema nodosum: a report, world literature review and mechanism of pathogenesis. *J Rheumatol* 1992; 19: 414–420.
- Uysal H, Vahabogly H, Inan L, Vahabogly G. Acute febrile neutrophilic dermatosis (Sweet's syndrome) in neuro-Behçet's disease. *Clin Neurol Neurosurg* 1993; 95: 319–322.
- Lee MS, Barnetson RS. Sweet's syndrome associated with Behçet's disease. *Aust J Dermatol* 1996; 37: 99–101.
- Ginarte M, Toribo J. Association of Sweet syndrome and erythema nodosum (letter; comment). *Arch Dermatol* 2000; 136: 673–674.
- Bartelmeyer JA, Petrie RH. Erythema nodosum, estrogens and pregnancy. *Clin Obstet Gynecol* 1990; 33: 777–781.