Isospora induced diarrhea in a pemphigus vulgaris patient

Sir,

A 50-year-old woman with pemphigus vulgaris for four years was treated with oral steroids and five pulses of methylprednisolone for one year before she was seen at our institution and started on intravenous dexamethasone-cyclophosphamide pulse therapy. She received intravenous dexamethasone 100 mg for three days along with cyclophosphamide 500 mg on the second day; the cycle was repeated every 28 days with daily cyclophosphamide 50 mg and supplementary oral steroids (starting with tablet prednisolone 30 mg/day and tapered after every pulse). Her lesions improved but smouldered on and she received 23 pulses monthly for two years. Since the disease was recalcitrant, she was then given four doses of injection rituximab 375 mg/m^2 body surface area every week for 3 weeks followed by a fourth dose given three months after the first dose. Her lesions healed and oral steroids were tapered and stopped over a period of three months. The disease was then under control, and she was continued on modified dexamethasone-cyclophosphamide pulse therapy practiced at our institution i.e. dexamethasone 48 mg and cyclophosphamide 500 mg without additional oral steroids.

During this period, she developed recurrent diarrhea associated with crampy abdominal pain, occasional fever and loss of appetite. The consistency of stool was semi-solid with traces of mucus but it was not blood stained or foul smelling. Microscopic examination of the stool specimen and gastroduodenoscopy with biopsy performed at a local hospital situated in another state were inconclusive. She skipped her routine monthly pulse therapy dose and presented to our institute after two months when her symptoms persisted and she also noticed weight loss upto 10 kgs within this period.

General examination of the patient revealed mild pallor. Laboratory findings showed normochromic normocytic anemia (hemoglobin 10.2 g/dl) and a WBC count of 5,400/mm^3 with no peripheral eosinophilia. Other laboratory results including liver function and renal function tests were normal. The chest X-ray was within normal limits. The HBsAg and antibodies to HIV and HCV were negative. When specifically looked for, repeat microscopic examination of a fresh stool specimen showed oocysts of *Isospora belli* on a wet mount preparation using 0.85% normal sterile saline. Immature sporulating oocysts of *I. belli* were seen on modified Ziehl–Neelsen staining technique [Figure 1].

After the report of stool examination was obtained, the patient was started on trimethoprim-sulfamethoxazole (160/800 mg) four times daily for 10 days and twice daily for the next three weeks. The gastrointestinal symptoms resolved within three days of initiating the treatment. Two repeat fecal specimens collected at one week intervals post treatment did not reveal oocysts of *I. belli* thus indicating parasitological cure.

Infections are an important complication in pemphigus vulgaris due to the loss of epidermal barrier caused by the disease and immunosuppression caused by systemic steroids and immunosuppressants that are the mainstay of treatment.[1,2] Recalcitrant cases have been successfully treated with intravenous rituximab. With the concurrent use of intravenous corticosteroids and rituximab, infectious adverse effects such as pneumonia, herpes simplex, cytomegalovirus (CMV) gastritis/retinitis, septic arthritis, and sepsis have been reported.[3,4] It is observed that several complications such as oral candidiasis, localized herpes simplex, bacterial skin infection, urinary tract infection (UTI), pulmonary infections, and sepsis are associated with high doses of corticosteroids and immunosuppressive therapies in patients with pemphigus vulgaris. The most common pathogens isolated from cultures were *Staphylococcus aureus* from skin infections and *Escherichia coli* from the urinary tract.[5] In another study conducted by Belgnaoui *et al.*, bacterial (52%), fungal (50%), herpetic (19%), and parasitic (1.5%) infections were found in these patients.[6] Bilateral herpes

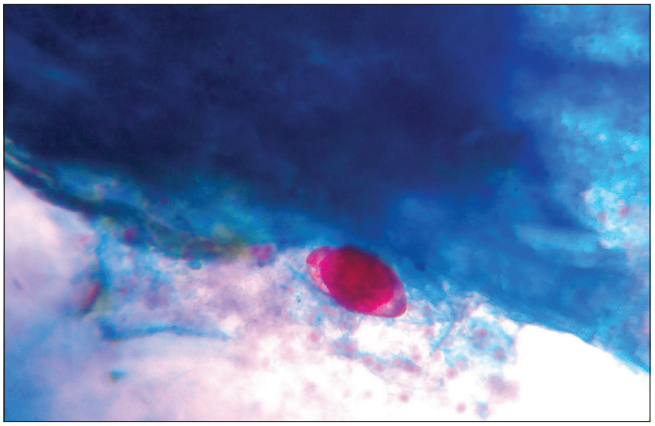

Figure 1: Modified Ziehl–Neelsen staining showing immature sporulating oocyst of Isospora belli (×1000)

simplex virus keratitis in a patient with pemphigus vulgaris has also been reported.[7] Concurrent CMV and herpes simplex virus infection have also been reported in patients with pemphigus vulgaris.[3]

Isospora belli, a coccidian protozoan parasite, causes chronic diarrhea in immunocompetent as well as HIV-infected and non–HIV-infected immunocompromised hosts. Once considered to be an AIDS-defining illness in the US in HIV-infected individuals, it has become a rare entity as a result of the widespread use of trimethoprim-sulfamethoxazole for preventing *Pneumocystis jirovecii* pneumonia. Stray cases of isosporiasis do occur in developing countries in 10-20% of immunocompromised individuals.[8] *Isospora belli* infection has been reported in patients with non-Hodgkin's lymphoma, thymoma, adult T-cell leukemia, renal transplant, and in a chronic alcoholic.[9] However, it has not been previously reported in a patient suffering from pemphigus. Isosporiasis is acquired by the ingestion of infected sporulated oocysts which transform into sporozoites that penetrate the mucosa of the small intestine to complete the life cycle. In immunocompromised individuals, infection usually results in protracted, severe diarrheal illness with resultant dehydration and malabsorption which can also progress to extraintestinal dissemination.

Patients with pemphigus vulgaris on long-term immunosuppressants or treated with rituximab, presenting with diarrhea or any gastrointestinal symptoms should be screened for opportunistic intestinal parasites. Stool examination with a modified Ziehl–Neelsen stain for parasites should be advised in such patients to detect isosporiasis.

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