An unsuspected cause of diarrhoea and gastrointestinal bleeding during corticosteroid therapy

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Abstract

We report on a fatal case of disseminated strongyloidiasis during corticosteroid treatment presenting with abdominal pain, diarrhoea and lower gastrointestinal bleeding. The patient emigrated from Thailand 16 years before the current hospitalisation. Complicated strongyloidiasis is a relatively unrecognized complication of corticosteroid therapy in non-endemic areas. In individuals who have resided in endemic areas, even decades before treatment, strongyloidiasis should be excluded before initiation of immunosuppressants. (Acta gastroenterol. belg., **2014**, 77, **259-261**).

Key words : disseminated strongyloidiasis, strongyloides stercoralis, immosuppressants, corticosteroids.

Introduction

We describe the unusual feature of development of disseminated strongyloidiasis, presenting with abdominal pain, diarrhoea and lower gastrointestinal bleeding during treatment with corticosteroids 16 years after leaving an endemic area. We make a case for screening not only patients in endemic regions, but also those who have emigrated from endemic regions, before initiation of immunosuppressive therapy.

Case report

A 59-year old female patient was referred to us because of abdominal pain and diarrhoea. She emigrated from Thailand 16 years before the development of symptoms and had not returned to southeast Asia since then. One week before admission, she started complaining of loose stools three to four times per day, intermittently tinged with bright red blood and mild dyspnea.

The patient's medical history included idiopathic focal segmental glomerulosclerosis with a nephrotic syndrome and acute renal failure two months prior to the current hospitalisation. She was treated with corticosteroids and haemodialysis up to six weeks before admission. At the moment of admission her daily medications included methylprednisolone 32 mg per day.

On examination at the time of admission, the blood pressure was 116/68 mmHg, heart rate 104 beats per minute, temperature was 37.2°C and oxygen saturation 91% while breathing ambient air. Bilateral inspiratory crackles were present at the lung bases. The abdomen was moderately distended with limited diffuse tenderness on deep palpation. On digital rectal examination, which was painless, semi-liquid feces with a small amount of red blood were found on the tip of the glove.

Biochemical analysis was remarkable for an elevated C-reactive protein (CRP) of 80 mg/L (upper limit of normal (ULN) 5 mg/L) and haemoglobin of 9.8 g/dL (normal range 12 to 16 g/dL). Chest radiography showed a slightly increased reticular attenuation of the bases of the lungs. Since a pulmonary infection was suspected, intravenous administration of amoxicillin-clavulanate was initiated. A gastroduodenoscopy, performed because of upper abdominal pain and gastrointestinal blood loss, showed white plaques in the stomach and duodenum without obvious ulcerations or blood. Duodenal and gastric biopsies were obtained and a lower gastrointestinal endoscopy was scheduled. During bronchoscopy, small amounts of blood-tinged mucus were seen from the pharynx down to the segmental bronchi without lesions. A bronchial aspirate was sent for pathological examination.

The day after admission, her clinical condition quickly deteriorated with expectoration of bloody mucus, moderate rectal blood loss and desaturation to 70% while breathing 15 litres of oxygen per minute through a non-rebreather mask. Despite endotracheal intubation, mechanical ventilation and inotropic support, her condition further deteriorated and she died 32 hours after admission.

On the next day, haemocultures showed growth of *Escherichia coli* sensitive to amoxicillin. Microscopic evaluation of faeces, bronchial aspirate specimen and gastric and duodenal biopsies (Fig. 1) revealed adult worms and larvae of *S. stercoralis*. At autopsy, the lungs showed macroscopic signs of diffuse bleeding. Multiple larvae and adult worms of *S. stercoralis* were demonstrated in biopsies of liver, stomach, duodenum and colon.

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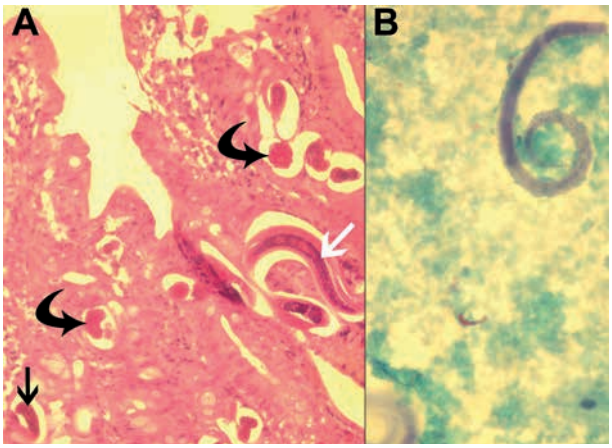

Fig. 1. — (A) Duodenal biopsy showing an adult worm (white arrow), rhabditiform larvae (black arrow) and eggs (curved arrow). (B) Multiple *Strongyloides stercoralis* larvae in a bronchial aspirate.

Discussion

S. stercoralis is a nematode that is widely distributed in tropical and subtropical areas. In southeast Asia, a prevalence of 11% has been reported (1). The life cycle of *S. stercoralis* is similar, but not identical, to other nematodes. Filariform larvae, which are the infective larvae and are found in the soil, penetrate the skin and reach the alveoli by the pulmonary circulation. The larvae ascend the tracheobronchial tree to the pharynx and are swallowed. They develop into adult worms and burrow in the small bowel mucosa. The female worms produce eggs that hatch into the non-infective rhabditiform larvae. These are excreted with the faeces, moult into filariform larvae and enter a new parasitic cycle (direct cycle). The larvae can also further develop into adult worms and reproduce by parthenogenesis or sexually to form new rhabditiform and eventually filariform larvae (indirect cycle). Contrary to other helminthic parasites, *S. stercoralis* has the unique ability to complete its life-cycle within the host by autoinfection. This phenomenon occurs when rhabditiform larvae transform into filariform larvae in the intestinal tract. The filariform larvae penetrate the colonic mucosa or perianal skin and then spread hematogenously to the lungs. They are subsequently coughed up and swallowed, completing the autoinfection cycle (2-5).

Symptoms are generally mild and include intermittent gastrointestinal (diarrhoea, constipation, abdominal pain, mild rectal blood loss), pulmonary (cough) and cutaneous symptoms (pruritus ani, urticaria or a typical 'larva currens' rash) or asymptomatic eosinophilia. These symptoms can appear for the first time decades after leaving an endemic area, due to the persistent autoinfection cycles. In immunocompetent individuals, autoinfection mostly occurs to a limited extent, allowing the parasite to persist in the host indefinitely after the primary infection. However, when cell-mediated immunity is impaired, e.g. in case of HIV, malnutrition or immunosuppressive medication, the autoinfection cycle can be accelerated and amplified (2-5). Corticosteroids are known to induce apoptosis of Th2-lymphocytes and reduce eosinophil count and thus impair anti-parasitic immunity (5,6). Increased larval burden can lead to the strongyloides hyperinfection syndrome (SHS), characterized by more severe gastrointestinal or pulmonary symptoms or disseminated strongyloidiasis (DS), with spread of the larvae to virtually every organ. Symptoms of SHS and DS are nonspecific and refer mostly to the respiratory (cough, hemoptysis, dyspnoea and, rarely, respiratory insufficiency) or gastrointestinal tract (abdominal pain, diarrhoea, hematochezia). Strongyloidiasis can also lead to systemic manifestations and sepsis caused by dissemination of the helminthic infection or by bacteraemia because of interruption of the intestinal barrier by the parasite (2,7-9). The majority of patients with bacteraemia have a fatal outcome. In a review of 38 cases of bacterial infections associated with disseminated strongyloidiasis, a 87% mortality rate was reported (8).

To avoid complicated strongloidiasis during immunosuppressive therapy, screening for strongyloidiasis before initiation of therapy is warranted in epidemiologically high-risk groups. However, diagnosis of latent strongyloidiasis is difficult because, in uncomplicated disease, the burden of worms excreted in the stools is variable and mostly limited. Examination of a single stool sample has a poor sensitivity of 25-30% (2-4). Multiple stool examinations, concentrating techniques and agar plating can increase sensitivity. Compared to stool microscopy, serologic testing is more sensitive, although less specific (4). Unfortunately, serodiagnostic testing is only available in specialized centres and cross-reactions with other parasites occur, which is more problematic in screening situations than in symptomatic patients. Furthermore, it is difficult to differentiate between active or past infection because antibodies may persist for many years after treatment (4).

Albendazole, thiabendazole and ivermectin have been shown to have adequate activity against *S. stercoralis*. Ivermectin is the drug of choice because of lower incidence of side effects and higher efficacy. A treatment with two single doses of ivermectin 200 μg/kg with an interval of two weeks is proposed for latent strongyloidiasis (10). Prompt initiation of ivermectin in combination with broad-spectrum antibiotics is critical in SHS and DS, since the frequent association with bacteraemia results in high mortality rates (8). In severe strongyloidiasis oral therapy is frequently impossible due to ileus or impaired consciousness. To date, parenterally administered antihelminthics have not been approved for human use. Case reports on subcutaneous administration of veterinary formulations of ivermectin in DS in humans show variable results (11,12).

Conclusion

Disseminated strongyloidiasis is an uncommon and relatively unrecognized complication of corticosteroid therapy. In non-endemic countries, diagnosis is often missed with fatal outcome for several reasons : 1/ eosinophilia is frequently absent, partly due to concomitant corticosteroid treatment ; 2/ blood cultures can be positive for enterobacteria and hence only anti-bacterial medications are initiated ; 3/ reactivation can occur even decades after emigration from endemic areas ; 4/ experienced staff and specialized diagnostic methods are not available in many hospitals in non-endemic countries. To avoid this potentially lethal complication of immunosuppressive therapy, patients who have emigrated from high-risk areas, even many years before, should be tested for strongyloidiasis. If tested positive, patients should be treated by ivermectin prior to initiation of corticosteroid treatment.

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