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Case Report

Systemic Lupus Erythematodes (SLE) Patient with an Unexpected Finding: Case Report

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ABSTRACT

We report the case of a 44-year-old female with systemic lupus erythematodes who presented with a severe case of strongyloides infection after immune- suppressant therapy with high dose steroids and rituximab. Due to the endemic nature of this helminthic disease we suspect an asymptomatic infection at least a year prior during visits to the patient's home country Brazil. As a result from the intensified immunosuppressant therapy, a manifest disseminated infection via accelerated auto-infection developed which caused the clinical symptoms. The infection was successfully treated with the antimycotic drugs ivermectine and albendazole. A follow-up of more than two years later showed signs of ongoing, though clinical asymptomatic infection. This was treated again successfully with ivermectine. Because of the patient's underlying autoimmune disease and listing for kidney transplantation due to end stage renal disease, regular follow-ups will be continued for early detection of signs of (auto) infection.

Keywords: Strongyloidiasis; *S. stercoralis*; Systemic lupus erythematosus

INTRODUCTION

Strongyloidiasis is a disease caused by infection with the parasitic helminth. *Strongyloides stercoralis (S. stercoralis).* It is endemic in tropical and subtropical regions (regional prevalence up to 25 percent) and occurs sporadically in temperate areas. It is assumed that up to 100 million people are infected worldwide [1]. The adult worms live in the host's small intestine. Contrary to other helminth parasites *S. stercoralis* can complete its entire life cycle in the human host [2]. The worm burden can therefore increase significantly via autoinfection. Autoinfection is generally limited by the host's intact immune system. Nevertheless a low level of autoinfection can lead to the parasite's persistence for decades and can cause clinical symptoms long after the initial infection [3-4]. The parasite usually affects the gastrointestinal, pulmonary and dermatologic system but can also merely present as asymptomatic eosinophilia in the immune competent host. In an immune deficient state uncontrolled auto infect on can lead to invasion of the larvae into multiple organs and tissues and cause severe organ dysfunctions. An exacerbation of autoinfection and can lead to potentially fatal hyper infection which can even lead to septic shock [5-7]. Thus, early diagnosis of strongyloidiasis is essential.

CASE REPORT

A 44-year-old female was referred to us from a community hospital. She presented with rapid deterioration of her general state of health and progressive colic type abdominal cramps which were not dependent on food intake. The bowel movement showed no diarrhea. The patient complained about difficulties swallowing and a non-productive cough. Intermittently a fever developed. Within the last month she had lost approximately 10 kilograms of body weight.

The patient's medical history consisted of a systemic lupus erythematodes (SLE) which was first diagnosed 13 years before. Renal involvement in form of lupus nephritis type IV had been confirmed via kidney biopsy in 2002. In the year 2004 a bolus therapy with cyclophosphamide had been initiated. Since 2007 a

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mono therapy with mycophenolate mofetil had been performed. Due to an acute progression of the lupus activity, the patient had been in our medical care about three months prior to the current admittance. Back then she had presented with a dialysis-dependent acute renal failure and suspected cerebral lupus involvement (dysarthria, one episode of generalized tonic-clonic seizure; cerebral MRI with patchy signal elevations in the medullary layer with subcortical focus in T2-weighted image compatible with alterations due to SLE, no signs of intracerebral ischemia or bleeding). A kidney biopsy had been performed and showed membranous lupus nephritis Type V with severe tubulus atrophy and approximately 70% in erstitial fibrosis. Nevertheless, to try to save some of the kidney function and because of the suspected cerebral vasculitis, a corticosteroid pulse therapy (1 mg/kg) and a therapy with rituximab had been initiated. Four single doses of rituximab of each 375 mg/m^2 had been administered over the course of four weeks. Under this therapy regimen the neurological symptoms had been regressive. Unfortunately the renal function showed no lasting recovery so that dialysis therapy had to be continued. Therefore a permanent vascular access via arteriovenous fistula and a temporary dialysis catheter into the jugular vein were surgically implemented. The corticosteroid dosage was slowly tapered to 20 mg per day. On resent admission the blood work showed increased inflammation markers (CRP 43 mg/l (normal <5 mg/l), leukocytes 16.4/nl (normal 3.5-10/nl), procalcitonin 2.3 ng/ml (normal <0.5 ng/ml)). The white blood cell imaging count showed the elevated leukocytes with 16.4/nl with an elevated neutrophil percentage of 90.9% (normal 43-75%), the eosinophil count was negative. The lymphocyte count was decreased with 6.3% (normal 16-45%), as was the percentage in monocytes (2% (normal 3-8%)). Hemoglobin (Hb) concentration was low with 8.8 g/dl (normal 12-16 g/dl) depicting a normochrome, normocytic anemia. The platelet count was low with 98/nl (normal 150-360/nl). Though the LDH concentration was increased with 370 U/l (normal <245 U/l), there were no signs of hemolysis with an elevated haptoglobin of 3.28 g/l (normal 0.35-2.5 g/l) and an amount of erythrocyte fragments in the normal range of <5/per million, giving no evidence for a thrombotic microangiopathy. The global coagulation-related tests were normal. Following liver enzymes were slightly increased: gamma-GT with 48 U/l (normal 9-36 U/l), alkaline phosphatase with 111 U/l (normal 35-104 U/l) and GLDH with 10.1 U/l (normal <5 U/l). The other liver enzymes and bilirubin were within the normal range. The creatinine concentration was elevated fitting the known end stage renal disease under regular dialysis therapy. There were no serological hints for lupus activity. HIV-Antigen and antibody screening was negative. Because of the elevated inflammation markers and fever in this immune compromised state an empiric antibiotic therapy was rapidly established with piperacilline/tazobactam und ciprofloxacine. Regular microbiological examinations such as blood cultures and urine cultures did not lead to bacterial or fungal growth. Due to an unexplained reduction in the patient's vigilance a CCT was performed which ruled out an acute pathology such as intracranial hemorrhage or thrombosis. CT-Scans of the thorax and abdomen showed no pathological findings. An ultrasound of the stomach revealed increased fluid filled intestinal loops but other than that no significant findings. Endoscopy of the sigma brought no pathologic results macroscopically and histologically. Gastric track endoscopy on the other hand showed unspecific erythema of the mucous membrane. Multiple biopsies from the stomach and duodenum were taken. The histological examination revealed signs of inflammation in the pars descendens duodeni with partial destruction of crypts. Between the crypts lay abundant amounts of worms. In the gastric regions scattered worm eggs were detected. The microbiological work-up identified the worms as Strongyloides stercoralis larvae (Figure 1).

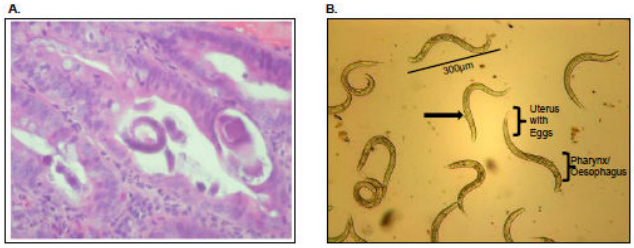

Figure 1: (A) Histological finding of the biopsies taken from the duodenum. The histological examination revealed signs of inflammation in the pars descendens duodeni with partial destruction of crypts. Between the crypts lay abundant amounts of worms (Photomicrograph, Institute of pathology, University of Mainz). (B) The photomicrograph displays the Strongyloides stercoralis larvae (Rhabditiforme larves with pharnyxbulbus) in the stool.

Because of the patient's highly immunoincompetend status after treatment of an acute Lupus flare, an oral antimycotic therapy with ivermectine in combination with albendazole was immediately initiated. Two single doses of ivermectine (200 mcg/kg each, 11 days apart) were given and albendazole was applied over the course of 15 days (400 mg twice daily) until no larvae could be detected in stool specimens. The antibiotic therapy was de-escalated. The preexisting steroid therapy with prednisolone was tapered from 20 mg/d on admission to 7.5 mg/d. In the course of this therapy the clinical symptoms subsided quickly and the patient could be discharged from the hospital. In a follow-up examination approximately two and a half years after the first diagnosis and treatment of the strongyloidiasis the patient presented herself without clinical symptoms. She was on no immunosuppressant therapy. The microbiological stool specimen examination detected no Strongoloides stercoralis larvae. In the serum, however, a positive strongoloides antibody titer with 1:160 was found (performed by indirect immunofluorescence testing). The peripheral differential blood count showed fluctuating values of eosinophilia up to 22.6%. Our patient had not been outside of Europe since first being diagnosed with strongyloidiasis. This asymptomatic infection of Strongyloides stercoralis was treated with two single doses of ivermectine 200 mcg/kg each given 15 days apart. A second follow-up two months later showed a decrease in the antibody titer to a borderline result. A PCR testing in the stool specimen detected no Strongoloides stercoralis DNA.

DISCUSSION

Our patient presented with a massive, clinical apparent strongyloidiasis after iatrogenic immunosuppression after the application of rituximab and high-dose corticosteroids in order to control a highly active systemic lupus erythematodes flare with renal and suspected cerebral involvement.

Strongyloidosis is endemic in rural areas of tropical and subtropical regions. In general, patients should be tested for strongyloidiasis when presenting with clinical manifestations and epidemiologic exposure, especially in an immunosuppressed state. Clinical signs can consist of unexplained eosinophilia, urticarial or serpiginous skin lesions, or pulmonary or gastrointestinal symptoms. Interestingly, there have been reports about donor-derived strongyloidiasis in solid organ transplant recipients with donors from endemic areas [8].

Our patient originates from northeastern Brazil but has been living in Germany for over 25 years. The last visit to her home country had been about one year prior to the start of the immunosuppressant therapy with corticosteroids and rituximab. We therefore assume a preexisting, asymptomatic infection, which developed into a manifest disseminated disease via accelerated autoinfection as a consequence of the patient's immune compromised state. It has been described that even short courses of corticosteroids of 6 to 17 days have led to overwhelming hyper infection and death [9-10].

CONCLUSION

Though parasitic infections such as strongyloidiasis often present with an eosinophilia, our patient did not present with this on admission, which led to not taking a parasitic infection into consideration in the first place. This is likely to have been due to the ongoing steroid therapy. In the follow-up many months after the first diagnosis, after immunosuppressant therapy had been reduced for a long period of time, an ongoing, though asymptomatic, infection was detected via focused stool examination. In the meantime the blood count developed a very considerable eosinophilia up to 22.6%. Since our patient is suffering from the autoimmune disease lupus erythematodes and is listed for kidney transplantation due to end stage renal disease, it is very likely that immunosuppressant therapy will have to be initiated again in the future. Therefore we will continue performing regular follow-ups with differential blood count and focused stool examination even if the patient stays clinically asymptomatic.

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