

Case report of *Strongyloides stercoralis* hyperinfection – a lesson for the immunocompromised patients` treatment

Prikaz bolesnika sa *Strongyloides stercoralis* hiperinfekcijom – lekcija za liječenje imunokompromitiranog bolesnika

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Abstract

Strongyloides stercoralis is an intestinal nematode that causes chronic gastrointestinal infection. In immunosuppressed patients this persistent disease can lead to disseminated disease and/or hyperinfection that are life threatening conditions. We present a fatal case of *S. stercoralis* hyperinfection and the appropriate treatment for immunosuppressed patients is discussed.

Sažetak

Strongyloides stercoralis je crijevna nematoda koja uzrokuje kroničnu gastrointestinalnu infekciju. Kod imunokompromitiranih bolesnika ova perzistentna bolest može dovesti do diseminirane bolesti i/ili hiperinfekcije koje su životno ugrožavajuće. Prikazujemo slučaj hiperinfekcije *S. stercoralis* sa smrtnim ishodom te odgovarajuće liječenje kod imunokompromitiranih bolesnika.

Introduction

Strongyloides stercoralis is a common intestinal nematode and it is estimated that it affects up to 100 million people worldwide. It is endemic in Africa and Asia, as well as in

Central and South America. Human infection occurs when filariform larvae penetrate intact skin. The life cycle of *S. stercoralis* can be divided in two parts: part where it is outside a host as a free living rhabditiform larvae and a

parasitic part inside a host as an infective filariform larvae. During the free living cycle rhabditiform larvae transform into filariform ones which can actively penetrate the human skin reaching venous circulation, right heart and finally lungs. From alveoli larvae migrate up the pulmonary tree reaching trachea and larynx from where they come to pharynx. Reaching the pharynx they are swallowed and in the small bowel the larvae mature into adults. They embed into the small bowel mucosa and start producing eggs by parthenogenesis. Within the intestinal lumen the eggs hatch into non-infective rhabditiform larvae that are excreted along with the stool reaching the soil. Sometimes rhabditiform larvae transform into filariform larvae even inside the host's small bowel. The filariform larvae penetrate intestinal mucosa reaching the blood stream or they actively penetrate perianal skin causing autoinfection [1]. In people with impaired cellular immunity this persistent infection can lead to disseminated disease and/or hyperinfection that are life threatening conditions. In this article we present a fatal case of *S. stercoralis* hyperinfection in a patient with plasma cell myeloma.

Case presentation

A 63-year-old male with plasma cell myeloma, presented to our Emergency Room with a four days history of fever, cough, abdominal pain and diarrhea up to three times a day. The last 19 months he was treated with lenalidomide, dexamethasone and zoledronic acid for the myeloma. At the admission he was febrile 38°C and chest auscultation showed bilateral crepitation while the rest findings was unremarkable. Initial laboratory tests showed that his white blood cells were $6 \times 10^9/L$ with 40% neutrophils, 31% lymphocytes, 27% monocytes and 2% eosinophils while CRP was 103 mg/L. Chest x-ray at the admission showed bilateral infiltrations so the empirical treatment with piperacillin with tazobactam 4,5 g TID, levofloxacin 500 mg OD and oseltamivir 75 mg OD was started. After the admission he started to desaturate so he was put on Bilevel Positive Airway Pressure (Bi-PAP) mode of noninvasive ventilation. Chest CT showed bilateral upper and mid zones of peri bronchial and ground glass opacities while the abdominal CT revealed features of colitis in the descending and sigmoid colon and to lesser extent of similar changes in the rectum. Bronchoscopy was done and bronchoalveolar lavage (BAL) cytology showed mixture of alveolar macrophages, bronchial epithelial and squamous cells. Many roundworm organisms with notched tails were noticed in BAL and their morphology was suggestive of *Strongyloides* nematodes (Figure 1). Blood, urine and BAL cultures were negative, cytomegalovirus (CMV) polymerase chain reaction (PCR) in blood was negative, legionella and pneumococcus antigen were negative in urine and acid-fast bacilli (AFB) smear and PCR as well as pneumocystis pneumonia (PCP) PCR were negative in BAL. *S. stercoralis* was found in the stool sample and the treatment with albendazole 400 mg

BID was started. In the next 24 hours his general condition further deteriorated. He was intubated and shifted to the ICU where ivermectin 200 mg/kg was added. His condition stabilized however during the next two days his blood pressure decreased. He had to be on inotropic support and laboratory results showed multiorgan failure. The patient died on the seventh day of his hospitalisation.

Discussion

The majority of infected people have chronic but asymptomatic gastrointestinal tract infection. *S. stercoralis* has the unique ability to complete its life cycle in the human host causing the autoinfection that can lead to persistent infection for decades. If the patient has impaired cell-mediated immunity (e.g. steroid or other immunosuppressant treatment, transplant patients, patients infected with human T-cell lymphotropic virus type 1) normal *S. stercoralis* life-cycle is accelerated leading to excessive worm burden within the usual migration route (skin, gut, lungs). This condition is labeled as hyperinfection syndrome (HIS). If larvae are spread even to other organs (liver, brain, heart, urinary tract) the condition is labeled as disseminated infection syndrome (DIS). Clinical presentation of HIS and DIS is similar to usual strongyloidiasis symptoms including nausea, vomiting, diarrhea, weight loss, abdominal pain, cough, fever, dyspnea and gastrointestinal bleeding. However, because of massive infection and dissemination, HIS and DIS patients can have catastrophic presentation like shock, disseminated intravascular coagulation, meningitis, renal and/or respiratory failure [2].

It seems that in the last years the global prevalence of *S. stercoralis* infection is increasing, especially in previously known endemic areas where the poor sanitary measures, poor personal hygiene, as well as the insufficient drinking water supply are the main reasons for the infection rate increase. At the same time there are many isolated *S. stercoralis* infection cases occurring in non-endemic areas mostly associated with patients with immunosuppressive diseases, corticosteroid therapy, organ transplant recipients, hematological malignancies or other debilitating conditions [1]. Data about the *S. stercoralis* prevalence in non-endemic areas are scarce and the increasing number of high-risk patients emphasizes the importance of appropriate diagnosis and treatment of this potentially fatal infection. The actual human prevalence in Croatia is not known although the *Strongyloides* spp was detected in 0,5% of Croatian wild wolves faecal samples [3].

The microbiological diagnosis of strongyloidiasis can be challenging. Initially eosinophilia and/or increased total-IgE may raise suspicion of *Strongyloides* but may be absent in immunocompromised patients. It is based on either finding the larvae in stool samples or on demonstrating specific antibodies to *S. stercoralis* in blood. Fecal microscopy can detect the first stage larvae whereas the eggs or adults are not common to see. Microscopy has low

sensitivity as larvae are shed sporadically and in numbers which depends on the stage and severity of the infection. In order to increase the sensitivity of microscopy it is recommended that few stool specimens collected over several consecutive days are examined. Coproculture is an additional stool examination method which aims to detect larvae in freshly passed stool samples.

Detection of anti-*Strongyloides* antibodies in blood samples should be done as a screening test or as an additional test for making diagnosis. Together with the eosinophil count it can be used to monitor the treatment. The drop in antibody levels is variable. Usually it could be seen only after 6 months of the effective treatment. The sensitivity of commercially available EIA tests using *Strongyloides* filariform antigen is estimated to be around 90 percent but in the case of profound immunosuppression sensitivity can be lower. At the same time, cross reactions with other nematodes can't always be excluded [4]. In cases when serology is positive it is suggested to confirm or rule out the cross reaction using direct microscopic or culture diagnostics. Molecular test for diagnostic have been developed recently but their use has not been routine yet.

The objective of strongyloidiasis management is to treat symptomatic patients, to eradicate the parasite from the host thus eliminating the possibility of autoinfection, and to prevent possible complications in asymptomatic patients. Today, the first-line treatment for strongyloidiasis is ivermectin that eradicates the parasite in approximately 80% patients. It is highly effective as it targets both adults and larvae. For uncomplicated *S. stercoralis* infection oral ivermectin is given 200 mg/day for two days. Alternative treatment is albendazole 400 mg twice a day for 7 days but it is shown to be less effective most probably because it primarily targets adult worms. HIS/DIS should be considered as medical emergencies so the treatment should be started as soon as this diagnosis is considered. In these situations ivermectin 200 mg/day should be given for at least two weeks or until the parasite has not been detected in the stool for the full two weeks. There are some reports about improved efficacy of the ivermectin and albendazole combination but so far there are no randomized trials confirming this conclusion [5]. The additional management that could benefit the patients is the reduction of immunosuppressive treatment if this would be possible due to patient's underlying condition.

After our patient's death, a review of his medical record showed that four months prior this admission he complained on abdominal pain and diarrhea. At the same time eosinophilia of 14-27% in his peripheral blood was detected and *S. stercoralis* was found in the stool. He was treated as an outpatient with albendazole 400 mg twice a day for 7 days advising him to take medications with fatty food. At the same time the dexamethasone dose was reduced from 40 to 20 mg daily. After the treatment his bowel movement normalized, he didn't complain on the abdominal pain and eosinophilia was not present any more. Unfortunately no

further stool examination was done. The HIS that our patient presented with four months later confirms that 7 days of albendazole was not the adequate treatment as it didn't eliminate the possibility of autoinfection. In high-risk patients it is imperative to repeat diagnostic studies (stool, duodenal fluid, endoscopy) in order to confirm or rule out the parasite eradication [2]. Eosinophilia is not a reliable parameter for the treatment surveillance but can be used in combination with serial antibody titers [6].

Conclusions

In immunocompetent people *S. stercoralis* often causes chronic and asymptomatic infection that can be lifelong. In patients that are immunosuppressed, especially in those who are treated with steroids, the number of parasites can substantially increase leading to potentially fatal hyper or disseminated infection. To prevent these serious sequelae all chronically infected patients should be diagnosed and treated. This suggestion is obvious for *Strongyloides* endemic areas but as it is little known about the strongyloidiasis prevalence in non-endemic areas, it should be applied in non-endemic areas too. In non-endemic areas the prevalence studies should be done in order to assess the risk of *S. stercoralis* infection. Also it would be advisable to include *S. stercoralis* screening in the pretreatment workup for the high risk patients that are prepared for immunosuppressive treatment.

Conflicts of interest

Authors declare that they have no conflicts of interest.

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Figure 1. Strongyloides nematode in bronchoalveolar lavage

