Strongyloides stercoralis hyperinfection in a diabetic patient: Case report

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Abstract. *Strongyloides stercoralis* is a widespread, soil-transmitted helminth affecting humans. Autoinfection occurs in *S. stercoralis* infection and this leads to a continuous build-up of worm burden in human host. This may lead to hyperinfection syndrome which has the potential to cause serious life-threatening disease especially in immunocompromised and immunosupressed patients. Thus, patient with underlying risk factors should be suspicious of having this infection as severe strongyloidiasis carries a high mortality rate if the diagnosis is delayed. Here, we report a case of *S. stercoralis* hyperinfection in a diabetic patient.

INTRODUCTION

Strongyloides stercoralis is a widespread, soil-transmitted helminth affecting humans. It is endemic in tropical and subtropical countries. Strongyloidiasis is generally benign and asymptomatic, eosinophilia and larvae in stools being the only indications of infection. The disease is classified as acute, chronic and severe strongyloidiasis and commonly manifests as cutaneous, pulmonary and intestinal features. Common clinical features of acute strongyloidiasis include macularpapular rashes of the feet, epigastric discomfort, diarrhoea, occasional nausea and vomiting. Other manifestations include cough, dyspnoea, wheezing, low grade fever or constipation (Tsai *et al.*, 2002). In chronically infected individuals as well as in immunocompetent person the disease is generally asymptomatic (Mora *et al.*, 2006). Severe strongylodiasis is commonly seen in patients with underlying comorbidities such as malnutrition, corticosteroid therapy, chronic obstructive pulmonary disease, chronic liver disease or cirrhosis and peptic ulcer disease (Tsai *et al.*, 2002). It manifests

as skin rash, nausea, vomiting, diffuse abdominal pain and tenderness, diarrhoea, fever with chills, cough, dyspnoea and wheezing. Meningism and altered mental functions are usually seen in patients with central nervous system involvement.

Strongyloides stercoralis is capable of causing autoinfection in host. This condition may lead to hyperinfection syndrome (HS) which has the potential to cause serious life-threatening complications especially in immunocompromised and immuno-supressed patients. HS can be described as a syndrome with accelerated auto-infection, which is a quantitative distinction, and not clearly defined. Systemic manifestations in such patients suggestive of the diagnosis of hyperinfection is attributable to increased larval migration. These manifestations include an exacerbation of gastrointestinal and pulmonary symptoms (Siddiqui & Berk, 2001).

The majority of cases of severe HS are associated with a predisposing, immuno-suppressing condition, such as haematological neoplasias, human T-cell lymphotropic virus type 1 (HTLV-1), and

organ transplantation. Chronic malnutrition, diabetes mellitus, chronic obstructive pulmonary disease, alcoholism, and chronic renal failure are also recognized predisposing conditions for the hyperinfection syndrome (Fardet *et al.*, 2007).

Case report
A 75-year-old Malay male, is a known case of pemphigus vulgaris since 1999 and on oral prednisolone 30mg once daily and azathioprine 100mg once daily. He was diagnosed to have diabetes mellitus 3 years later most probably secondary to steroid therapy. He is a vegetable seller for many years.

He was first seen on Mac 2001 when he presented with diarrhoea for 2 days which was associated with nausea and vomiting. On April 2001, he was readmitted due to similar presentation. There were history of loss of weight and loss of appetite for a month. He had no melaenic or watery stools, and no abdominal pain. Microscopic examination of the stool sample revealed numerous *S. stercoralis* rhabditiform larvae. He was treated as acute gastroenteritis. Intravenous fluid, oral rehydration salt, oral albendazole 400mg stat dose and oral metronidazole 400mg eight hourly for seven days were prescribed. His symptoms improved and he was discharged after 3 days of admission.

Two weeks later he was readmitted (in late April 2001) due to high grade fever for one week duration prior to admission which is associated with poor oral intake, abdominal pain and altered sensorium. However, there was no diarrhoea, vomiting, urinary tract infection or upper respiratory tract symptoms noted.

On examination, he was noted to have spiking temperature of 38.2ºC, pale and dehydrated. He had oral candidiasis. Multiple hyperpigmented pemphigoid scars were noted over the trunk and limbs. There were dry ulcer noted on medial aspect of distal left foot and bilateral pitting edema. His blood pressure was 126/82mmHg and pulse rate of 100 beats /minute. There was generalized abdominal tenderness with normal bowel sound. Per rectal examination was unremarkable. Mild crepitation was heard at the base of the left lung. Other systemics reviews were unremarkable.

He was diagnosed as having sepsis secondary to infected ulcer and cellulites and was treated with intravenous cefuroxime 750mg every 8 hourly and cloxacillin 500mg every 6 hourly.

Microbiological examinations of blood, urine, stool and swab from ulcer did not reveal any growth. Stool microscopic examination for intestinal parasites was negative. Other related investigations of sepsis such as blood film for malarial parasite, Widal-Weil Felix test and enzyme immunoassay dot blot for *Salmonella typhi* were negative.

He was severely anaemic with haemoglobin level of 7.2 g/dl., thrombocytopenia of 99.0 X 10 ^{9}/L and borderline low total white cell count (3.2 X 10^3/υL). His full blood picture – showed macrocytic anaemia with normal total white blood cell count and morphology, however, eosinophil was absent.

He was noted to have hyponatraemia and hypokalaemia with sodium of 125 mmol/L and potassium of 3.3 mmol/L. The urea level was borderline high with 8.8 mmol/L. Hypoalbuminaemia with albumin level of 11 g/L was noted. Liver function test was impaired with raised transaminases and alkaline phosphatase while the bilirubin level was within normal limit. The erythrocytes sedimentation rate was raised with 100 mm/hour.

His fever did not settle down despite treatment. His condition deteriorated after 6 days in the ward where he became restless, confused and developed aystole. He was pronounced death due to cardiorespiratory arrest secondary to sepsis.

DISCUSSION

Hyperinfection syndrome (HS) is known to be associated with immunocompromised as well as immunosupressed patients. In these two conditions, there are defect in the cellular immunity that could predispose to

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hyperinfection. Pertaining to this case, the patient was treated for three years with immunosuppressive drugs which include steriod and azathioprine for his underlying autoimmune disease. Of all the immuno-suppressive drugs prescribed, corticosteriod are the most widely used and it is the most specifically associated with transformation of chronic strongyloidiasis to hyperinfection. Corticosteroid use is the most frequent risk factor for development of HS in developed countries. It is associated with a two- to three-fold increase in the risk of being infected by *S. stercoralis* (Armignacco *et al.*, 1989). This drug is able to induce hyperinfection by acute suppression of eosinophilia and lymphocyte activation. Some researchers have suggested that corticosteriod may also have a direct effect on the parasites which is able to accelerate the transformation of rhabditiform into invasive filariform larvae (Keiser & Nutman, 2004).

The clinical manifestations of *S. stercoralis* hyperinfection vary widely. The onset may be acute or insidious. Fever and chills are not uniformly present and should prompt a search for an associated bacterial infection. Other constitutional symptoms include fatigue, weakness and total body pain. In immunocompromised individuals, blood counts performed during hyperinfection may show eosinophilia, but more often they show a suppressed eosinophil count (Keiser & Nutman, 2004). Gotuzzo *et al.* (1999) found that eosinophilia was absent in more than 92% of cases with *s*trongylodiasis hyperinfection (Gotuzzo *et al.*,1999) as noted in this patient.

Immunosuppressed patients who experience any unusual gastro-intestinal or pulmonary symptoms or suffer from unexplained Gram-negative bacilli sepsis should be suspected of having strongyloidiasis. They are at risk of having severe stongyloidiasis especially in patients with travelling history to endemic area (Fardet *et al.*, 2007). This patient has been a vegetable seller for many years. Vegetable sellers are not a known risk factor for acquiring strongyloidiasis, however, the nature of his job which brings him in contact with contaminated soil and water would pose a risk of infection in this diabetic patient.

Hyperinfection has been reported to be seen in patients with negative stool smears for intestinal parasites. In this patient, although a stool smear for intestinal parasites was negative for this current admission, the diagnosis of HS could not be easily excluded. Underlying immuno-compromised and immunosupressed state as well as positive stool smear for *S. stercoralis* during previous admission may give a suspicion of *S. stercoralis* hyperinfection. Generally, it is difficult to identify *S. stercoralis* larvae in view of low sensitivity of routine direct stool smear for intestinal parasites examination. A single stool examination has low sensitivity of about 50% for making the diagnosis of *S. stercoralis* infection in someone with symptomatic chronic disease. In the asymptomatic individual, direct stool smear examinations are probably even less sensitive (Siddiqui & Berk, 2001). Patterns of detection of *S. stercoralis* larvae in the faeces of infected persons can be characterized on the basis of examination of a minimum of four stool specimens. Low adult parasite load and irregular larval output were two other contributing factors to low yield of detection (Marathe & Date, 2008). Thus, stool culture using Harada Mori technique is very useful to detect low infection of *S. stercoralis* which was not done in this patient. This technique employed a strip of filter paper that is partially submerged in a test tube containing water. Any larvae present in the specimen migrate against the current water that arises by capillary action and accumulate at the bottom of the tube (Engbaek *et al.*, 2003). This technique make use of the ability of *S.stercoralis* to enter a free living cycle of its development, but this technique is rarely adopted as standard procedure in clinical parasitology due to involvement of life infective larvae (Blantt & Cantos, 2003).

Though other investigations of sepsis were negative, secondary bacterial infection following HS cannot be excluded from the diagnosis. High erythrocytes sedimentation

rate found in this patient could suggest underlying active infection or inflammation process.

Septicaemia from enteric bacteria as well as yeast particularly candida were frequently associated with severe strongyloidiasis. The postulated mechanism of sepsis in those cases was transmission of enteric bacteria through invading track of the bowel wall by *S. stercoralis* filariform larvae (Fardet *et al.*, 2007). In this patient, the oral candidiasis is not part of the features of HS. This localized oral mucosa lesion resulted from a combination of immunosuppressive therapy and poor glycaemic condition from uncontrolled diabetes.

In this patient, the liver function test was found to be impaired with raised transaminases and alkaline phosphatase which indicate damage of the liver cells. It might be caused by immunosuppressive drug, azathioprine or liver dissemination of filariform larvae causing hepatitis. Rare cases with liver dissemination of filariform larvae may show an obstructive pattern in the liver enzymes, with elevations of the alkaline phosphatase and bilirubin, while alanine aminotransferase and aspartate aminotransferase were minimally elevated (Keiser & Nutman, 2004).

Although *S. stercoralis larva was* negative for this episode, suspicion of HS should be made and treatment should be started in this patient. The treatment should be continued until the clinical features resolves and/or larvae are no longer detectable especially in those who receive immunosuppressive therapy (Davidson *et al.*, 1984). Treatment and screening should be continued for at least two weeks which is actually based on the duration of autoinfective cycle (Keiser & Nutman, 2004). Each patient suspected of strongyloidiasis should be treated with prompt anti-parasitic treatment and any patients who were treated with corticosteroid should be monitored carefully. By tapering the dose of corticosteroid, it may have an impact on the prognosis of patients infected with this parasite (Marcosa *et al.*, 2008).

Strongyloidiasis is present in our local setting. Patient with underlying co-morbidities such as immunocompromised and immunosupressed would increase susceptibility to hyperinfection syndrome. Thus, patients with underlying risk factors should be suspected of having strongyloidiasis as the outcome might be fatal. Identification and early treatment of strongyloidiasis in such patients would improve morbidity and mortality. Culturing the stool will increase the sensitivity of identifying *S. stercoralis* larvae.

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