BJMS
Borneo Journal of Medical Sciences

CASE REPORT

Strongyloides Hyperinfection Syndrome in an Immunosuppressed Patient

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Received: 20 August 2018

Accepted: 29 October 2018

Keywords: *Strongyloides stercoralis*, hyperinfection syndrome, immunosuppressed patient

ABSTRACT

Strongyloides stercoralis **is an intestinal nematode which is endemic in tropical and subtropical countries. The global prevalence of *Strongyloides* is unknown. Strongyloidiasis is found more frequently in the socioeconomically disadvantaged, in institutionalized populations, and in rural areas. The spectrum of disease varies. It may cause asymptomatic infection, mild eosinophilia or hyperinfection syndrome in the most severe form. Here we reported a case of *Strongyloides* hyperinfection syndrome in an immunosuppressed patient. This patient is a 54-year-old man with myasthenia gravis on long term azathioprine and prednisolone. He presented with fever associated with diarrhoea and was in septic shock. His blood culture was positive for *Klebsiella pneumoniae*. *Strongyloides stercoralis* larvae were detected in his sputum and stool sample. He was diagnosed to have *Strongyloides* hyperinfection and was treated with subcutaneous ivermectin. He recovered well. Our case demonstrated the association of *Strongyloides* hyperinfection with superimposed gram-negative sepsis as a consequence of prolonged immunosuppression. A high index of suspicion is needed in approaching patient with risk factors of hyperinfection syndrome.**

INTRODUCTION

Strongyloidiasis is caused by *Strongyloides stercoralis*. Strongyloidiasis is often asymptomatic. Eosinophilia and larvae in stools being the only indication of infection[1]. Opportunistic disseminated strongyloidiasis

is an important cause of morbidity and mortality in immunocompromised patients. In Malaysia, cases of *Strongyloides* hyperinfection have been reported previously[2]. Risk factors for *Strongyloides* hyperinfection include congenital immunodeficiency, malignancy, malnutrition, immunosuppression, alcoholism and haematopoietic stem cell transplantation[3]. In general, immunosuppression is defined as suppression of body immune system to fight off infection, prevent graft rejection or as treatment of autoimmune diseases. It may occur as a result of disease or deliberately by immunosuppressive drugs such as azathioprine, methotrexate, cyclophosphamide, etc.[2].

CASE PRESENTATION

A 54-year-old man with underlying myasthenia gravis on long-term prednisolone and azathioprine, hypertension and well-controlled diabetes mellitus presented with fever associated with diarrhoea for 3 days. He was on 2 years of azathioprine and prednisolone for his myasthenia gravis and 1 year of metformin for his diabetes prior to this. On arrival to emergency department, he was in shock, blood pressure was 60/37 mmHg. His pulse rate was 104 beats per minute and his temperature was 37°C. His respiratory and abdominal examination were unremarkable.

Initial blood investigation showed anaemia, haemoglobin of 8.7 g/dl, leukocytosis of 20 $\times$ 10^9/L. His renal profile was impaired with urea of 6.2 mmol/L and creatinine of 118 **µmol**/L. He had metabolic acidosis with pH of 7.41 and bicarbonate of 14.4 mmol/L (Table 1). He had low albumin level with albumin of 9 g/L and his C-Reactive Protein (CRP) was 87 mg/L. His chest radiograph was normal. His provisional diagnosis was Gram-negative sepsis in septic shock. He was then given boluses of intravenous crystalloids, noradrenaline and intravenous meropenem.

After 48 hours, his blood culture grew *Klebsiella pneumoniae*, his sputum was positive for *Strongyloides stercoralis* larvae and stool was positive for rhabditidiform larvae (L1). Antibiotic was deescalated to intravenous amoxicillin-clavulanic acid and started on oral albendazole 400 mg and subcutaneous ivermectin. Diagnosis was revised to *Klebsiella pneumoniae* septic shock with *Strongyloides* hyperinfection syndrome. He made good clinical recovery and discharged 2 weeks later. He was prescribed monthly subcutaneous ivermectin for 6 months.

Table 1 Blood investigation of the patient

	Unit	Normal range	Day 1	Day 2	Day 7	Day 8	Day 14
Haemoglobin	g/dL	13 – 18	8.7	10.8	7.6	9	9
Total white blood cell	10^9/L	4.0 – 10.0	20.7	30	8.69	12	12.6
Platelet	10^9/L	150 – 400	102	57	84	358	358
Sodium	mmol/L	135 – 148	129	133	136	137	137
Potassium	mmol/L	3.5 – 5.1	3.8	3.5	2.7	4.1	4.3
Urea	mmol/L	2.8 – 7.8	6.2	5.5	2.1	7	3.8
Creat	**µmol**/L	61 – 110	118	86	61	59	36
pH		7.35 – 7.45	7.41	7.337	–	–	–
PCO2	mmHg	33 – 48	22	34	–	–	–
PO2	mmHg	80 – 100	206	45	–	–	–
HCO3	mmol/L	23 – 29	14.4	14.4	–	–	–
Total bilirubin	**µmol**/l	0 – 17	19	11	10	9	9.1
ALT	IU/L	0 – 41	12	22	35	32	32
AST	IU/L	0 – 40	26	23	34	30	20
ALP	IU/L	40 – 129	171	366	260	203	233
Albumin	g/L	34 – 48	9	12	14	22	22
Globulin	g/L	20 – 35	25	26	25	33	33

DISCUSSION

Strongyloides stercoralis infection was first reported in 1876 in French soldiers on duty in Vietnam[4]. The first report of disseminated infection dates back to 1966, with occurrence of fatal strongyloidiasis with immunosuppression[5]. *Strongyloides* is unique among helminths due to its persistence and ability for autoinfection. Risk factors for *Strongyloides* hyperinfection include congenital immunodeficiency, malignancy, immunosuppression, etc. In our patient, we believe that his risk factor for hyperinfection syndrome was long-term azathioprine and prednisolone for 2 years which rendered him to be immunosuppressed.

The lifecycle of *Strongyloides stercoralis* begins with rhabditiform larvae in the intestine excreted in the stool. The rhabditiform larvae then developed into infective filariform larvae or develop through succeeding rhabditiform stages into free-living adults. It infects adult human by penetrating intact skin[6]. The filariform larvae can enter the circulation, transported to the lung, penetrated the alveolar and swallow into digestive tract of human. Rhabditiform larvae can develop into infective filaform in the gastrointestinal tract and trigger off autoinfection.

The clinical manifestation of strongyloidiasis may vary depending on organs involved. Patient may develop local reaction at the site of entry of the larvae. Respiratory symptoms such as cough, dyspnoea, haemoptysis and tracheal irritation can occur when the larvae migrate through respiratory system[7]. In the gastrointestinal tract, patient may complain of diarrhoea, constipation, abdominal pain and loss of appetite[8]. Sometimes it may cause intestinal obstruction, haemodynamically significant gastrointestinal bleeding or ileus.

In the hyperinfection syndrome, the classic life cycle of *Strongyloides stercoralis* from skin to lungs and gastrointestinal tract is accelerated with increased reproduction leading to excessive worm burden. The clinical symptoms of hyperinfection syndrome can vary. Fever with chills and rigors are not typically

present. We should look for presence of Gram-negative infection when there is fever with chills and rigors[9].The likelihood of developing hyperinfection is increased in patient with impaired cell-mediated immunity[10].

Diagnosis of strongyloidiasis is made by detecting rhabditiform larvae in stool or by serological method[11]. However, the sensitivity of a single stool examination to make the diagnosis is only about 50%[12]. Hence, stool study alone is inadequate for diagnosing hyperinfection syndrome. There have been reports of hyperinfection syndrome with negative screening stool exams and the larvae are excreted intermittently. Other techniques such as Beaermann and formalin-ethyl acetate concentration techniques and Harada-Mori filter paper technique have been used to improve the sensitivity[13].

In term of treatment, thiabendazole has been the treatment of choice in the past. The efficacy of thiabendazole in treating chronic strongyloidiasis is said to be around 67 – 81% if given at a dose of 25 mg/kg twice a day for 3 days[14]. However, in recent days, the recommended choice of treatment is ivermectin with albendazole as alternative. Two single dose of 200 mcg/kg of ivermectin is usually administered on two consecutive days for uncomplicated infection.

The optimal treatment for hyperinfection is still uncertain. Some experts give 3 to 11 doses of ivermectin in disseminated disease and certain experts give a combination of ivermectin and albendazole until patient shows clinical response[15]. Besides that, treatment and screening of *Strongyloides* should be done until faecal cultures are negative for at least two weeks as the autoinfective cycle lasts at least two weeks. The same apply to those who have positive urine or sputum samples.

In term of prevention of hyperinfection syndrome, measures such as wearing shoes and screening of family members will be helpful in endemic area[16]. Patient also should be screened for asymptomatic *Strongyloides* infection, either by serological testing or stool examination[17]. For patient who requires prompt initiation of immunosuppression, empirical treatment for strongyloidiasis may be administered to prevent hyperinfection syndrome.

CONCLUSION

Strongyloides hyperinfection is a treatable condition but can cause potentially life-threatening infection. This present case has illustrated the association of *strongyloides* hyperinfection with superimposed gram negative sepsis as a consequence of prolonged immunosuppression. Clinicians should often have high index of suspicion of possible hyperinfection when treating patients with risk factors. Aggressive treatment is often warranted and immunosuppressant need to be adjusted.

ACKNOWLEDGEMENTS

The authors would like to thank the Director of Health Malaysia for the permission to publish this paper.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this case.

CONSENTS

Written informed consent was obtained from the patient to publish the case. A copy of written consent is available for review by the Chief Editor.

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