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Disseminated strongyloidiasis in an immunocompromised host: A case report

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ABSTRACT

Infections caused by *Strongyloides stercoralis* (*S. stercoralis*) in human are generally asymptomatic, however in immunocompromised individual, hyperinfection may develop with dissemination of larvae to extra-intestinal organs. The diagnosis could be easily missed due to asymptomatic presentation and insufficient exposure towards the infection itself, which may lead to low index of suspicion as a consequence. In this report, a case of a Malaysian male with underlying diabetes mellitus, hypertension, cerebrovascular accident, bullous pemphigus and syndrome of inappropriate antidiuretic hormone secretion who initially complained of generalized body weakness and poor appetite without any history suggestive of sepsis is presented. However, he developed septicemic shock later, and *S. stercoralis* larvae was incidentally found in the tracheal aspirate that was sent to look for acid fast bacilli. Regardless of aggressive resuscitation, the patient succumbed due to pulmonary hemorrhage and acute respiratory distress syndrome. It was revealed that the current case has alarmed us via incidental finding of *S. stercoralis* larvae in the tracheal aspirate, indicating that the importance of the disease should be emphasized in certain parts of the world and population respectively.

1. Introduction

Strongyloides stercoralis (*S. stercoralis*) is a nematode belonging to the class of Secernentasida, order of Rhabditorida, family of Strongylidae and the genus of *Strongyloides*. *Strongyloides* infection is endemic in humid tropical regions including Africa, Southeast Asia, and Latin America [1,2]. *Strongyloides fuelleborni* which is mainly found in Africa and Papua New Guinea [3], is another important causative agent of human strongyloidiasis, but in a lesser frequency in contrast to *S. stercoralis*.

Strongyloidiasis begins with the penetration of a susceptible host by filariform larva (infective stage) into the skin. The larva enters the venous or lymphatic channels, and is subsequently transported to the lungs, where it migrates to the trachea. As it matures, it will then be swallowed into the gastrointestinal tract. A female parasite then lodges in the lamina propria of the duodenum and proximal jejunum where it lays egg. The eggs hatch into rhabditiform larvae, where they migrate into the intestinal lumen and go into either one of the two pathways – autoinfection or excreted to the external environment (free-living stage).

In general, strongyloidiasis can cause acute infection, autoinfection and chronic infection, hyperinfection and dissemination syndrome. However, majority of human infections are manifested themselves as chronic strongyloidiasis. The chronic state is probably maintained by a relatively low and stable number of adult worms that reside in the intestine and is survived by a means of well-regulated auto-infection [4]. Once the host immunity is compromised, the rate of autoinfection and

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population of adult worm increases, hence hyperinfection occurs. Ultimately, the larvae migrate extra-intestinally and lodge themselves into meningeal spaces, brain, liver, lymph nodes, kidney, cutaneous and subcutaneous tissues. This migration and penetration into other organs can lead to inflammation and complicate further with hemorrhage.

2. Case report

A 56-year-old man was presented with generalized body weakness and poor appetite two days prior to admission. He denied any history of fever, cough, shortness of breath, headache, and blurring of vision. There were no abdominal pain, urinary and bowel symptoms associated with the main complaints. Past medical history revealed that the patient has been diagnosed with diabetes mellitus and hypertension for more than ten years, and has suffered from cerebrovascular accident (CVA) for the past seven years. However, the patient has been able to ambulate independently. He had recently diagnosed as having bullous pemphigus and syndrome of inappropriate antidiuretic hormone secretion (SIADH) four months prior to the current admission. In relation to that, he was on multiple drugs for his underlying problems including oral prednisolone 30 mg once daily (OD) for the bullous pemphigus. He was a former government servant and had no history of recent travel.

Upon physical examination he was alert, conscious but appeared dehydrated. The vital signs were normal with a temperature of 37 °C, blood pressure of 100/70 mmHg and pulse rate of 80 beats/minute with regular rhythm. There were no oral thrush, abnormal cutaneous lesions and cervical lymphadenopathy present. A cardiovascular system and fundoscopy examinations were unremarkable. A central nervous system (CNS) examination was also normal except for lower muscle power that revealed at 4/5 for both upper and lower limbs. Respiratory examination revealed crepitation at the right lower zone bilaterally, with no dullness on percussion. Tenderness at the epigastric region was noted per abdomen. A provisional diagnosis of acute kidney injury secondary to dehydration with uncontrolled diabetes mellitus was clinically suspected.

Initial blood investigations showed hemoglobin of 7.6 g/dL, total white cell count of 10×10^9/L without eosinophilia, and normal platelet count at 200×10^9/L. Biochemically, there were evidence of hyperglycemia (16 mmol/L), impaired renal function with electrolyte imbalances; hyponatremia (115 mmol/L) and hypokalemia (2.6 mmol/L). Liver function profile was unremarkable except for low albumin level (13 g/L). The C-reactive protein (CRP) was elevated at 5.90 mg/dL (0.01–0.82 mg/dL).

Chest radiograph was done and it revealed the consolidation of the right lower zone with patchy opacity over the left lower zone of the lung. Blood for bacterial culture and sensitivity was collected on day 3 of admission. Empirical intravenous (IV) cefepime 1 g 8 hourly was commenced immediately after that while waiting for further identification of the organism. After 48 h of incubation, carbapenem resistant *Klebsiella pneumoniae* (CRE) was isolated. The patient was deescalated to IV polymyxin E 4.5 µ twice daily and imipenem 500 mg 6 hourly. Full blood picture was collected too, and features suggestive of iron deficiency anemia with neutrophilia likely due to infection are detected.

In spite of having appropriate antibiotics and improvement of his repeat renal profile, except for persistent hyponatremia, the patient developed septicemic shock on day 9 of admission. The respiratory examination revealed generalized rhonchi with prolonged expiratory phase. At the same time, tracheal aspirate was sent to look for acid fast bacilli (AFB) (immunofluorescence; Auramine O staining QBC Diagnostics, Inc.) to exclude the possibility of pulmonary tuberculosis. Upon reviewing the AFB smear, presence of apple-green fluorescent larvae (Figure 1) was noted. Following that, a wet smear (Figure 2) was performed and live helminthic larvae were seen with the esophageal lengths of approximately half of the body, while the ends were pointed with some demonstrated hooked or notched appearance. Trichrome and Giemsa staining (Figure 3) were also carried out to verify the wet smear findings. This incidental finding was informed to the clinician, thus a combination of albendazole (400 mg oral, twice daily) with ivermectin (200 µg/kg oral, daily) were administered. Unfortunately, regardless of aggressive resuscitation, the patient succumbed to illness on day 13 of admission due to pulmonary hemorrhage and acute respiratory distress syndrome (ARDS).

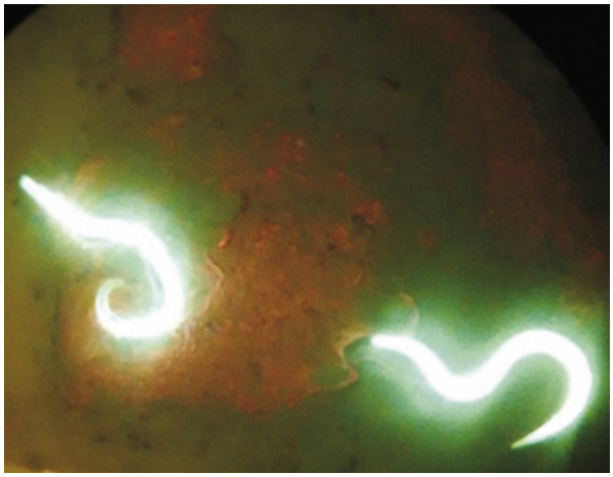

Figure 1. Presence of apple-green fluorescent larvae using Auramine-O-stain.

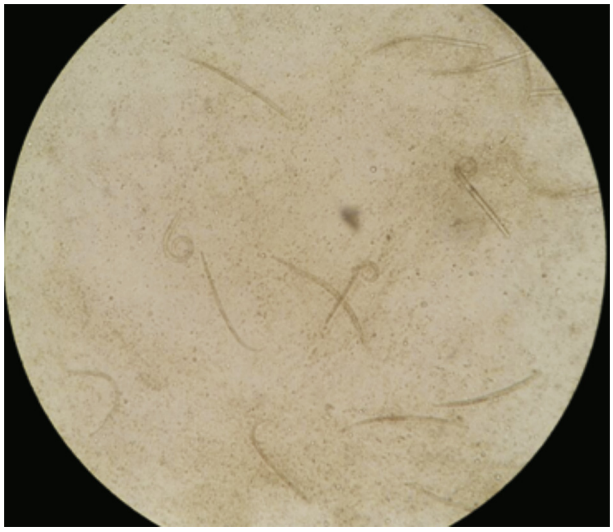

Figure 2. Larvae of *S. stercoralis* in unstained wet mount.

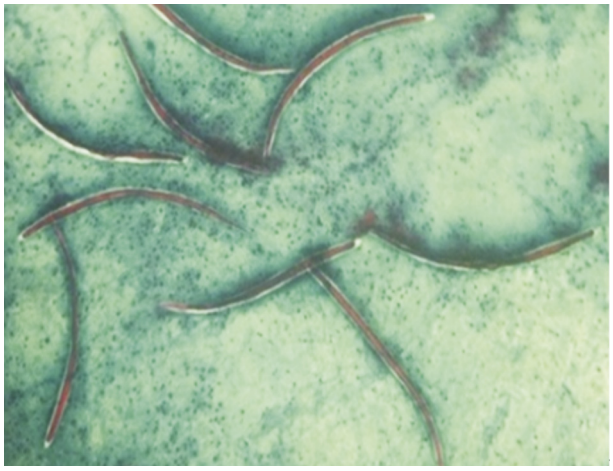

Figure 3. Larvae of *S. stercoralis* stained with Trichrome stain demonstrated notched tail and short buccal cavity. Image taken at 400× magnification.

3. Discussion

S. stercoralis is a soil transmitted intestinal nematode causing strongyloidiasis that was first reported in 1876 from the stool of French soldiers in Vietnam [3] who had severe diarrhea. Vietnam, Cambodia, and Laos remain as endemic countries for strongyloidiasis, with prevalence of 10% or less [5]. It is ubiquitous in tropical, subtropical countries and was once considered as one of the re-emerging diseases in northern Italy. In Malaysia, cases of strongyloidiasis were found in certain state including Penang among the fishermen (1.2%) [6] and *Strongyloides* larvae were detected in 7.1% of stool samples from Selangor [7]. Nevertheless, the actual prevalence might still be underestimated as microscopy has low sensitivity [8] in diagnosing this condition.

The clinical manifestations of strongyloidiasis vary, depending on the acuity of infection and the underlying host immune response. Vast majority of patients with strongyloidiasis have remained asymptomatic [9] and can survive decades undiagnosed. It is noteworthy, that our patient may had underlying chronic *S. stercoralis* infection, yet asymptomatic when he was diagnosed as having bullous pemphigus. Asymptomatic or chronic presentation of strongyloidiasis in this case could be one of the contributing factors to the delay in making accurate diagnosis. Furthermore, the multiple underlying diseases that this patient has had could mask the presentation of strongyloidiasis, which may lead to low index of suspicion. Thus, both epidemiological and clinical aspects are crucial in reaching to appropriate diagnosis and warranting the attending clinicians to be adequately exposed to such clinical conditions.

In symptomatic strongyloidiasis, gastrointestinal (GI) manifestations are more common in contrast to extra-intestinal (pulmonary, dermatology and neurology) presentations. These include epigastric pain, anorexia, weight loss, vomiting, chronic diarrhea, and constipation. While in pulmonary strongyloidiasis, the manifestations may resemble clinical features for bronchial asthma, as migrating larvae triggers wheezing [10] and mild cough [9]. These findings explained the underlying causes of rhonchi and it corresponds to the patient presentation while he was in septicemic shock. Furthermore, the features of the chest radiograph in the report suggest the presence of pneumonia, and this was in agreement to previous reports which described that some of the patients were having pneumonia, alveolar hemorrhage, ARDS and pulmonary fibrosis [11–13].

Most of the reported cases of strongyloidiasis worldwide involved immunocompromised hosts including AIDS, leukemia, lymphoma, solid organ transplant recipient, long term corticosteroid usage and chronic pulmonary disease. In this report, the patient too, is categorized as immunosuppressed individual by having multiple chronic diseases as well as receiving multiple doses of immunosuppressive agents such as steroid. In relation to that, nematode transmits its molting signals by means of molting hormones (ecdysteroids). In healthy adult, level of ecdysteroid-like substances is generally negligible [14], but in immunocompromised host, it could be vice versa. Administration of exogenous or endogenous corticosteroids may result in amplified amount of ecdysteroid-like substance in the host's tissues including intestinal wall where the adult female worm reside. This substances act as molting signal for eggs or rhabditiform larvae for the transformation into filariform larvae. Once intestinal population has become very large, it continues to expand rapidly, even at low molting rates. At this moment, discontinuation of steroids is insufficient to arrest the population growth. With the presence of voluminous amount of ecdysteroid-like substance and the immunosuppressive state that our patient had, this would most likely explain the causes of an increase in filariform larvae and subsequent increase in autoinfection. This will further attract more larvae to penetrate the bowel [15] and cause hyperinfection and dissemination. These postulations could be one of the most appropriate justifications for the development of disseminated strongyloidiasis in this patient.

The prednisolone that the patient had consumed for almost four months could be a triggering factor for the occurrence of hyperinfection syndrome. This finding was consistent with the previous reports of *Strongyloides* hyperinfection syndrome that were ensued after courses of steroid as short as six days [16] and with a dose of oral prednisolone as low as 20 mg per day [17]. Additionally in this case, there was concomitant infection caused by CRE that could add to more outrageous consequence, although appropriate antimicrobial therapy was instituted. This outcome was compatible with earlier reports which stated that concomitant infections should be treated aggressively, and any immunosuppressant, including exogenous corticosteroids, should be quickly tapered [17], as hyperinfection syndrome and disseminated strongyloidiasis carry high mortality rate.

Microscopic identification of *S. stercoralis* larvae is the definitive diagnostic test for strongyloidiasis. The larvae of *S. stercoralis* resemble those of hookworms, but they can be distinguished by their short buccal cavity (Figure 3). Other diagnostic methods include cultures that are cumbersome and may produce false-positive test results in patients with hookworm infection. While ELISA was reported to have a negative predictive value of 98%, hence is an excellent screening test for strongyloidiasis [18], however its sensitivity may be lower in severely immunocompromised patients. Stool and serum specimens were unfortunately not sent for the presented case.

Keiser PB. *et al.* [19] reported that, absence of eosinophilia is considered as poor prognostic sign in hyperinfection syndrome. The present case, had no evidence of eosinophilia and this was in agreement to cases reported by Babak M. *et al.* in 2004 [20] and Weam EH. *et al.* in 2016 [21] recently. Nevertheless, eosinophilia serves as a reliable indicator in majority of parasitic infection case, however, its diagnostic value in this case could be limited and affected due to steroid consumption and concurrent bacterial infection.

The presented case corresponds to the description of disseminated strongyloidiasis. It is supported with the combination of pulmonary strongyloidiasis, concomitant CRE infection, and immunosuppression which results into septicemic shock and is complicated further with pulmonary hemorrhage and ARDS. The diagnosis of disseminated strongyloidiasis is considered difficult and nearly always fatal. To date, strongyloidiasis is not commonly encountered in our country, yet the incidental finding of *S. stercoralis* larvae in the tracheal aspirate was an awakening. Indeed, it is a challenge in managing strongyloidiasis particularly in immunocompromised group of patients, in the country that has uncertain prevalence of the disease. Therefore, the importance of disseminated strongyloidiasis should be acknowledged, especially in this current era that involves increasing needs to travel and migrate to and fro endemic and non-endemic countries.

In conclusion, the possibility of disseminated strongyloidiasis should always be considered in any immunocompromised patient who suddenly deteriorates. Prognosis tends to be grave in this population and delay in diagnosing strongyloidiasis frequently results in death, despite vigorous treatment.

Ethical approval

Ethical approval was granted from Medical Research Ethics Committee (MREC), Ministry of Health Malaysia.

Conflict of interest statement

The authors declare that they have no conflicts of interest concerning this article.

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