Steroid-induced Strongyloidiasis with Cholestasis Post-COVID-19 Pneumonia

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Abstract

The use of immunosuppressive agents has recently been raised during the coronavirus disease 2019 (COVID-19) pandemic to manage the COVID-19 induced systemic inflammatory response and improve mortality. This widespread use of steroids and other immunomodulators for severe COVID-19 diseases might pose a potential risk of reactivation of latent diseases and the emergence of opportunistic infections such as strongyloidiasis. We report a case of strongyloidiasis with cholestasis in a middle-aged man; who was otherwise healthy and had no history of recent travel, developed three weeks after a prolonged course of steroids for management of severe COVID-19 pneumonia. The patient was managed with a combination of albendazole and ivermectin. A high index of suspicion of strongyloidiasis in symptomatic patients post immunosuppressant therapy for severe COVID-19 is required to prevent unfavorable outcomes. In selected high-risk patients post prolonged steroid therapy for COVID-19 pneumonia screening for strongyloidiasis and ivermectin empirical treatment might be considered even in non-endemic areas.

Keywords: *Strongyloides*, COVID-19, Steroids, Ivermectin

Introduction

Strongyloides stercoralis is a soil-transmitted intestinal nematode. Its clinical spectrum varies from subclinical to life-threatening disseminated infection. Endogenous autoinfection is a unique feature in strongyloidiasis that may result in a long-lasting infection.[1] In the immunocompetent host, cell-mediated immunity plays a role in regulating the population density of adult worms in the intestine. Once the immune system gets compromised, even one adult female can multiply rapidly leading to accelerated autoinfection and/or dissemination.[2] Administration of corticosteroids regardless of dose, duration, or route has been described as a risk factor of Strongyloidiasis.[3] Dexamethasone therapy, due to its powerful anti-inflammatory effects, has been widely used for the management of hospitalized patients with severe COVID-19 as it showed a survival benefit.[4] In Oman, the prevalence rate for Strongyloides stercoralis is 3% according to studies done in 2013.[5] We reported a case of strongyloidiasis with cholestasis post a course of steroid therapy for the management of severe COVID-19 infection.

Case report

A 55 years old Omani man who works as administrative in ministry of education, presented in May 2021 with three weeks history of profuse diarrhea associated with mucus and a frequency of 10 times per day. The patient had nausea, poor oral intake, and weight loss of approximately 10 kg. He had no history of fever, skin rash, jaundice, or respiratory symptoms. There was no history of travel, change in dietary habits, or ingestion of unusual

food and none of his family members had similar symptoms. His medical background was only remarkable for COVID-19 pneumonia in April 2020 for which he required hospital admission for 7 days. During his admission, he received 5 days course dexamethasone 6 mg/day and was discharged on a prolonged course of tapering dexamethasone regime 10 mg for 5 weeks.

The patient was initially evaluated at local primary health care and suspected to have pinworms (*Enterobius vermicularis*) for which he was treated with a single dose of albendazole 400 mg to be followed by a second dose after 2 weeks but the second dose was not taken. His symptoms persisted, therefore he presented to the Royal hospital for further management. On presentation, the laboratory workup showed high eosinophilia 1.2 x 10^9/L (normal range: 0.1-0.5 x 10^9/L) and picture of cholestasis as alkaline phosphatase 217 IU/L (normal range: 46-116 IU/L), alanine transaminase 76 IU/L (normal range 10-49) and normal bilirubin 6 umol/l (normal range 5-21). Stool microscopy showed *Strongyloides* larvae in 3 stool samples Figure 1. Abdomen Ultrasound showed common bile duct dilation Figure 2. Magnetic resonance cholangiopancreatography (MRCP) showed no abnormalities.

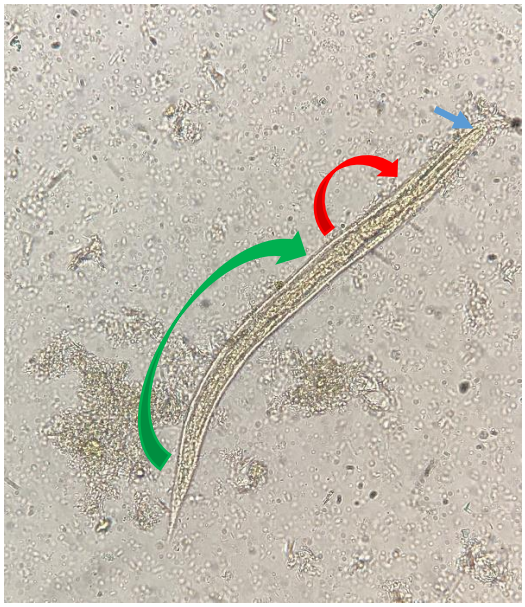

Figure 1: Rhabditiform larva of *S. stercoralis* in iodine stain stool sample. It has a short buccal canal (blue arrow), a bulbar portion of the rhabditoid esophagus with 3 portions (red arrow), and a prominent genital primordium (green arrow).

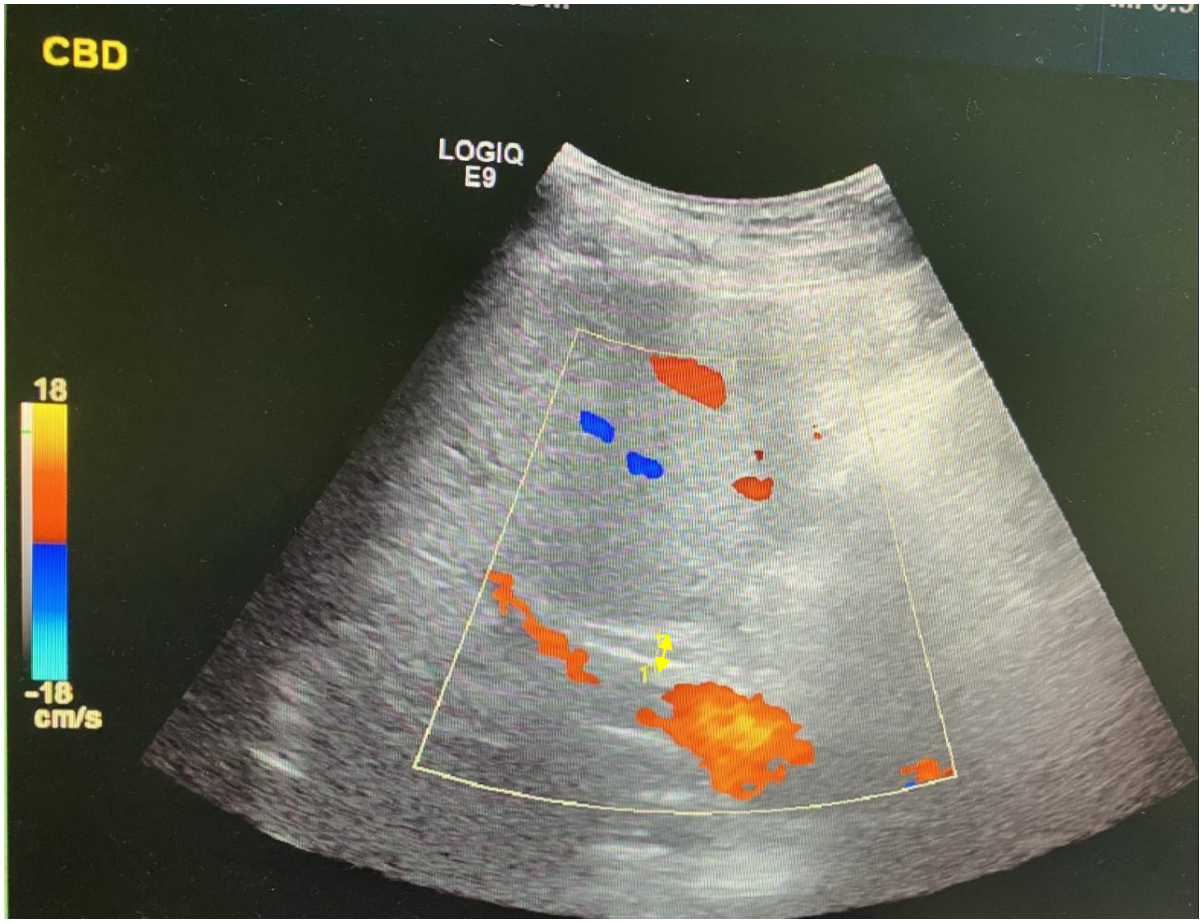

Figure 2: Abdomen Ultrasound showed mildly dilated common bile duct.

The patient was admitted for hydration and was treated initially with 2 doses of albendazole 400 mg for 2 days due to the in-availability of ivermectin. He clinically improved and was discharged home. One week later, he was reviewed in the clinic and he complained of persistent diarrhea, so he was given ivermectin 12 mg for 2 days and repeated after 2 weeks. After 1 month of follow-up, patient reported complete resolution of his symptoms and microbiological clearance as a repeated stool sample tested negative for *Strongyloides stercoralis*.

Discussion

In this report, we are discussing a case of strongyloidiasis with cholestasis in an immunocompetent man who has been on a prolonged course of steroid therapy for the management of severe COVID-19 infection and recovered well after three doses of albendazole and two courses of ivermectin.

Most *Strongyloides* infections (51-64%) are asymptomatic.[6] Acute infection may give a characteristic cutaneous reaction as the larvae penetrate the skin or respiratory symptoms, such as a dry cough or wheeze as larva migrate to lungs which were both not present in our patient. They can stimulate vague gastrointestinal symptoms once the adult worms reach the small intestine, such as diarrhea, vomiting, and epigastric pain, and our patient had these symptoms.[6] Hepatobiliary manifestations of strongyloidiasis seem to be rare, the larvae can cause granulomatous hepatitis with or without larval remnants. Steatosis and cholestasis are other hepatobiliary features and our patients had laboratory and radiological features suggestive of cholestasis.[6] Diagnosis of Strongyloidiasis by microscopic examination of a single stool sample can detect larvae in about 25% of uncomplicated *Strongyloides* infections.[5] However repeated examination of concentrated stool samples increases the sensitivity;a a number of stool samples recommended is 3 to 7 samples.[5] In our patient, the larva was seen in all three stool samples that were sent. Peripheral eosinophilia may be associated with parasitic infection and is commonly believed to be a good clinical marker for *Strongyloides stercoralis* infection as was seen in our patient. However, eosinophilia has poor sensitivity, specificity and predictive value especially, in predicting hyperinfection syndrome.[7]

In our patient, the only risk factor for acquiring strongyloidiasis is the use of steroids as part of COVID-19 management. The strongest risk factor for strongyloidiasis seems to be the corticosteroids, even at a dose of oral prednisolone as low as 20 mg per day and as short as six days.[8,9] Corticosteroids found to increase susceptibility to this parasitic infection through their suppressive effects on some of the major mediators of the immune response like eosinophils.[10] There are two previous case reports of patients who developed strongyloidiasis after receiving steroids for COVID-19 treatment, one from Italy and one from the US. Similar to our patient, the 2 cases have severe COVID pneumonia and received prolonged steroids, 1st case presented with abdominal pain and itching and improved with ivermectin but the second case has respiratory symptoms and required the addition of albendazole to ivermectin for 2 weeks.[9] Ivermectin 200 mcg/kg orally once a day for 2 days has been used for the management of uncomplicated infection and is generally well-tolerated as have been with our patient.[11] However, in our patient we had to repeat another course of ivermectin as he remained symptomatic. His parasitic load was high due to the prolonged course of dexamethasone that was extended to 5 weeks. In addition, our patient has cholestasis which could explain his requirement for 2 courses of ivermectin in addition to 3 doses of albendazole which also could play a role in his recovery. However, this will be individualized according to clinical response to treatment. In patients who require prolonged use of steroids for conditions such as necrotizing pneumonia, we propose a risk assessment and screening algorithm for strongyloidiasis in COVID-19 patients. Patients deemed at high risk (including travelers or migrants from endemic areas, farmers, military personnel, refugees, barefoot walkers, contacts with human sewage) may need empirical treatment with ivermectin, which has an efficacy of 85% as a single dose.[12]

Conclusion

In patients with COVID-19 pneumonia, we suggest avoiding using prolonged steroids to mitigate the risk of Strongyloidiasis. For those who will still require steroids as part of COVID-19 treatment, a high index of suspicion and epidemiological risk assessment are the cornerstones for the diagnosis. In such patients, we should consider a screening test and an empirical treatment for *Strongyloides* to have a better outcome.

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