Strongyloides in bronchoalveolar lavage fluid: practical implications in the COVID-19 era

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Highlight

Latent infections caused by *Strongyloides* sp. may become symptomatic years after initial exposure in endemic areas especially in specific contexts such as following administration of corticosteroids (for COVID-19 or other diseases). Heightened awareness of these reactivations and timely diagnosis may be critical to prevent complications and improve outcome.

Certain helminth infections such as strongyloidiasis may be underdiagnosed in non-endemic areas due to the presence of asymptomatic individuals, the lack of awareness of the disease and the poor sensitivity of diagnostic methods. Life-threatening complications of these infections may occur especially in patients with altered immune responses.[1]

Case Report

A 69 year-old Colombian male presented with abdominal pain and vomiting. He had been living in Spain for 20 years and had last traveled to his country 6 years previously. The patient was receiving treatment with prednisone 5mg daily and docetaxel, atezolizumab and ipatasertib as part of a clinical trial for stage IV prostate cancer with bone metastases.

On examination he was afebrile, basal oxygen saturation 96%, with normal renal/hepatic function, mild neutrophilia (12900 neutrophils/uL) and no eosinophilia. Nasopharyngeal PCR for SARS-CoV-2 was negative; pneumococcal antigen in urine was positive. Chest X-ray showed interstitial diffuse bilateral infiltrates.

In the following hours he developed progressive shortness of breath (oxygen saturation 80%). An urgent CT pulmonary angiogram confirmed bilateral pulmonary infiltrates and ruled out pulmonary emboli (see figure).

He was admitted on antibiotic treatment with levofloxacin and piperacillin-tazobactam and iv methylprednisolone (drug-induced pulmonary toxicity could not be excluded). Due to lack of improvement iv gancyclovir was initiated (CMV viremia was positive in blood, 2200 IU/mL).

Despite treatment the patient´s condition deteriorated over the next 72 hours and a diagnostic bronchoscopy was performed. Microscopic examination of the broncheoalveolar lavage fluid revealed nematode larvae identified as *Strongyloides* spp. (see figure). *Strongyloides* serum ELISA was positive (*NovaLisa® Strongyloides, NovaTec Immundiagnostica GmbH, Dietzenbach, Germany*). An initial stool sample for parasites was not processed. HIV, hepatitis C, HTLV-1/2 and *Trypanosoma cruzi* serologies and hepatitis B surface antigen were all negative.

A diagnosis of *Strongyloides* hyperinfection syndrome (SHS) was established, methylprednisolone was discontinued and treatment with oral ivermectin (200mcg/Kg/ daily) was administered for 14 days with gradual improvement of respiratory symptoms (basal oxygen saturation of 97%) and resolution of the pulmonary infiltrates on discharge. Stool samples for parasites/nematode larvae culture, sent after ivermectin treatment was initiated, were repeatedly negative.

Discussion

SHS may be a fatal complication of *Strongyloides stercoralis* infection. The life cycle of *S. stercoralis* may occur completely in the soil or in the host (autoinfection) and if this process becomes dysregulated large numbers of infective larvae may penetrate the gut, cycle through the lungs and re-enter the intestine leading to hyperinfection. In some patients with hyperinfection, migrating larvae invade ectopic sites, affecting other organs (disseminated strongyloidiasis). The most important risk factors for SHS are corticosteroid use and HTLV-1 co-infection.[1] A study reviewing over 130 patients with this syndrome found >80% had received corticosteroids.[2] Cases have occurred as soon as 5 days after steroid initiation and development of the syndrome may not be dependant on dose, duration or route of administration. Possibly due to underdiagnosis and undereporting there are no reliable data on the incidence and prevalence of *Strongyloides* hyperinfection.[1] During hyperinfection, feces usually contain a high load of larvae, and this was most probably not found in this case as stool samples were eventually processed days after ivermectin treatment had been initiated. Complicated cases of strongyloidiasis are generally associated with peripheral eosinophilia, although, as occurred in this case, eosinophilia may be absent (possibly also due to concomitant steroid use).

Awareness of this complication has been raised during the current COVID-19 pandemic. The use of dexamethasone for hospitalized patients with COVID-19 increased following publication of data from the RECOVERY trial showing a survival benefit in these patients and reports have been published of SHS in patients with COVID-19 treated with dexamethasone and tocilizumab. [3-6] Increased rates of COVID-19 have been noted in specific populations, including migrants, who may also be at higher risk for occult strongyloidiasis. Untreated SHS is associated with a high

mortality rate and the possibility of underdiagnosis of this syndrome in fatal cases of COVID-19 has been raised previously especially as symptoms and possible complications of these two entities may overlap. The World Health Organization issued an alert informing of the risks of this complication following administration of corticosteroids (in the context of COVID -19 or other diseases) and recommended presumptive treatment (with/without laboratory screening) with ivermectin as advisable for those at high or moderate risk of hyperinfection. [1, 7] Increased vigilance for *Strongyloides* infection, especially in the current pandemic era, is thus warranted.

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All authors contributed to the clinical management of the patient and interpretation of the data. FFN wrote the paper, the co-authors reviewed the final draft.

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Conflict of interest:

There are no conflicts of interest to declare

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Figure:

Top row: Chest X-ray and CT scan on admission

Bottom row: *Strongyloides* spp. larvae in broncheoalveolar lavage fluid (Papanicolaou stain) (filariform larvae identified based on their long esophagus and notched tail).