CASE REPORT

Strongyloides hyper infection in a steroid dependent leprosy patient

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Accepted for publication 5 October 2016

Summary

Background: Immunosuppression caused by corticosteroids predisposes leprosy patients to *Strongyloides stercoralis* infection which if untreated can be fatal. Patients acquire infection by walking barefoot in infested soils and can be infected for life because of the auto infective cycle of the parasite. Corticosteroids have precipitated death in more than 60% of disseminated strongyloidiasis cases.

Objective: The aim of this article is to report a successfully treated case of SS infection in a low resourced leprosy hospital in rural India and increase awareness of the unique features of *S. stercoralis* and also to outline the important role that dermatologists and leprologists have in diagnosing and treating chronic strongyloidiasis, thus preventing cases of fatal hyperinfection.

Discussion: Leprosy patients live in tropics and subtropics which are also endemic for SS infestation and hence are prone to develop this infection. Chronic strongyloidiasis does not have typical symptoms and clinical features. Those who have unexplained eosinophilia must be checked for the presence of the parasite before initiation of steroid therapy for reactions and neuritis. Leprosy heath workers must have the awareness and a high index of suspicion to diagnose disseminated SS infection. Otherwise these patients, if infected, may develop hyperinfection syndrome, which has a high fatality rate.

Introduction

Leprosy is a disease of the poor, implying poor nutrition, housing, sanitation, and hygiene. Complications of leprosy include DDS reaction, neuritis, Type 1 and Type 2 reaction for which corticosteroids are used in variable doses, sometimes for prolonged periods. Adverse effects of steroids involve many systems of the body, causing myriad infections, a frequent cause of morbidity and mortality. Helminthiasis is one such infection that occurs in the general population and more so in an immunosuppressed state. Infection with helminths,
especially Strongyloides Stercoralis (SS) is a poorly studied and reported condition. SS infects about 100 million people mainly in the tropics and subtropics.\textsuperscript{1–3} Its three unusual features make eradication difficult, i.e. autoinfection,\textsuperscript{4} parthenogenesis and external phase of life cycle with a free living adult.\textsuperscript{5} Literature describes SS infection as chronic and asymptomatic, but a change in immune status can lead to an increase in parasite load, hyper-infection syndrome, dissemination, and death.\textsuperscript{6} Corticosteroid use causing immunosuppression is commonly associated with hyperinfection syndrome and have precipitated death in more than 60% of cases. Leprosy patients on corticosteroids are at potential risk of developing this syndrome.

Chronic infections with \textit{S. stercoralis} can be clinically in apparent or can lead to cutaneous, gastrointestinal, or pulmonary symptoms. Skin involvement is characterised by a migratory, serpiginous, urticarial rash and termed larva currens. Gastrointestinal symptoms of strongyloidiasis include diarrhea, abdominal discomfort, bloating, nausea, and anorexia. The symptoms of pulmonary strongyloidiasis include cough and shortness of breath. Bacterial and fungal infections often occur in cases of hyperinfection because of the leakage of gut flora from a bowel damaged by the motile larvae. The enteric bacteria are disseminated by the larvae to other organs resulting in septicemia, pneumonia, meningitis and death.

Diagnosis of Strongyloides is often overlooked and delayed because of its vague signs and symptoms.\textsuperscript{7} A definitive diagnosis of strongyloidiasis is usually made by the detection of larvae in stools but is a difficult intestinal parasite to diagnose because of the low parasite load and irregular larval output.\textsuperscript{8} Ivermectin is the drug of choice and a single dose therapy is sufficient for asymptomatic patients. For disseminated cases it needs to be tailor-made till complete eradication of the parasite.\textsuperscript{5} Disseminated SS infection has a high mortality (85–100%).\textsuperscript{9}

Strongyloidiasis hyper infection is rarely reported in leprosy, but this may be due to under-reporting as the diagnosis could be missed.\textsuperscript{10} A Pubmed search shows in 12% of reported cases the diagnosis was made post mortem.\textsuperscript{5}

This paper describes a successfully treated case of Strongyloides Stercoralis hyper infection in a Leprosy patient on long-term steroid therapy from a rural hospital in West Bengal, India.

Case Report

A 35 year old man with lepromatous leprosy was admitted in the hospital on 9th April 2016 for uncontrolled ENLs on prednisolone 40 mg per day. He had typical features of steroid dependence like moon facies, central obesity, thin extremities, pedal edema and easy bruisability. He had been treated with WHO MDT at an outside facility for a year and varying doses of prednisolone for 2 years.

On admission his smears were 3 +, BP was 100/70 mm and Pulse Rate 94/min. Prednisolone dose was continued at 40 mg per day. Cap Clofazimine 300, Tab Ranitidine 150 mg twice daily, Tab Calcium 500 daily and Tab Albendazole 400 mg daily for 5 days was added. Thalidomide was started at a dose of 300 mg daily. Over the month prednisolone was successfully tapered to 20 mg. The patient had fluctuating low potassium levels, intermittent vomiting, right upper quadrant abdominal pain, distension with alternate loose stools and constipation throughout the month. Upper Gastro Intestinal scopy revealed mild hepatomegaly with Grade 1 fatty changes. On May 16 he was hypotensive with blood
pressure 80 systolic and pulse rate 140/min. He vomited twice, had three episodes of watery foul smelling diarrhea, developed breathlessness, oxygen saturation dropped to 60 % and he became semiconscious.

Table 1 tabulates the investigations that were done during the period of illness. Stool examination revealed large numbers of Strongyloides Stercoralis larvae and Entamoeba Histolytica cysts.

He was provisionally diagnosed to have hyper infection syndrome secondary to Strongyloides Stercoralis with gram negative sepsis. All oral medications were stopped. IV Ceftriaxone, Gentamicin, metronidazole was started along with Ionotrope support and Naso gastric dependent drainage. Abendazole, ivermectin and thalidomide were administered through an NG tube. He developed oliguria; bowel sounds were sluggish to absent, abdomen distension persisted, and there was severe abdominal tenderness with no passage of stool or flatus. Breathlessness was managed by intermittent oxygen therapy. Oliguria was managed with IV fluids and IV frusemide. There was generalized anasarca with tachypnea. Hemoglobin dropped to 7 gm /dl and was transfused 2 pints of blood. On day 7 he passed a stool and the abdominal distension started subsiding. He was off ionotrope support after 11 days. The abdominal symptoms gradually subsided and repeat stool examination after 2 weeks and one month did not show any Strongyloides Stercoralis larvae. He did not have further ENLs during this period.

Discussion

The course of this patient’s illness with diarrhea, breathlessness, peripheral eosinophilia and the presence of many SS larvae in the stool was strongly suggestive of Strongyloides hyper infection. Severe abdominal pain and ileus indicated gram negative sepsis. The Nonspecific symptoms experienced by the patient made us provisionally diagnose him as steroid dependent with chronic adrenal insufficiency. The right upper quadrant pain was being attributed to hepatic congestion and gall bladder pathology but an Upper GI scopy did not reveal any such cause. Retrospectively, we learned that it was acute duodenitis due to hyper infection. Stool tests positive for SS, peripheral eosinophilia, hypokalemia and clinical features clinched the diagnosis.

Strongyloides is unique among the commonly occurring helminths, as it can complete its life cycle within the human host, thereby allowing it to persist and replicate indefinitely. In the life cycle of other helminths, such as hookworms and roundworms, one larva gives rise to only one adult worm. Strongyloides infection, in contrast, can lead to autoinfection in which rhabditiform larvae can re-penetrate the gastrointestinal mucosa or the perianal skin.4,11 Immunosuppresion stimulates the auto infective cycle resulting in dissemination. Autoinfection also makes eradication of this parasite difficult. Stool microscopy to identify S. stercoralis larvae or ova has variable sensitivity.12 A direct stool microscopy has only a sensitivity of 30% and three specimens will increase the sensitivity to 60–70%.12 Peripheral blood eosinophilia >5% is associated with strongyloidiasis, in immunocompetent hosts.12–15 Thus, physicians in endemic regions should strongly suspect strongyloidiasis when patients present with gastrointestinal and/or pulmonary symptoms with peripheral eosinophilia.16 However, patients on corticosteroids may not have eosinophilia since their immune response is blunted. Eosinophilia is a good prognostic indicator but patients on Thalidomide also have peripheral eosinophilia, so even if this test is positive it may not be predictive enough.
### Table 1. Laboratory Investigations during the period of illness

<table>
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<tr>
<th>S. No</th>
<th>Investigation</th>
<th>9th April</th>
<th>17th May</th>
<th>19th May</th>
<th>21st May</th>
<th>23rd May</th>
<th>27th May</th>
<th>30th May</th>
<th>1st June</th>
<th>6th June</th>
<th>21st June</th>
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<td>7</td>
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<td>7</td>
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<td>16</td>
<td>Stool micro</td>
<td>17th May</td>
<td>Plenty of SS larvae and EH cysts</td>
<td></td>
<td>19th May</td>
<td>Plenty of SS larva</td>
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<td>No larva and cysts</td>
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* SGOT- Serum Glutamic Oxaloacetic Transaminase, SGPT – Serum Glutamic Pyruvate Transaminase.
Serology again in such patients may not be sensitive due to the immunosuppression. Hence diagnosis depends on risk factors, peripheral eosinophilia, and positive stool tests with a strong clinical suspicion.

Broad-spectrum antibiotics were administered to cover Gram negatives and anaerobes. Hypokalaemia resulted from continuing gastric aspiration, poor intake and chronic diarrhea. Due to ileus, IV correction was done. Oliguria was treated like acute renal failure. Clinical presentation involved Pulmonary, Gastrointestinal, Genitourinary, hematological systems and sepsis.

Strongyloidiasis is a difficult to treat because of its auto infective filariform larva more so in cases with paralytic ileus due to poor absorption of the drug.17

Ivermectin is registered as the drug of choice for the treatment of strongyloidiasis in the WHO’s list of essential drugs.18 The recommended dose is 200 mcg/kg/day taken as a single dose.12,19 In SH, daily ivermectin is administered for a minimum of 2 weeks (duration of auto infective cycle) and often until there has been evidence of 2 full weeks of negative stool examination. Despite treatment, fatal progression to acute respiratory distress syndrome cans occur even with successful eradication of larvae.20

Patients with paralytic ileus can have difficulty absorbing oral ivermectin due to tissue edema. Ileus can be prolonged in patients due to bowel deposits of clofazimine mimicking obstruction since chronic ENL patients are usually on high dose clofazimine. Parenteral formulations of ivermectin are not approved currently for use in humans. It can be administered under compassionate use Investigational New Drug exemptions. Some cases have reported improved serum drug levels with subcutaneous ivermectin.21 We had procured the veterinary formulation of intravenous ivermectin but did not use it since the patient started responding to oral medication.21 Oral combination of Albendazole and ivermectin twice daily for 2 weeks was used for this patient. Though there are no RCT using this, it seems a reasonable approach.

Albendazole has been recommended as a well-tolerated and safe treatment for strongyloidiasis at a dose of 400 mg orally twice daily for 5 days which a cure rate of 95%.18 In our case Albendazole prophylaxis was not effective since our patient had received 5 days of the drug one month ago. Administration of Albendazole and Ivermectin combination had added benefits since the patient had coinfection with Entamoeba Histolytica.

Steroids were stopped to allow for clearance of the parasites. However if there is a risk of ENL eruption then it must be continued in the lowest effective dose. Since our patient was on Thalidomide, we could completely stop prednisolone. This can be a real dilemma in countries where thalidomide is not available and in the steroid dependent patient.

We found the return of bowel sounds and movements considerably prolonged. Again this could be attributed to the high dose clofazimine deposits in the intestines impeding the return of peristalsis. After 2 weeks, the patient had two stool samples that were negative for parasites, no GI symptoms and no ENLs.

Financial constraints prevented the patient to be referred to a higher treating facility which is about 120 km away. Blood cultures, duodenal fluid aspiration were not done due to non-availability. Chest X-ray and erect abdomen X-ray were not done since the patient was too sick to be shifted.
Conclusions and recommendations

Primary prevention includes hand washing habits, use of footwear, avoidance of outdoor toilets and bathing in ponds and rivers and thorough washing of vegetables.

Albendazole and Ivermectin must be administered during initiation of Multidrug therapy for leprosy in patients living in endemic areas for Strongyloidiasis. Patients at risk for long term steroids should prophylactically be treated with ivermectin for chronic strongyloidiasis. Symptoms of infestation are vague and similar to chronic steroid dependence. Clinicians must make an effort to look for and be familiar with its management. This information must be disseminated to all the health carers. Stool tests must be performed frequently to diagnose the infection. Laboratory personnel need to be educated to recognise this larva during stool microscopy. Protocols for steroid use must be rewritten keeping the latest therapeutic guidelines for Strongyloides in mind. Since it is in the model WHO essential drug list for NTD, every treating facility must make this drug available for use.

In developing countries, over-the-counter availability of steroids is the rule rather than the exception. Therefore, every physician working in a strongyloidiasis endemic region, or treating patients from endemic regions, needs to persistently enquire about potential steroid use or look for other signs of steroid abuse.

Rigorous screening of leprosy patients at risk for chronic steroid use from Strongyloides-endemic areas is of utmost importance to prevent this often missed fatal complication.

References


