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Trichuris dysentery syndrome: Do we learn enough from case studies?

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Abstract. Trichuris Dysentery Syndrome (TDS) is a severe persistent trichuriasis associated with heavy worm build-up in the colon that continues to be neglected and underestimated in endemic countries. Trichuriasis is most prevalent in children in tropical countries, and that increases the risk of TDS. We reported a series of four preschool children of both genders chronically having TDS over a period ranging from several months to years presenting with anaemia. The hemoglobin levels ranged from 4.6 to 9.1 g/dl on first admissions. Despite treatment, the cases were reported to have failure to thrive with persistent anaemia. It was concluded that TDS should be considered in endemic areas among children presenting with chronic bloody diarrhea and anaemia.

INTRODUCTION

Trichuris trichiura is a soil-transmitted intestinal helminth found primarily in tropical countries with poor sanitation and hygiene. Human acquires the infection when embryonated eggs are ingested via contaminated food or water. The eggs hatch and the larvae inhabit the large intestine where they develop into adult males and egg-laying females (Cooper 2004).

Trichuris trichiura infection (trichuriasis) constitutes an important public health problem that may cause asymptomatic infection or severe persistent infection termed Trichuris Dysentery Syndrome (TDS). TDS is associated with heavy worm build-up in the colon and manifested by chronic mucoid dysentery that leads to systemic consequences such as anaemia, due to direct loss of red blood cells from the gut followed by iron deficiency, and impaired growth (Cooper 2004; Krishnamurthy *et al.*, 2009;). The mechanism for the impaired growth is not clear. It was postulated that increased circulating TNF-α may inhibit patient's appetite, as well as, metabolic processes (Cooper 2004).

Stool microscopy and colonoscopy provide differential diagnosis of TDS which differentiates the infection from other causes of infective dysentery or idiopathic colitis (Cooper 2004). Here, we report four cases of TDS in preschool children, who presented with chronic bloody diarrhea, anaemia and failure to thrive.

CASE DESCRIPTION

Case 1

A 5-year-old Malay boy was admitted to the pediatric ward four times within a 2-year period for chronic diarrhea and symptomatic anaemia. He had a medical history of epilepsy and was suffering from chronic diarrhea for two years. He presented with recurrent bloody diarrhea (15 times/day) associated with abdominal pain, vomiting and low-grade fever. However, he did not have any cough or abdominal distention. His weight is 11.7 kg and height is 95.5 cm which is below 3rd

centile. During his first admission, worm infection or polyps were suspected, thus colonoscopy was done which revealed numerous *T. trichiura* worms seen all the way from the rectum to the splenic flexure. Rectal biopsy showed stromal infiltration by eosinophils, lymphoplasma cells and neutrophils, suggestive of chronic colitis with eosinophilia. The haemoglobin was 4.6 g/dl with full blood picture showing thrombocytosis, leukocytosis with eosinophilia; hypochromic microcytic anaemia with elliptocytosis and target cells. The serum immunoglobulin G was 21.8 g/L (normal value: 5.5-14.0 g/L), Ig A was 2.27 g/L (normal value: 0.35-2.50 g/L) and Ig M was 1.45 g/L (normal value: 0.40-1.50 g/L). Stool examination showed presence of occult blood, mucus, pus cells and *T. trichiura* ova. The patient was treated with albendazole 400 mg daily for 5 days and blood transfusion (1 unit of packed cells) to raise his hemoglobin level. The patient was discharged after symptoms resolved with hemoglobin of 7.9 g/dl. However, the patient suffered from the same symptoms and was admitted two times to the hospital and treatment was repeated. On the fourth and last admission, the patient was treated with mebendazole 100 mg twice daily for 3 days. The diagnosis of recurrent/ relapsed TDS with chronic anaemia was made. Longer hospitalization was needed for treatment of symptomatic anemia and for blood transfusion to correct the haemoglobin level.

The full laboratory investigation profile, treatment and patients' outcome (for cases 1 to 4) are shown in Table 1.

Case 2

A 6-year-old Malay boy was admitted to the ward two times for a similar problem of bloody diarrhea, nausea, vomiting and fever for 2 months. On examination the child was noted to be pale and small for age. His weight was 14 kg while his height was 99.8 cm. which is below 3rd centile. The haemoglobin was 5.2 g/dl and the full blood picture showed hypochromic microcytic anaemia with thrombocytosis and eosinophilia. Stool examination showed presence of occult blood and *Trichuris trichiura* ova. The patient was treated with syrup albendazole 400 mg daily for 3 days and was transfused with whole blood and post transfusion hemoglobin was 10.2 g/dl. After six weeks, stool examination done during follow up in the clinic showed parasitological clearance of the ova.

After three years, the patient was seen again at the Child and Adolescence Psychiatric Clinic for learning difficulties. He was not performing well at school. At 9 years of age, he is only able to write his name and was not able to calculate simple mathematics. It was planned for him to be transferred out to a special school for children with learning disabilities. Thus, he was referred to a child psychiatrist for assessment and further treatment. However, he has defaulted follow up after the first visit.

Case 3

A 5-year-old Malay boy had a previous history of recurrent hospital admission for chronic diarrhea since early age. He was admitted for diarrhea associated with food intake (defecate 5 min after a meal), no fever or vomiting. His weight is 10 kg and his height is 101 cm below 3rd centile. His stool was negative for any parasite infection. He has been given supplements to improve his clinical state and was discharged. One week later, the patient was readmitted with complain of abdominal pain. His weight has decreased to 7.5 kg and his hemoglobin was 6.1 g/dl. His full blood picture showed dimorphic blood film with hypochromic microcytic anaemia, thrombocytosis and leukocytosis. Stool examination showed presence of occult blood, *T. trichiura* ova and threads of bloody mucus. He was treated and discharged. Two weeks later, the patient was readmitted again to the hospital with similar symptoms. Hemoglobin was 4.3 g/dl and stool examination showed presence of *T. trichiura* and *Ascaris lumbricoides* ova and threads of bloody mucus. The final diagnosis for this case is ascariasis, TDS, failure to thrive and malabsorption. The patient was treated with mebendazole 60 mg twice daily for 3 days, albendazole 400 mg daily for 3 days and oral hematinics.

Table 1. Laboratory profiles, treatment regimen and outcome for all cases of TDS

		TWBC (10^9/L)	Hb (g/dl)	Plt (10^9/L)	ANC (10^9/L)	AEC (10^9/L)	Treatment	Outcome
	Normal values*	10±5	12.6±1.5	200–490	1.5–8	0.1–1.0		
CASE 1								
First admission		34.94	4.6	619	4.79	22.78	Albendazole 400mg for 5 days and blood transfusion	
Second admission		19.8	4.0	732	5.15	7.02	Albendazole 400mg for 3 days and blood transfusion	
Third admission		14.23	3.9	733	5.31	5.62	Albendazole 400mg for 3 days	
Fourth admission		17.01	11.1	492	7.92	3.72	Mebendazole 100mg 12 hourly for 3 days	Relapsed TDS
CASE 2								
First admission		12.7	5.2	504	5.70	1.41	Albendazole 400mg for 3 days and blood transfusion	Cured
Second admission		14.1	7.1	788	NA	NA		
CASE 3								
First admission		17.1	6.1	788	6.54	0.21	Albendazole 400mg for 3 days. Haematinics.	
Second		14.6	4.3	605	6.11	1.31	Albendazole 400mg for 3 days.	Cured
CASE 4		20.7	9.1	578	6.77	7.7 7	Albendazole 400mg for 3 days. Haematinics.	Cured

Note: TWBC= total white blood cells, Hb=hemoglobin, Plt= platelet, ANC= absolute neutrophil count, AEC= absolute eosinophil count, NA= not available. * Normal values for children 2-6 years (Imelda and Mitchell, 2011).

Table 2. Summary of clinical features for all cases

Cases	Age	Gender	Age at diagnosis	Duration of illness	Chronic dysentery anaemia	Hypochromic microcytic	Short stature	Pallor
1	5 years	Male	3 years	2 years	Present	Yes	Yes	Present
2	6 years	Male	6 years	2 months	Present	Yes	Yes	Present
3	5 years	Male	Since infancy	4 years	Present	Yes	Yes	Present
4	6 years	Female	4 years	2 years	Present	Yes	Yes	Present

Subsequent follow up showed parasitological clearance of the ova and corrected hemoglobin level of 9.6 g/dl.

Case 4

A 6-year-old Malay girl suffered from chronic diarrhea for 2 years associated with abdominal pain and was previously diagnosed as TDS. On admission, she was noted to be slightly pale and small for age. Haemoglobin was 9.1 g/dl and full blood picture showed monocytosis, eosinophilia, thrombocytosis, reactive lymphocytes and mild hypochromic microcytic anaemia. Her weight was 14.5 kg and her height was 101.5 cm below 3rd centile. Stool examination showed presence of occult blood, *Trichuris trichiura* and *Ascaris lumbricoides* ova. Colonoscopy showed numerous worms and ulceration of the sigmoidal intestinal mucosa and bleeding. Biopsy specimen was not taken during the colonoscopic procedure. The patient was treated with 400 mg albendazole daily for 3 days and syrup folate 25 mg daily and showed parasitological clearance of the ova on subsequent follow up.

DISCUSSION

Infections with soil transmitted nematodes are still being neglected and underestimated. Chronic infection state may develop due to misdiagnosis, incomplete treatment or absence of follow up. These infections may persist as dormant asymptomatic infections, such as chronic strongyloidiasis that may cause fatal hyperinfection syndrome as a complication in immunocompromised patients (Zueter *et al.*, 2014) or chronic life threatening Trichuris dysentery syndrome. Sometimes, trichuriasis may cause chronic dysentery like syndrome that mimics other inflammatory bowel disease like ulcerative colitis and celiac disease (Cooper 2004).

There were cases reported for chronic strongyloidiasis, as well as strongyloides hyperinfection syndrome (AbdelRahman *et al.*, 2012; Norsarwany *et al.*, 2012) and its prevalence were observed among all age groups. On the contrary, there are few published reports of TDS in children, with no previous reports in adults (Khuroo & Khuroo, 2010). The prevalence of trichuriasis is higher in children, in particular among school-age children of tropical countries (Stephenson *et al.*, 2000). Noorizan & Mahendra Raj (2001) had reported TDS cases in children in Kelantan state, Malaysia. They suffered from persistent bloody diarrhea and anemia and the diagnosis was confirmed with the detection of *T. trichiura* by colonoscopy.

Human trichuriasis begins when embryonated eggs of *T. trichiura* are ingested via contaminated food or water and hatch inside the small bowel to yield the first-stage larvae that migrate to the caecum, where they mature into adult worms that penetrate the mucosa of caecal wall and female worms start releasing eggs that appear in faeces 3 months after the infection. Most of the affected people are asymptomatic. However, in cases of incomplete or no treatment, the disease progresses to heavy infection, a specific disease stage known as Trichuris dysentery syndrome (TDS). TDS commonly affects children between 2 and 10 years of age and is characterized by chronic symptoms of mucoid diarrhoea, rectal bleeding, anaemia, rectal prolapse, and finger clubbing (Azira & Zeehaida, 2012).

In this series, all the children were aged between 5 to 6 years old with predilection of males. All the children presented with chronic dysentery, hypochromic microcytic anaemia and failure to thrive. They were seen regularly since the symptoms persisted after a single treatment and thus repeated anti-helminthic drug administration was necessary to ensure parasitological clearance of the ova. In case 1, the child had recurrent trichuriasis, requiring multiple hospital admissions. It was not clear whether the parasite was not adequately treated or there had been reinfection by *Trichuris trichiura*. The same patient was also serologically positive for toxocara antibody. Multiple parasitic infections could contribute to the severity of the illness in this patient.

For the laboratory profile characteristics, all patients presented with thrombocytosis and eosinophilia except for case 3 who had normal eosinophil count. In case 1, the serum immunoglobulin G level

was high, which could indicate previous and/or possible recurrent infection. However, the Ig A and Ig M levels were normal in this patient. The serum immunoglobulin levels were not done for the other 3 cases. In all cases, serum albumin, serum iron, serum ferritin and Erythrocyte Sedimentation Rate (ESR) were not requested. There were specific risk factors seen in all four cases illustrated in this series. All patients live in rural villages in Kelantan state, Malaysia with low socio-economic backgrounds that reflect possible poor sanitation and poor hygiene which increase the risk of infection. As *T. trichiura* is prevalent in Kelantan, there is a possibility of underdiagnosed cases in this state that may have developed into TDS.

In Malaysia, many surveys were conducted using a panel of diagnostic tests to investigate for trichuriasis. A study done among Orang Asli (arborigines) communities in Selangor, Malaysia on children aged between 2-15 years showed that up to 98% had trichuriasis (Al-Mekhlafi *et al.*, 2006). A case report was documented on a 4-year-old girl with chronic TDS complicated with iron deficiency anemia. Definitive diagnosis was made by colonoscopy and blood transfusion was given to correct anaemia. It was concluded that a longer duration of anti-helminthic treatment up to three days is required to achieve effective and better outcome (Azira & Zeehaida, 2012). Mebendazole has been proven as the treatment of choice in trichuriasis. Standard dose regime of mebendazole of 100 mg twice daily for 3 days provides about 70% cure rate. A second course of mebendazole is indicated if patient is not cured within 3 to 4 weeks (Bartoloni *et al.*,1993). In this series, three patients were cured with repeated administration of albendazole. However, in the recurrent TDS, mebendalzole should be the treatment of choice and should be regularly repeated as recommended by Bartoloni *et al.* (1993).

Many anti-helminthic drugs effective against *Ascaris* have been shown to be inactive against *Trichuris*. A single dose of mebendazole 100 mg to 500 mg; or albendazole 400 mg give a good cure rate in most light infections. For clinically significant infections, mebendazole 200 mg per day for 3 successive days, or albendazole 400 mg per day for 3 days is recommended to treat TDS. Clinical cure will be obtained following worm expulsion but if the environment is unchanged with poor sanitation, re-infection is likely to occur and re-treatment every 3 months is advised (Cooper 2004). Recurrent TDS may result in some complications. In this series, two patients had complications of symptomatic anaemia and learning disabilities affecting their school performance. In one study, treatment for relatively heavy infections of *Trichuris trichiura* had improved cognitive performance in school-going children (Stephenson *et al.*, 2000). All patients in this series had failure to thrive. The growth retardation in TDS can be reversed by repeated treatment for the infection. Oral iron supplement should be part of the treatment regimen. In patients with significant developmental and cognitive deficits, positive psychological stimulation in the child's environment helps to minimize the effect (Stephenson *et al.*, 2000).

TDS is a chronic problem especially when prevention of the infection is not specifically addressed. The issues of reinfection after a successful treatment arise because the affected child still lives in the same environment which acts as a source of infection. The education on hand and personal hygiene practices should be delivered to the patients and all their family members to reduce the chance and possibility of reinfection. These will include hand washing before eating, after using toilet, after contact with soil, drink boiled water, proper washing of fruits and vegetables and eat cooked food.

In conclusion, TDS is a chronic problem among young children in endemic areas. The infection need to be diagnosed and treated accordingly. The children need to be closely followed up to monitor their symptoms, complications such as anaemia and the treatment regimen. There should be a guideline for the management of children with TDS. The multidisciplinary team should consist of pediatrician, gastroenterologist, dietitian, psychologist and a child psychiatrist . These patients should be seen

at the combined clinic to organize the treatment plan for TDS since this disease is of chronic course with multiple complications. The role of home visits and contact tracing among defaulted cases should be ascertained and adhered. Health education to the family members to break the chain of transmission of this soil-transmitted helminth requires support from everyone including the hospital staff, the public health care workers as well as the family members of the affected patients.

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