

Hepatosplenic Schistosomiasis Presenting as Melena in an Adolescent Filipino Male: A Case Report and Literature Review

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ABSTRACT

Schistosomiasis, a snail-borne disease caused by infection with a trematode parasite of the genus *Schistosoma*, is one of the most neglected tropical diseases in the world. One of its rare complications is hepatosplenic schistosomiasis which ultimately leads to fibrosis and presinusoidal portal hypertension.

We report a case of a 13-year-old Filipino male from Quezon City with previous one year residence in the endemic island of Leyte, presenting with melena. Diagnostic work-up revealed hepatosplenomegaly and periportal fibrosis with multiple hepatic nodules on ultrasound, positive *Schistosoma japonicum* eggs on Kato-Katz stool examination technique, and findings of esophageal varices on upper endoscopy. The patient was managed with praziquantel, propranolol, and endoscopic rubber band ligation of the esophageal varices, with note of resolution of bleeding, and improvement on sonographic liver findings.

The degree of liver fibrosis from schistosomiasis is affected by poorly understood mechanisms which affect its severity, progression, and complications, regardless of biosocial factors including egg burden and duration of parasite exposure. This is the first case report on a Filipino adolescent to document significant interval improvement, within four weeks of treatment, of the characteristic fibrotic pattern in hepatosplenic schistosomiasis. Hepatosplenic schistosomiasis is still often missed out as the diagnosis in patients who consult with common symptoms, and high index of suspicion is recommended for those with history of residence in endemic areas. Likewise, treatment focusing on parasite eradication can aid in promptly addressing the resulting fibrosis and its complications.

Keywords: Hepatosplenic schistosomiasis, fibrosis, portal hypertension, gastrointestinal bleeding, case report

INTRODUCTION

Schistosomiasis is a snail-borne disease caused by infection with a parasitic blood fluke and is one of the most neglected diseases in the world, particularly in tropical and subtropical regions.¹ It is also known as "bilharziasis" after Theodor Bilharz, who first identified the parasite in 1852. These parasites live in certain types of freshwater snails, and individuals can become infected when skin comes in contact with contaminated water and is penetrated by the infectious form of the parasite called cercariae. Seven schistosome species are known to cause infection in humans and among these, the most common are *S. japonicum* in East and Southeast Asia, *S. mansoni* in Africa and South America, and *S. haematobium* in Africa and Middle East. Among these, *S. japonicum* and *S. mansoni* are known to cause intestinal tract diseases, while *S. haematobium* causes genitourinary tract diseases.²

It is estimated that schistosomiasis affects 250 million people worldwide with 779 million people in endemic areas remaining at risk, many of whom develop severe and permanent



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disabilities.³ The global health burden of schistosomiasis has been estimated at 9 to 36 million disability-adjusted life years (DALYs), a value similar to that of malaria or tuberculosis, which are also both endemic in the Philippines.⁴ Schistosomiasis caused by *S. japonicum* affects approximately 12 million Filipinos, with 2.5 million directly exposed to the infection.⁵

Although the national prevalence has decreased significantly from 20% in 1940⁶ to 4% in 2011, this is still far from the World Health Organization (WHO) target of <1% by 2025.⁷ Among Filipino children, the Philippine Pediatric Society (PPS) registry from 2006 to 2024 reported 84 cases of schistosomiasis from *S. japonicum* (ICD B65.2).

In the Philippines, *Schistosoma* remains endemic in 28 provinces found in 12 regions.⁴ However, schistosomiasis is still commonly missed as signs and symptoms are non-specific and a high index of suspicion is recommended for those with history of residence in endemic areas. We report an adolescent male with a history of melena and with exposure in a schistosomiasis-endemic area. He was eventually diagnosed and managed as a case of hepatosplenic schistosomiasis.

CASE PRESENTATION

A 13-year-old Filipino male from Quezon City presented with a five-month history of occasional melena three to five times per week, around 50 to 100 ml per episode, associated with epigastric pain. An abdominal ultrasound revealed hepatic nodules and splenomegaly. The patient had unknown diagnosis on consult but was prescribed with oral cefuroxime for seven days with no relief of symptoms. He had undocumented weight loss, easy fatigability, and decreased appetite, but with no fever, vomiting, and bowel or urinary changes. He has no known comorbidities and no previous hospitalizations. Family history is unremarkable. He and his family used to reside in the island of Leyte, Philippines for a year, two years before consult, where the patient used to play in a nearby pond which had different types of freshwater snails. There was no known exposure to persons diagnosed with or suspected of having COVID-19 infection.

On physical examination, the patient was noted to be pale, with severe wasting and severe stunting, afebrile, and not in respiratory distress (Figure 1). Pertinent findings included pale palpebral conjunctivae and hepatosplenomegaly; his abdomen was slightly distended with engorged abdominal veins, liver was firm with edge palpable 7 cm below right costal margin, 4 cm subxiphoid; and spleen edge was palpable 5 cm below left costal margin. No fluid wave was noted. There was no clubbing nor palmar erythema.

Initial diagnostics revealed anemia (hemoglobin 35 g/L, reference: 135-180 g/L), with hypochromia, moderate anisocytosis, and slight poikilocytosis, but with normal white cell and platelet count. There was no evidence of cholestasis (total bilirubin 0.55 mg/dL, reference: 0.2-1.3 mg/dL), with normal liver enzyme levels (AST 41 U/L,



Figure 1. Photographs of the patient in the presented case. On physical examination, noted were gross wasting and stunting, generalized pallor, abdominal distention, and hepatosplenomegaly. (With permission from the patient's family).

reference: 17-59 U/L; ALT 22 U/L, reference: <50), and normal serum albumin level (37 mg/dL, reference: 35-50 mg/dL), but with prolonged prothrombin time (19.6 secs. vs. control of 12.6 secs., INR1.59) which normalized after one dose of intravenous vitamin K administration. On imaging, ultrasound revealed hyperechoic bands along the portal vein branches representing periportal pipestem fibrosis, (Figures 2A and 2B) corresponding to pattern C of the Niamery image pattern score for hepatic fibrosis.⁸ The liver parenchyma demonstrated mosaic pattern (Figure 2C), with multiple isoechoic nodules with hypoechoic rim (Figure 2D).

Upon admission at the emergency room, nasopharyngeal SARS-CoV-2 RT-PCR showed positive result; hence, the patient was admitted in the COVID-19 isolation ward. Diagnostics were done to determine the cause of the pallor and the hepatosplenomegaly. Tuberculosis workup including sputum, stool, and urine AFB showed negative results. Serologic markers for Hepatitis B, A, and C were all nonreactive. Serum Alpha-Fetoprotein, to exclude malignancy like hepatocellular carcinoma, showed normal level (3 IU/mL, reference: 0.74-7.3 IU/mL). Stool examination using Kato-Katz technique on two specimens revealed the presence of *Schistosoma japonicum* eggs.

In the presence of the stool examination findings, with the pallor and hepatosplenomegaly, a diagnosis of hepatosplenic

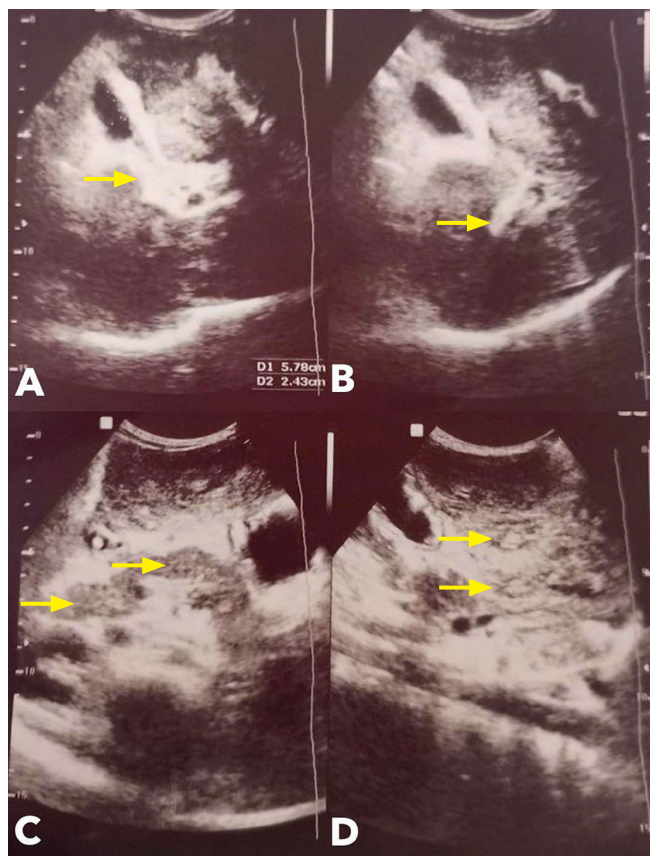


Figure 2. Liver ultrasound of the patient prior to treatment with praziquantel. There are hyperechoic bands of fibrosis along the portal vein branches (A and B, arrows). The liver parenchyma demonstrates mosaic pattern seen in cases of schistosomiasis (C, arrows). Note the multiple isoechoic nodules with hypoechoic rim within the liver parenchyma (D, arrows). (Photo courtesy of the patient's family, reproduced with consent).

schistosomiasis was made and praziquantel was given at 20 mg/kg/day divided into 3 doses for one day, to be repeated after one month.

Esophagogastroduodenoscopy (EGD) was facilitated to screen for the presence of esophageal and gastric varices from suspected portal hypertension (Figure 3). There were noted three columns of tortuous vessels 22 cm from central incisors, two of which continuously descended into the gastric cardia, both with red wale sign. Gastroesophageal junction was at 29 cm from central incisors with no mucosal breaks and with good lower esophageal sphincter tone. The stomach was distensible with non-erythematous, non-edematous gastric mucosa. Hematin stains were observed, with probable isolated tortuous vessel seen in the gastric body. No mosaic mucosal pattern was seen, nor were there erosions, ulcerations, masses, or any source of active bleeding. The rest of the endoscopic findings were unremarkable. Rubber band ligation (RBL) of the three esophageal varices was then done (Cook Medical 6

Shooter Saeed® Multi-Band Ligator®) with minimal mucosal bleeding and no significant complications during and after the procedure. The patient was then started on propranolol at 1 mg/kg/day.

The patient completed treatment with praziquantel. The hemoglobin improved from 35 g/L to 108 g/L after four blood transfusions with packed red blood cells. Repeat abdominal ultrasound after four weeks revealed persistence of hepatosplenomegaly with heterogenous echo pattern but with resolution of the previously noted multiple hepatic nodules and hyperechoic bands along the portal vein branches, with unremarkable Doppler studies of the portal veins, hepatic veins, and hepatic artery. He was advised readmission for repeat EGD for monitoring of gastroesophageal varices and possible RBL.

DISCUSSION

We report a rare case of hepatosplenic schistosomiasis in a 13-year-old male who presented with a 5-month history of intermittent melena and on physical examination was noted to be stunted, wasted, and with pallor and hepatosplenomegaly suggestive of portal hypertension. Stool samples examined on Kato-Katz technique revealed *Schistosoma* eggs and confirmed the diagnosis. His episodes of melena were secondary to pre-hepatic portal hypertension as evidence by the presence of esophageal and gastric varices on endoscopy, fibrosis on ultrasound, splenomegaly, and a preserved hepatic function, assessed biochemically by a normal bilirubin, liver enzymes, prothrombin time, and serum albumin.

In our patient, there was regression of the pipestem fibrosis and the hepatic nodules on ultrasound, four weeks after praziquantel treatment was given. The degree of accelerated portal hypertension of the patient can be explained by the advanced fibrosis which could have been affected by several factors. Of note, studies have shown disparities between prevalence of infection and levels of tissue morbidity, characterized by the stage of advancement of hepatic fibrosis and the presence of periportal fibrosis, with dissimilar progression in patients with same characteristics such as *Schistosoma* egg burden and biosocial features.⁹ Hence, the progression of liver fibrosis might be affected by poorly defined host intrinsic factors which might play a defining role in the regulation of liver fibrosis. There is a complex mechanism involved in the pathophysiology of hepatic schistosomiasis and the development of its complications, particularly portal hypertension, which involve a myriad of reactions of host regulators including pro- and anti-fibrotic processes. In the pro-fibrotic processes involved, granuloma formation is a helper T cell-mediated delayed hypersensitivity reaction driven by cytokines. Once *Schistosoma* eggs are embedded in hepatic tissues, their antigens stimulate a reaction in which injured hepatocytes release certain interleukins, particularly IL-4 and IL-33, which signal a cascade of cytokine production which, together with the high mobility group box

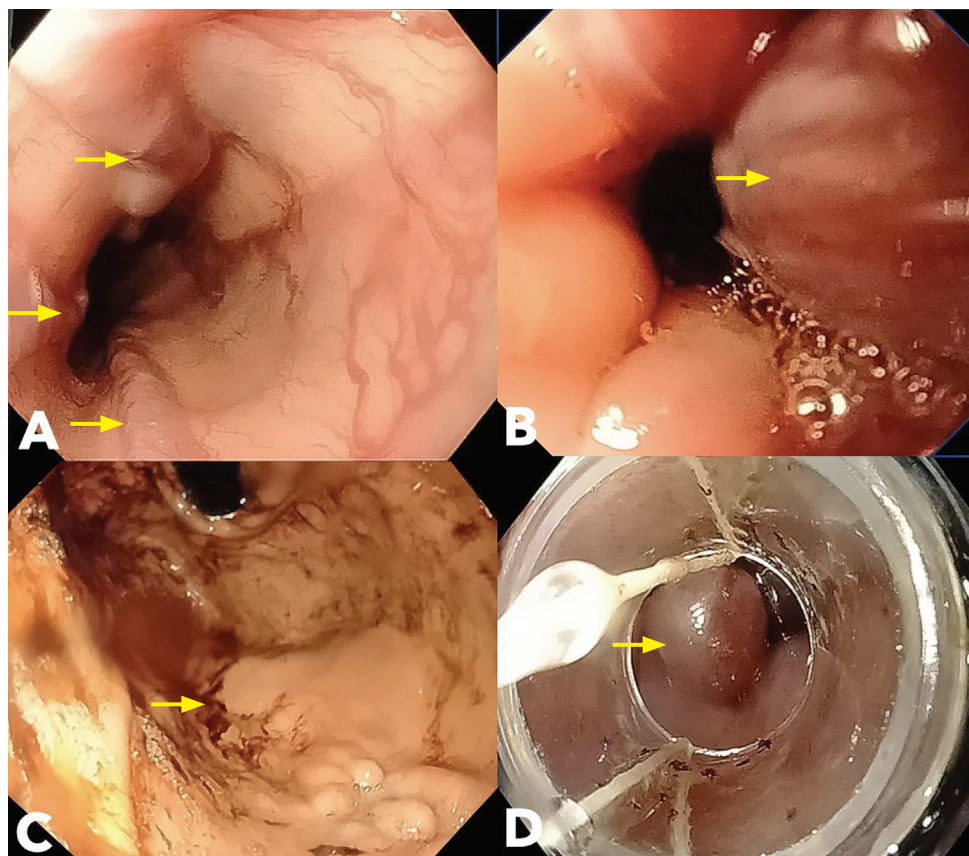


Figure 3. Upper endoscopic findings of the patient in the presented case. There were three columns of esophageal varices (A, arrows) with positive red wale sign (B, arrow) which are evidence of collateral vessel formation from portal hypertension. Gastric examination revealed hematin stains (C, arrow) which could be from a recent episode of bleeding from the esophageal varices. Upon doing rubber band ligation, there was flattening of the proximal varices (D, arrow).

1 (HMGB1) released from damaged hepatocytes, cause the activation of the quiescent hepatic stellate cells (qHSC) to become activated hepatic stellate cells (aHSC). These aHSC produce large amounts of collagen which accumulate and later lead to fibrosis, eventually progressing to cirrhosis if not controlled. On the other hand, anti-fibrotic processes are also involved and may occur simultaneously. Three possibilities can account for regression of fibrosis: apoptosis, senescence, and/or reversion of aHSC to their quiescent stage. Upon stimulation, hepatic resident macrophages will produce IL-12 which will drive the differentiation of Naïve T-cell to Th1. Th1 cells will release INF- γ which will classically activate macrophages (M1). A host of cytokine production can also block the activation of qHSC to consolidate an anti-fibrotic effect. aHSC might return to the quiescent or senescent state under the action of several of these cytokines by undergoing apoptosis depending on how strong the pro-fibrotic signal was, and this might be related to the number of eggs deposited in the liver. Another cytokine involved, INF- γ can also activate matrix metalloproteinases (MMP) to digest the deposited

collagen, and this action is reinforced by higher levels of estrogen in women. This antifibrotic processes may explain the regression of fibrosis, as supported in animal studies, especially if there is predominance of type III over type I collagen, as the latter is reported in end-stage liver fibrosis and its turnover was thought to be a much slower process.¹⁰ The fibrosis caused by the chronic granulomatous reaction around *Schistosoma* eggs embolized around the sinusoidal area eventually results in presinusoidal portal hypertension¹¹, as seen by the presence of hepatosplenomegaly and esophageal varices in our patient.

Eight pediatric cases of hepatosplenic schistosomiasis have been reported, with age ranging from 5 to 18 years¹²⁻¹⁸, with five patients from Africa, two from Brazil, and one from Laos. There is no local report of hepatosplenic schistosomiasis in the Philippines based on published literature and on the PPS Registry. Seven patients were cases of hepatosplenic schistosomiasis involving *S. mansoni* and one with *S. mekongi*. There was none with *S. japonicum*. Five patients had signs and symptoms of gastrointestinal bleeding, with one with concomitant dyspnea and cough. The latter patient succumbed

to severe pulmonary hypertension and was eventually diagnosed with hepatosplenic schistosomiasis post-mortem.¹⁷

The diagnosis of hepatosplenic schistosomiasis is based on the establishment of *Schistosoma* infection in the patient, and on the presence of portal hypertension. Simple microscopic examination of stools for the presence of *Schistosoma* eggs via Kato-Katz smear examination remains the gold standard test for the diagnosis of an active infection.¹⁹ Although it has lower sensitivity compared to other diagnostic methods, its sensitivity increases with the number of stool samples from 26.2% with single stool specimen to 53.8% with two stools, and 69.2% with three stools from consecutive days.²⁰ Kato-Katz technique is the favored method due to its low cost and ease of use in epidemiologic studies, particularly in diagnosing *S. japonicum* and *S. mansoni*.²¹

In our case, the diagnosis was confirmed by the presence of *S. japonicum* eggs in the stool via Kato-Katz technique on two determinations. Other methods in diagnosing schistosomiasis include serum antibodies detection thru indirect hemagglutination assay (IHA) and enzyme-linked immunosorbent assay (ELISA), and DNA identification of *Schistosoma*. IHA has the highest sensitivity at 97%, followed by ELISA at 93%, and polymerase chain reaction (PCR) at 89%.²² However, these methods are expensive and are more tedious to perform.²³ In the reported cases, four were diagnosed by Kato-Katz stool examination technique, similar to our patient, while other methods used included ELISA, indirect immunofluorescence test (IIT), rectal biopsy, and post-mortem liver biopsy.

Ultrasound is used as a major imaging tool for diagnosis of hepatosplenic schistosomiasis and in the follow up of patients. Typical ultrasonographic findings at onset include periportal fibrosis which are graded and correlated with severity of the disease.⁸ Other ultrasonographic findings may include left liver lobe hypertrophy with right lobe atrophy, gall bladder wall thickening, splenomegaly, and dilated collateral vessels. With the presented case, ultrasound revealed characteristic fibrotic pattern in schistosomiasis known as pipestem fibrosis (Figures 2A and 2B). The liver parenchyma demonstrated mosaic pattern commonly seen in liver involvement in schistosomiasis (Figure 2C), and the multiple isoechoic nodules may represent lodged *S. japonicum* eggs with resulting surrounding fibrosis (Figure 2D).

The management of hepatosplenic schistosomiasis should include eradication of the *Schistosoma* in the body and the control of the portal hypertension. For eradication, praziquantel (2-(cyclohexylcarbonyl)-1,2,3,6,7,11b-hexahydro-4H-pyrazino[2,1-a]-isoquinoline-4-one) is the drug of choice^{24,25} which was given to our patient and in the published cases. This drug works by targeting β subunits of voltage-gated calcium ion channels causing severe spasms and paralysis of the muscles of the worms by a rapid Ca^{2+} influx inside the schistosome.²⁵ A meta-analysis showed that at a dose of 30 to 60 mg/kg, praziquantel has an efficacy of 76% compared to placebo in treating schistosomiasis.²⁶ In the eradication of *S.*

japonicum, praziquantel was documented to have a cure rate as high as 90.3%²⁷, with a 90% reduction in mean schistosome egg counts after administration of a single dose at 40 mg/kg among patients with *S. japonicum* in the Philippines²⁸. Although therapy with praziquantel is the established mode of treatment for hepatosplenic schistosomiasis, this is the first case report to document resolution, within four weeks of treatment, of the characteristic fibrotic pattern in hepatosplenic schistosomiasis: the previously noted hepatic nodules, which may represent the immediate hepatic fibrosis surrounding the *Schistosoma* eggs lodged in the liver, and pipestem fibrosis or the hyperechoic bands along the portal vein branches. Despite being the first case to demonstrate interval improvement of signs of fibrosis as early as one month after treatment with praziquantel, a clinical study in Filipinos with *S. japonicum* hepatosplenic schistosomiasis has already noted improvement in sonographic liver findings in as early as six months²⁹, while animal models have already shown that praziquantel treatment can improve hepatic fibrosis in as early as eight weeks³⁰. Nevertheless, the case presented is the first to document significant sonographic improvement in the least amount of time after anti-parasitic therapy. Note, however, that the persistence of heterogenous echo pattern of the liver may represent incomplete resolution of fibrosis in the case, which is consistent with the observed significant improvement in human subjects 6 to 24 months post-treatment.³⁰

For the control of portal hypertension, our patient was managed with both medical and endoscopic treatment to control the bleeding esophageal varices. Although the use of propranolol for the management of portal hypertension in children with hepatosplenic schistosomiasis has not been well studied, studies have shown that propranolol can decrease portal pressure in non-cirrhotic liver with presinusoidal portal hypertension from hepatosplenic schistosomiasis as evidenced by the reduction in transmural variceal pressure and wall tension, as well as in the reduction of portal vein diameter.^{31,32} In fact, several studies have looked into this, and even a comparison with another non-selective beta blocker, carvedilol, showed no significant difference between the two drugs, with a reduction of variceal bleeding as high as 90%.³³

Rubber band ligation of the esophageal varices was also done to prevent further bleeding. In the eight reported cases of hepatosplenic schistosomiasis, only four had therapeutic endoscopy. Of these, three had RBL but one later required transjugular intrahepatic portosystemic shunt (TIPS); and another had initial esophageal sclerotherapy who eventually had Warren distal splenorenal anastomosis.¹²⁻¹⁸

The prognosis in hepatosplenic schistosomiasis is favorable with treatment. The patient adhered to the treatment with praziquantel and propranolol with no noted untoward events. The endoscopic intervention was also tolerated well with no complications. Only one patient in the case reports with hepatosplenic schistosomiasis died from pulmonary hemorrhage who was only diagnosed post-mortem.¹⁷

Our patient completed treatment with praziquantel with noted resolution of the abdominal pain and with no recurrence of melena thereafter. Repeat imaging with abdominal ultrasound and Doppler studies still revealed findings of hepatosplenomegaly and heterogenous parenchymal echo pattern but with no signs of the previously noted periportal fibrosis and hepatic nodules. In addition, there was unremarkable Doppler studies of the portal veins, hepatic veins, and hepatic artery. Unfortunately, the patient was lost to follow up but the plans on discharge were to repeat stool studies to document eradication of *Schistosoma* infection, repeat endoscopy to assess variceal status, assess the need for propranolol, and improve nutritional status.

CONCLUSION

This is a case of a 13-year-old Filipino male with hepatosplenic schistosomiasis who presented with upper gastrointestinal bleeding with a history of previous one-year residence in a schistosomiasis endemic area. This is the first case report from the Philippines looking into the unique presentation of rapid development of complications from hepatosplenic schistosomiasis in an adolescent patient, with documentation of the fast sonographic improvement of the liver after eradication of the parasite. The rapid progression of liver fibrosis might be highly affected by poorly defined host intrinsic factors which regulate liver fibrosis and could affect the effectiveness of treatment in terms of the resolution of fibrosis.

Hepatosplenic schistosomiasis should be considered in patients presenting with signs of portal hypertension, especially in those with history of residence or travel in endemic areas regardless of duration of exposure. Complications from this condition, particularly hepatic fibrosis and eventual collateral vessel formation, can develop in a matter of years as in the case presented. The hallmark of treatment remains eradication of *Schistosoma* with the anti-parasitic praziquantel, addressing variceal bleed with rubber band ligation, and controlling portal hypertension with beta blockers such as propranolol.

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Ethics Approval and Consent to Participate

This case report was registered in the Research Grants Administration Office of the University of the Philippines Manila and was exempted from full panel ethics review. Written consent was obtained from the legal guardian of the patient for the documentation and processing of this case.

Consent for Publication

Written consent was secured from the father of the patient for the publication of this case and the images included for documentation.

Availability of Data and Materials

Materials and data provided in this case study are available from all authors upon request.

Statement of Authorship

Both authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

Both authors declared no conflicts of interest.

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