PEDIATRIC PRIMARY SCLEROSING CHOLANGITIS WITH INFLAMMATORY BOWEL DISEASE: A DOUBLE JEOPARDY?

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Abstract

Introduction: Primary Sclerosing Cholangitis (PSC) is an idiopathic disorder which encompasses a spectrum of cholestatic conditions the ultimately lead to biliary cirrhosis and hepatic failure. 90% of cases are associated with inflammatory bowel disease (IBD). The incidence of PSC-IBD in the pediatric population is rare at only 0.2/100,000 per year worldwide, limiting data as to the manifestations, treatment, and prognosis in this age group.

Case: This is a case of a 10-year old Filipino male admitted due to jaundice, fever, and anorexia, preceded by bouts of abdominal pain and change in bowel habits. Laboratory tests showed anemia and leukocytosis with a hemoglobin 8.9 g/dL, hematocrit 26.5%, WBC 12.56 k/uL, platelet 326 k/uL; direct hyperbilirubinemia (19mg/dl), elevated ALT (1727 mg/dl); alkaline phosphatase (272); and a deranged protime (29.3 seconds/INR 2.64). Contrast abdominal CT scan showed edematous colonic walls with hepatic congestion. Colonoscopy revealed pancolitis consistent with IBD, and PSC was confirmed with liver biopsy which showed cholestasis with severe parenchymal damage and bile duct proliferation. The patient was started on UDCA, Prednisone, Azathioprine, and Mesalamine and discharged improved. He has maintained in remission up to present.

Conclusion: The clinical history, signs and symptoms in pediatric PSC-IBD are similar to that of adult patients, with the addition of failure to thrive and growth retardation. Ulcerative colitis is more commonly involved with PSC, with pancolitis as the most common colonoscopic finding, concomitant to the diagnosis of PSC. UDCA remains the only drug shown to have beneficial effects in PSC, while treatment with Mesalamine, Glucocorticoids, and immunosuppressants are effective in inducing remission for IBD.

INTRODUCTION

Primary Sclerosing Cholangitis (PSC) is an idiopathic disorder which encompasses a spectrum of cholestatic conditions that are characterized by patchy inflammation, fibrosis, and destruction of the intrahepatic and extrahepatic biliary tract which ultimately lead to biliary obstruction, biliary cirrhosis, and hepatic failure.[1]

Approximately 90% of all patients with PSC have concomitant Inflammatory Bowel Disease. Conversely, PSC is present in 2.4% to 4.0% of all patients with ulcerative colitis (UC) and 1.4% to 3.4% of patients with Crohn's disease.[2 3]

Most patients with PSC present between the ages of 25 and 45 years, with a median age of approximately 41 years. Pediatric-onset PSC, however, is rare, with a reported incidence of 0.2/100,000 per year, hampering the studies on clinical course and prognosis. The complexity of the clinical features and diagnosis of PSC also poses a great challenge especially in the pediatric population.[2 3]

CASE

This is a case of K.C., a 10-year old, male, from Dauis, Bohol, who presented with fever, jaundice, and abdominal pain. One month prior to admission, the patient had onset of intermittent fever and abdominal pain. Work-up done included a CBC with unrecalled results and the patient was managed as a case of dengue fever. Three weeks prior to admission, the patient developed jaundice with persistence of fever and abdominal pain. HBsAg and Anti-HAV taken were non-reactive. However, ALT, Alkaline phosphatase, serum bilirubin, and prothrombin time were all deranged (Table 1). Supportive treatment was given, but worsening symptoms with increasing severity of abdominal pain prompted the family to transfer to a private hospital in Cebu City for further work-up and management.

On transfer, physical exam findings showed stable vital signs, presence of jaundice, with an unremarkable abdominal exam. Repeat laboratory studies were taken and are summarized in Table 1. An ultrasound of the whole abdomen showed an unremarkable gallbladder, common bile duct, and biliary tree, a normal sized liver with subtle diffusely coarsened echotexture consistent with non-specific diffuse parenchymal disease, and a mildly enlarged spleen. Due to inconclusive findings, a contrast CT scan of the whole abdomen was then done and showed prominent, mottled enhancement of the liver parenchyma suggestive of congestion, non-dilated intra and extrahepatic bile ducts, a soft tissue mass in the distal ileum extending to the ileocecal valve measuring 1.7 x 2.4 x 1.4 cm showing mild rim enhancement on contrast study, and edematous walls of the ascending colon, sigmoid, and rectum, with no signs of obstruction. Symptomatic treatment was given.

A colonoscopy was done and revealed edematous mucosa at the terminal ileum but no mass noted, and edematous mucosa with areas of erythema and superficial ulcerations indicative of colitis at the level of the ascending colon, descending colon, sigmoid, and rectum consistent with a picture of inflammatory bowel disease. Colonic mucosal biopsy results showed chronic colitis and biopsy of the terminal ileum showed chronic ileitis with erosions. The patient was then started on Mesalamine 500mg/cap 1 capsule every 8 hours, Ursodeoxycholic acid 500mg thrice a day, Hydrocortisone 100mg IVTT every 8 hours, Rifaximin 200 mg thrice a day, and Ciprofloxacin 500 mg twice a day.

Due to the patient's clinical presentation and colonoscopic findings of IBD, PSC was entertained. Tests for autoimmune disease were taken including ANA, P-ANCA, anti-protein C and S but were all unremarkable. A liver biopsy to confirm the diagnosis was done and showed: altered hepatic architecture due to significant portal expansion and micronodular formation of the hepatic parenchyma. Heavy infiltrates of neutrophils and lymphocytes involving the bile ducts. Significant bile ductular proliferation was noted. The surrounding parenchyma showed prominent foamy degeneration of the hepatocytes associated with moderate cholestasis. Most of the hepatocytes are enlarged exhibiting foamy cytoplasm containing golden brown pigments. The findings are consistent with cholestasis with severe parenchymal damage and bile duct proliferation, to consider Primary Sclerosing Cholangitis.

During the course of hospital stay, the patient was noted to be improving. Hydrocortisone was shifted to oral Prednisone 10mg/tab 1 tablet once a day and Mesalamine was continued as maintenance therapy. Symptoms were improving. Repeat laboratory studies were taken for comparison and are shown in Table 1. The patient was then discharged improved with scheduled follow-up clinic visits.

DISCUSSION

We are presented with a 10-year old male who was admitted due to complaints of abdominal pain, jaundice, fever, and anorexia, and eventually diagnosed with PSC with IBD. The incidence of PSC in children is 0.23 cases per 100,000 persons. Median age at diagnosis is 11 years old. The patient's symptoms and physical exam findings which included fever, jaundice, icteric sclerae, a distended, non-tender abdomen, are similar to that of the adult presentation. Other notable features in pediatric patients are failure to thrive, growth retardation and delayed puberty, but were not seen in this patient. On work-up, abnormally elevated liver function tests with a deranged prothrombin time, elevated alkaline phosphatase, direct hyperbilirubinemia, and an elevated ALT was consistent with the cholestatic profile of PSC. Chronic elevation of serum alkaline phosphatase levels, typically 3 to 5 times normal, is the biochemical hallmark of PSC in adults but GGT is a more reliable indicator of biliary disease in children since alkaline phosphatase is affected by bone growth. Serum bilirubin levels were elevated with direct hyperbilirubinemia. Serum aminotransferase levels are typically elevated 4-5 times the normal in pediatric patients. The serum bilirubin level may be normal or elevated and often fluctuates and is predominantly conjugated. A hepatitis panel done was also unremarkable. MRCP/ERCP is the imaging study of choice to diagnose PSC in children however, in this patient, an ultrasound of the whole abdomen showed indeterminate results. This was followed by a contrast CT scan of the whole abdomen which showed hepatic congestion with no evidence of biliary obstruction, but with note of a soft tissue mass in the distal ileum extending to the ileocecal valve measuring 1.7 x 2.4 x 1.4 cm showing rim enhancement on contrast study. IBD is present in 83% of patients confirmed to have PSC. Pancolitis, consistent with ulcerative colitis, is the most common colonoscopic finding in both adult and pediatric patients with PSC-IBD and was also seen in this patient. Several immunologic markers and serum autoantibodies such as ANA (24% to 53%) and p-ANCA (65% to 88%) are found in patients with PSC, although none is specific for the disease. Both ANA and p-ANCA were tested in this patient but was negative. A liver biopsy is not recommended in all cases unless autoimmune hepatitis – PSC overlap is considered. This patient underwent liver biopsy and revealed findings consistent with cholestasis with severe parenchymal damage and bile duct proliferation, establishing the diagnosis of Primary Sclerosing Cholangitis.

Treatment of PSC-IBD includes immunosuppressive therapy with corticosteroids, anti-inflammatory agents, antibiotics, and ursodeoxycholic acid (UDCA). UDCA has been the most vastly studied drug in treating PSC and has shown to have beneficial effects in improving liver function tests and symptom resolution. Glucocorticoids and anti-inflammatory agents, although not proven to have any benefit in treating PSC, are beneficial in inducing remission in IBD. This patient was given Prednisone 10 mg/tab 1 tab once daily, Mesalamine 500 mg/cap 1 cap thrice daily, and UDCA 500mg/tab 1 tab thrice daily and has symptomatic improvement and decreasing values in liver function tests.

CONCLUSION

PSC is a rare disease in the pediatric population. The clinical history, signs and symptoms are similar to that of the adult, with the addition of failure to thrive and growth retardation in children. The typical presentation is that of a cholestatic type of jaundice associated with elevated levels of direct bilirubin, elevated ALT and alkaline phosphatase levels. PSC is usually accompanied by ulcerative colitis type of IBD in both adult and pediatric patients. MRCP is the imaging test of choice for pediatric patients while ERCP is the gold standard for diagnosis in adults. Liver biopsy is not indicated in all cases except for suspicion of autoimmune hepatitis – PSC overlap. The most common colonoscopic finding in both adults and pediatrics is pancolitis. Treatment consists of UDCA for PSC and corticosteroids, and mesalamine for IBD with good response and remission rates.

Table 1

Laboratory test	Before admission	On admission	Upon discharge
ALT	2302	1772	493
Alkaline phosphatase	272	231	218
Protime	20.8 secs/INR 2.3	33.6 secs/ INR 3.14	28.2 secs/ INR 2.52
Total Bilirubin	22.4	31.3	22
Direct Bilirubin	19	25	16

References:

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