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Clinical vignette: Importance of liver biopsy in diagnosing small duct primary sclerosing cholangitis

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INTRODUCTION:
• Primary sclerosing cholangitis (PSC) is characterized as progressive fibrosis, inflammation, stricture, and destruction of bile ducts due to unknown etiology.
• Primarily affects middle-aged men.
• 2:1 male to female ratio

CLINICAL COURSE:
• Symptoms may include fluctuating fatigue, pruritus, jaundice, and abdominal discomfort. (Very similar to chronic liver disease)
• Sometimes presentation may be asymptomatic.
• One prospective phosphatase is the classic finding.
• 60-80% of PSC patients have concomitant inflammatory bowel disease (IBD) such as ulcerative colitis (UC).

DIAGNOSTIC APPROACH:
• Complete HPI and PE is an important starting point.
• First rule out common causes such as viral, autoimmune, congenital, and malignant etiologies.
• Tests may include: CBC, chemistry 7, LFT, CA19-9, ferritin, autoimmune panel, viral panel, ceruloplasmin.
• Perinuclear anti-neutrophil cytoplasmic antibody (pANCA) prevalence of 30-94% in PSC. Not a reliable diagnostic tool.

RECOMMENDATIONS FOR LIVER BIOPSY IN PSC:
• European Association for the Study of the Liver Recommendations:
  • "Liver biopsy should be performed to diagnose small duct PSC if high-quality MRCP is normal."
  • "Liver biopsy may be helpful in the presence of disproportionately elevated serum transaminases and/or serum IgG levels to identify additional or alternative processes."
• American Association for the Study of Liver Diseases Recommendations:
  • "Liver biopsy "essential in suspected small duct PSC."
  • "In PSC patients with disproportionately elevated serum aminotransferase values, especially if the antinuclear antigen and/or smooth muscle antigen is positive and/or serum IgG levels are elevated, a liver biopsy may identify features of a PSC–autoimmune hepatitis (AIH) overlap syndrome."
• General liver biopsy indications from NEJM (one of ten indications):
  • "Evaluation of the cholestatic liver diseases primary biliary cirrhosis and primary sclerosing cholangitis."

CASE REPORT:
• A 58 year old male presented to the emergency department with worsening jaundice and icteric sclera. His other symptoms included pruritis, dark urine, yellow colored stool, and fatigue. Review of systems included a ten-pound weight loss over two weeks. The patient denied excessive alcohol or drug use. Pertinent exam findings included diffuse jaundice, icteric sclera, and hepatosplenomegaly. Laboratory findings showed elevated alkaline phosphatase (930), total bilirubin (23.7), and direct bilirubin (18.2); as well as decreased total protein (5.2) and albumin (1.8). Transaminase levels were relatively unremarkable – mildly elevated AST (74) and normal ALT (66). Extensive work up for other etiologies was unremarkable except for elevated ferritin (1191) and CA 19-9 (113). Abdominal ultrasound, CT, and MRCP were also unremarkable and non-diagnostic for PSC. A liver core needle biopsy demonstrated histologic features consistent with PSC. Colonoscopy showed no evidence of IBD, and biopsy samples were negative for malignancy.

SMALL DUCT PSC:
• Diagnostic criteria for small duct PSC:
  • Chronic cholestatic liver disease of unknown etiology
  • Perinuclear liver biopsy sample suggestive of PSC
  • Normal cholangiography studies
• Exclusion of other liver or biliary diseases
• According to one study, this variant rarely progresses to classic PSC and may be an early stage of classic PSC; however strong evidence is lacking for this claim.
• Median survival (23.5 years) was equal to the general white US population (control) in one study.
• Presents similar to classic PSC.
• In one prospective follow up study lasting 106 months, small duct PSC patients were less likely to present with symptoms compared to classic PSC.
• Rate of having concomitant IBD was approximately 88% in patients with small duct PSC compared to 83% in large duct in a small retrospective analysis.

DISCUSSION:
• The initial evaluation did not reveal a conclusive diagnosis, resulting in the need for a liver biopsy and a subsequent diagnosis of small duct PSC.
• A recent case series suggests that small duct variant of PSC tends to run a more benign course and thus has a better prognosis compared to the classic large duct variant.
• According to a recent study, PSC patients (all variant types combined) with concurrent inflammatory bowel disease (IBD) had a higher long-term risk of cancer compared to those patients who did not have IBD.
• One retrospective study suggests that small duct PSC patient do not progress to developing cholangiocarcinoma at the same rate as classic PSC patients.
• Our patient had a mildly elevated CA 19-9 level and made us concerned for possible malignancy, however, no ductal or pancreatic masses were found on CT or MRCP.
• There are no agreed upon guidelines for cancer surveillance in patients with PSC. As suggested by a very recent paper, a pragmatic approach including non-invasive imaging and serum CA 19-9 levels (despite poor sensitivity and specificity) annually may suffice.
• In our case, the small duct variant has a better prognostic outlook therefore requiring even less frequent non-invasive imaging and CEA 19-9 levels.
• Our patient had a colonoscopy with biopsies as recommended by the US Dept of Health and Human Services guidelines for all patients with newly diagnosed PSC.
• A high clinical suspicion for IBD in patients with PSC should be maintained by providers.

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