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SCLEROSING CHOLANGITIS IN THE SETTING OF PANCREATIC ADENOCARCINOMA

Gastroenterology

Bipneet Singh
Jahnavi Ethakota
Palak Grover
Gurleen Kaur

KEYWORDS

secondary sclerosing cholangitis, primary sclerosing cholangitis, pancreatic adenocarcinoma, cholangiocarcinoma

INTRODUCTION/BACKGROUND

Sclerosing cholangitis is a progressive, chronic cause of cholestatic liver disease. It is characterized by inflammation, obliterative fibrosis, and stricture development of the intrahepatic and/or extrahepatic biliary ducts, often progressing over time and might result in liver failure and cholestasis problems (1,2). Without a liver transplant, the median survival time from the time of diagnosis until death is about ten years (3). Disease can be primary (PSC) or secondary (SSC). PSC is generally associated with ulcerative colitis. Secondary causes vary from IgG4 disease, to HIV and so on.

The association of cholangitis with malignancy is studied in previous literature with cholangiocarcinoma causing secondary sclerosing cholangitis and PSC predisposing a person to hepatobiliary malignancies (4). Association with pancreatic cancer is rare and not frequently mentioned in the literature (5). Because bile duct carcinomas and pancreatic carcinomas can occur in the same site and are difficult to distinguish from one another.

Our case demonstrates a patient with no prior history of liver or biliary disease, presented with a newly diagnosed pancreatic cancer with secondary sclerosing cholangitis. Initial thought process involved the sclerosing cholangitis triggering the pancreatic cancer but the patient's age of diagnosis and symptoms of malignancy predating that of jaundice hinted otherwise.

Pancreatic cancer migrating along the biliary system is lesser known and the case demonstrates a tedious work-up taken for sclerosing cholangitis and finally a rare association between the two conditions.

CASE

A 62-year-old male presented with abdominal pain, jaundice, and 40 lb weight loss over the past year. Over the past year, the patient lost his appetite and progressively lost weight to go down from 265 lbs to 225 lbs. He lost a lot of muscle mass evident with temporal thinning and supraclavicular hollowing. Then he started noticing abdominal pain, initially 3/5 in intensity in the epigastric region, however, the pain worsened up to 8/10 in intensity and started radiating to the back. At this point, his wife started noticing yellowness in his eyes. Ultimately when the pain became unbearable, he was brought to the hospital.

The patient had a heart rate of 86 bpm and a blood pressure of 116/60 mm of Hg. He was in no respiratory distress, saturating well on room air. Further, there was icterus on examination, along with epigastric tenderness and fullness. Lab work included a WBC count of 4000 cells/mL, Hb of 10 g/dL, and platelet count of 200K/mL. Electrolytes were within normal limits. Liver function tests included AST of 80U/L and 90 U/L, ALP of 210 U/L and a bilirubin of 6.1 mg/dL. Upon CT of the abdomen and pelvis, he was found to have a mass in the head of the pancreas. He underwent an EUS-guided biopsy. At that time, the patient also underwent a cholangiogram for associated jaundice which interestingly showed intrahepatic strictures.

The biopsies from the pancreas demonstrated pancreatic adenocarcinoma. Further work was done for the intrahepatic strictures, including IgG4 levels, HIV, and autoimmune panel. The tests were unremarkable. Ultimately the patient underwent liver biopsies confirming pancreatic cancer migrating cranially to involve intrahepatic ducts. Given the hepatic involvement, the patient was scanned for metastatic disease and had metastasis to the lung and brain leading to the patient choosing hospice care.

DISCUSSION

Initial presentation with loss of appetite and weight loss indicated a brewing malignancy with jaundice hinting at pancreatic versus hepatobiliary origin. Upon confirmation of a primary pancreatic mass, mechanical obstruction was thought to be responsible for jaundice, however a cholangiogram during the ERCP showed intrahepatic structuring which was unusual.

The patient had no prior history of liver disease or inflammatory bowel disease which would predispose a patient to PSC. With an unusual presentation and negative anti-mitochondrial antibodies, primary biliary cholangitis was low on the differential. The patient was outside of the common age range of PSC as well. The initial hypothesis was undiagnosed SSC or less likely PSC with or without subsequent pancreatic adenocarcinoma.

With an unremarkable IgG4 level, an autoimmune liver panel including AMA, ANCA, ANA, anti-smooth muscle, anticardiolipin, and rheumatoid factor, common secondary causes were ruled out. With the thought process shifting towards PSC, a biopsy was planned to demonstrate fibrosing ducts. On biopsy ducts interspersed with columnar epithelia like pancreatic adenocarcinoma just diagnosed were seen indicating cranial migration and therefore SSC due to pancreatic cancer.

Disproving the previous hypothesis of PSC/SSC predisposing to cancer, it was the other way around with pancreatic cancer leading to SSC.

Sclerosing cholangitis frequently has an erratic and extremely variable history. A favorable prognosis is conferred by a serum alkaline phosphatase level that is consistently below 1.5 times the upper limit of normal. Further Mayo scoring greatly indicates prognosis. It can involve large ducts, small ducts, or both (6). Small duct PSC patients have a favorable prognosis; with advanced liver disease progression being less prevalent (7).

Progression to cancer especially cholangiocarcinoma is common but association to pancreatic cancer is not common and even less studied. The increased incidence of pancreatic cancer in PSC patients can be attributed to a number of factors. Reflux of bile acids, or potentially bacteria, into the pancreatic duct can be caused by distal common bile duct disruption and inflammation. The ensuing moderate or sporadic pancreatitis may not be severe enough to warrant medical attention, but the persistent, mild inflammation may have pro-neoplastic effects (8).

As per a retrospective analysis in 2002 in people with PSC compared to the general Swedish population increases the risk of pancreatic cancer by a factor of 14 (5). These findings point to a possible higher risk of pancreatic cancer in PSC patients. Subsequent studies in Sweden, without controlling for IBD, reported hazard ratios of 8 and cumulative probabilities of pancreatic cancer in PSC-IBD patients (9). Further, another Swedish study that did control for concomitant IBD found a cumulative probability of 2.3% of pancreatic cancer in patients with PSC-IBD, but only 0.5% in patients with IBD alone (10).

In a study amongst American veterans, patients with PSC had a significantly higher prevalence of pancreatic cancer compared to the general population and those with IBD without PSC (2.4% vs. 0.2% and 0.5%, respectively) (11).

On the other hand, 83% of 66 patients with any pre-existing pancreatic disease were found with sclerosing-cholangitis in a retrospective study. Despite the exclusion of patients with constriction of the distal common bile duct, more than half of the patients with acute pancreatitis, 3/4th of patients with chronic pancreatitis, and all of the patients with pancreatic cancer had these changes (12). The involvement with both inflammation and malignancy indicates some factors increasing the risk of SSC. Upstream metastasis could be a second factor conferring a higher incidence.

So, a two-way relationship between sclerosing cholangitis and pancreatic cancer has been reported and is possible. Our case can be approached either way but based on adenocarcinoma cells on biopsy, pancreatic cancer leading to SSC appears more reasonable.

CONCLUSION

Jaundice in the setting of pancreatic cancer should be investigated with MRCP or ERCP cholangiogram to look for causes other than extrinsic biliary duct compression. Secondly, any intrahepatic constriction needs to be worked up for PBC, PSC, and SSC. A low threshold should be kept for a biopsy and lastly, prognosis of SSC should be factored into decision-making with different morbidity and mortality with its presence.

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