Case Report

Mucosal Papillary Hyperplasia in Gallbladder: A Clue for Infectious Etiology in HIV Patients

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Abstract

Gallbladder specimens are ditzel in surgical pathology and opportunistic diseases like cryptosporidiosis where they are easy to miss. We describe three cases of gallbladders with mucosal papillary hyperplasia with acute and chronic inflammation, all of which revealed cryptosporidiosis on complete histological evaluation. The patients were found to be HIV positive on further chart review. In the absence of clinical history, which is often the case with gallbladder specimens, the finding of mucosal papillary hyperplasia can be a reactive response to an infectious cause and can serve as a helpful clue to look for organisms with patience at higher magnification.

Keywords: Cryptosporidiosis, gallbladder, hyperplasia, papillary

Introduction

Gallbladder is a ditzel specimen in surgical pathology, with the majority diagnosed as acute or chronic cholecystitis with cholelithiasis. Cryptosporidiosis is an opportunistic infection that involves the gastrointestinal tract and produces debilitating diarrhea in immunosuppressed patients.[1] We report three cases of gallbladder with mucosal papillary hyperplasia and cryptosporidiosis, identified on microscopic evaluation and in which the subsequent search in clinical chart revealed the patients to be HIV positive.

Case Report

Case 1 was received in consultation to rule out dysplasia, and Cases 2 and 3 were grossed routinely with three strips and a cross-section of the bile duct submitted. Due to marked mucosal hyperplasia, multiple additional sections were submitted in all cases and evaluated on hematoxylin and eosin (H and E) staining. Chart review was performed retrospectively.

Case 1 was a 58-year-old male with a 23-year long history of HIV, who presented with right upper quadrant abdominal pain of acute onset. His CD4 count was 6/ul. Computed tomography (CT) abdomen/pelvis and ultrasound showed gallbladder wall thickening, intrahepatic biliary ductal dilatation and mild pericholecystic fluid, changes that were concerning for acute cholecystitis. Gross examination revealed a gallbladder wall thickness of 0.4 cm without any lesions or choleliths.

Case 2 was a 49-year-old male with HIV diagnosed for 20 years (on and off antiretroviral therapy), who presented with diffuse abdominal pain, ascites, and leg edema. His CD4 count was 17/ul. CT showed gallbladder wall thickening and intrahepatic biliary ductal dilatation. There was absence of filling on hepatobiliary iminodiacetic acid (HIDA) scan, suggesting acute cholecystitis. Gross examination showed focal areas of hyperemia on the external surface with a 1.9-cm cholelith within. The wall thickness ranged from 0.2 to 0.4 cm.

Case 3 was a 38-year-old male with a history of AIDS (untreated for 5 years) and a CD4 count of 97/ul. He presented with worsening abdominal pain, watery diarrhea, nausea, and fever. Ultrasound showed gallbladder distension without gallstones, and HIDA scan revealed a nonfilling gallbladder, consistent with acalculous cholecystitis. On gross examination, the gallbladder was distended with a wall thickness of 0.2–0.4 cm. No choleliths were found.

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On histopathology, all the three cases showed acute and chronic cholecystitis with focal to diffuse papillary hyperplasia of the gallbladder mucosa [Figure 1a]. Case 1 also showed multifocal intestinal metaplasia. Multiple sections were submitted in all the cases to rule out metaplasia and dysplasia. All the cases showed multiple, small, round, blue organisms ranging from 3 to 4 microns in size on the surface epithelium associated with inflammation, which were morphologically consistent with *Cryptosporidium* spp. on H and E [Figure 1b] and fluorescence microscopy on Case 3 [Figure 1c]. Acid-fast, Gomori methenamine silver, and cytomegalovirus immunostains performed to exclude other infections were negative. Chart review revealed that serology for cryptosporidiosis was not performed in any of the cases.

Discussion

Cryptosporidiosis is a gastrointestinal illness caused by *Cryptosporidium* spp., transmitted by direct fecal contamination or through waterborne routes, and causes diarrhea in hosts. In humans, the infection is commonly found in children, with the small intestine being the primary site. In immunocompromised individuals, it can involve other organs such as the biliary tract, lungs, or pancreas.[2] Prevalence studies show that oocyst excretion rates vary between 1% and 3% in industrialized countries and 10% in less industrialized nations. In developed countries, the seroprevalence ranges from 25% to 35% and is as high as 60%–90% in the developing world.[3]

Cryptosporidiosis is usually a self-limiting illness in healthy individuals which may last up to 9–15 days. In immunocompromised individuals though, it can be life-threatening if misdiagnosed.[2] At present, nitazoxanide is the only Food and Drug Administration-approved drug for cryptosporidiosis with a moderate efficacy in children and immunocompromised patients.[4]

Biliary cryptosporidiosis that involves the bile ducts and the gallbladder has been reported much less frequently, both because of its rarity and the difficulty in diagnosing it.[1] The first case of gallbladder cryptosporidiosis was reported in an AIDS patient in 1983.[5] Several studies after that have reported intrahepatic and extrahepatic dilatation of the bile ducts, gallbladder wall thickening with accumulation of pericholecystic fluid, narrowing in the distal ducts with papillitis, and papillary stenosis on ultrasound, CT, and endoscopic retrograde cholangiopancreatography. Nonvisualization of the gallbladder on HIDA scan has also been reported, with acalculous disease being more common,[6] as identified in two of our cases.[1,3,6,7]

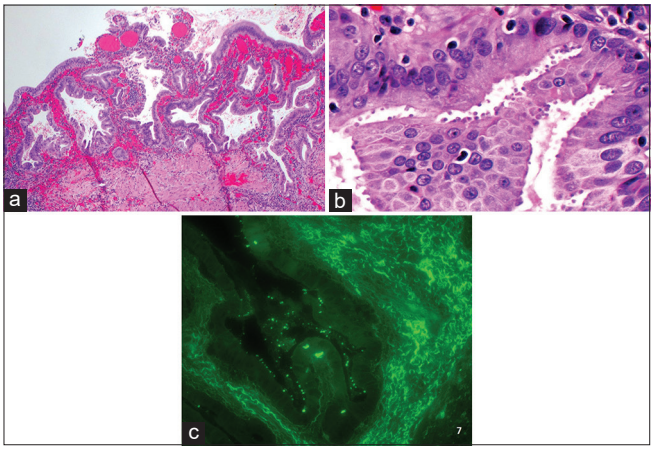

Figure 1: (a) Gallbladder epithelium showing papillary hyperplasia (H and E, ×100). (b) *Cryptosporidium* organisms on gallbladder surface epithelium (H and E, ×400). (c) *Cryptosporidium* organisms on fluorescence microscopy (auramine and eosin-yellowish YR, ×400, at 488 nm)

On histology, most of the findings described in the biliary tract are nonspecific and include a periductal inflammatory response with interstitial edema, mixed inflammatory cell infiltrates, hyperplasia, and dilatation of the periductal glands and neutrophils forming microabscesses within the lumina of dilated glands.[1,3] The largest study done on cholecystectomies from 107 patients with AIDS reported histologic findings similar to that in the intestine,[6] which is the most common site of involvement. Intestinal cryptosporidiosis shows blunting of villi, hyperplasia of intestinal crypt cells, inflammatory cell infiltrates in lamina propria, cryptitis, epithelial apoptosis, and reactive epithelial changes.[3] In any involved organ, the organisms may be overlooked because of their small size[1] and especially in a routine gallbladder specimen which is usually inflamed. Our cases also showed marked acute and chronic inflammation in the mucosa along with papillary hyperplasia of the gallbladder epithelium. The organisms were identified in these hyperplastic areas. The finding of papillary hyperplasia of gallbladder mucosa is a new addition to the histologic features described before and can be a hint to look for infectious organisms, for example, cryptosporidiosis.

To conclude, in cases known to be HIV positive with imaging studies suggestive of acalculous or acute cholecystitis, the finding of focal to diffuse mucosal papillary hyperplasia of the gallbladder in the presence of marked acute and chronic inflammation can be a clue for an infectious opportunistic cause.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Research quality and ethics statement:

The authors followed applicable EQUATOR Network (http://www.equator-network.org/) guidelines, notably the CARE guideline, during the conduct of this report.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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