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Intraductal papillary mucinous neoplasm with an invasive cancer in the background of primary sclerosing cholangitis. Coincidence or a genetic predisposition?

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Abstract

This is a rare case of an Intraductal Papillary Neoplasm of Bile duct (IPNB) in a 66 year old male presenting in the context of Primary Sclerosing Cholangitis (PSC) related cirrhosis for which true lineage has not yet been corroborated. He presented with biliary sepsis along with obstructed left hepatic ducts and a communicating cystic lesion. However following resolution of sepsis, proceeded for a liver resection that revealed a direct extension of the cystic lesion on to the body of the pancreas. A left hepatectomy and a marsupialization of the cyst performed with thermal ablation of the remaining cyst wall over the pancreas. Histology revealed an IPNB with an invasive component, though pancreatic margin was benign. Nine months postoperatively patient remains disease free and asymptomatic. In retrospect, comparing with three previous cases, we postulate an aggressive behaviour of IPNB in the background of PSC besides a true lineage.

Keywords

intraductal papillary neoplasm of bile duct; primary sclerosing cholangitis; mucinous lesions; premalignant lesions of bile duct.

Introduction

Intraductal Papillary Neoplasms of the Bile duct (IPNB) are intraductal, exophytic epithelial papillary masses with intrahepatic duct dilatation (Duct-ectatic type) that can be variably associated with mucus hyper secretion, which erupts either in the main biliary ducts with aneurysmal dilatation or in Peribiliary glands (Cyst forming type) but does not contain ovarian-type subepithelialstroma[1,2].

A multi centre, institutional based comparison revealed, prevalence for IPNB in western population is around 0.4% compared to 3.4% in the far east, but with a higher potential for malignancy [3]. Recognized risk factors include hepatolithiasis and clonorchiasis, resulting a higher prevalence in the far eastern world [4]. However, only in three cases, an association has been described with Primary Sclerosing Cholangitis (PSC), which needs corroboration.

Case Report

A 66-year-old male with Ulcerative Colitis (UC) since1968, had total Proctocolectomy and Ileoanal pouch reconstruction in 2007 for refractory colitis. PSC was diagnosed in 2012. He was under regular surveillance with Jaundice (Bilirubin of 35mg/dl) and normal liver synthetic functions. Computer Tomography (CT) scan in August 2014 revealed, slightly dilated left Intrahepatic Ducts (IHD) despite no mass lesion and normal tumour markers. Over the subsequent 18 months imaging showed progressive left ductal dilatation.

In November 2015 he presented with sepsis and repeat MRCP revealed left duct dilatation with new intraductal filling defects and a 6cm subcapsular cystic lesion in the left lateral segment communicating with segment III ducts and occlusion of the left hepatic vein and left portal vein. Ultrasound guided drainage isolated ESBL Ecoli which was treated with IV Ertapenum for 6 weeks. Cyst fluid cytology was negative for malignancy. Repeat MRCP in March 2016 (Figure 1) showed progression of the disease with further dilatation of left biliary ducts with intraductal filling defects. Additional stricture was demonstrated in the distal common bile duct (CBD). The segment III subcapsular lesion has increased in size from 6cm to 6.5cm. Sepsis had resolved and tumour markers were normal. ERCP demonstrated a 2 cm stricture in the CBD, which was dilated, with negative brushings for malignancy.

Appearances were of an IPNB and as he had well compensated cirrhosis (Childs A, MELD=18) with an adequate functional liver volumetry, was considered for resection. At surgery the inflamed liver cyst was densely adherent to the body of the pancreas. A left hepatectomy was performed. The portion of cyst wall densely adherent to the pancreas was left attached, cauterized with argon, with intra-operative biopsy confirming it was benign. He had a delayed postop recovery due to diagnosis of previously undiagnosed myasthenia gravis and prolonged cholestasis. Histology showed R0 resection of an IPNB, dilated ducts with moderate to severe dysplasia with a focus of invasive adenocarcinoma invading the liver parenchyma (Figure 2) and one hilar lymph node with metastatic disease (pT3N1). Pancreatic cyst wall margin was negative for dysplasia or malignancy.

Discussion

There are only three previous reported cases of IPNB in the background of PSC. One case occurred in a 60 year old lady with PSC for 1 year, investigated for mass lesion and upstream dilatation of the left intrahepatic bile ducts revealed a mucinous IPNB with a invasive component and a positive regional lymph node following surgical resection and remained disease free for 27 months [5]. In the second case 50-year-old lady with 26 years of UC and 3 years of PSC underwent orthotopic liver transplantation for recurrent cholangitis and the explant unravelled an IPNB with an invasive component in the right biliary ducts. Her preoperative imaging showed some dilated ducts in the right posterior segment with no mass lesion [6]. Third patient was a 46 year old lady with UC and PSC for 18 months, underwent a right hepatectomy for non-enhancing papillary lesion in the right posterior ducts revealed IPNB with only high grade dysplasia [7]. Our case is peculiar, as is the only male patient with longest duration of PSC (4 years) before the diagnosis of invasive cancer and with a direct extrahepatic spread in the series.

PSC is a chronic liver disease with prolong cholestasis secondary to inflammatory destruction of intra and extra hepatic bile ducts and a well renowned risk factor for cholangiocarcinomas (CCA) [7].

Prevalence of CCA secondary to PSC is around 5-7% [8]. Interestingly, longer time lag between UC and PSC is reckoned as a risk factor, but not the duration of PSC [9]. From the recorded data two cases including our patient had longer time lags between UC and PSC, thus evince a similar correlation towards IPNB. However, any association with preceding duration of PSC, which was relatively shorter in all four cases, is currently speculative of any synergetic effect. Furthermore, presence of an invasive component in all cases except for one intrigues the possibility of an aggrandized behaviour of IPNBs in the background of PSC.

In a disease with nonspecific clinical presentation, radiological features favouring IPNB such as intraductal filling defects, multilocular cysts with duct communication and dilatation and parenchymal atrophy [10] is of great value. Most of these features were variably present in all these cases, but background PSC alone could be of self-explanatory and reminds the usual gruelling has to be made on discovering CCAs in the background of PSC. Detection of abnormally dilated segmental ducts in the preoperative imaging was the only consistent radiological feature across all four cases. This along with the fact that all IPNBs occurred in first or second order ducts would suggest in clinical practice, an early cholangioscopic interrogation (with biopsy and witnessing mucin) could be anoptimistic tool in the modern era for early diagnosis.

IPNB is accounted for 9-38% of all resected bile duct carcinomas [2,11,12]. Malignant potential of IPNB varies from 49-74% and is extortionately higher compared to 2-3% in MCN of liver and 21-26% IPMN of pancreas [3,12], which justifies a obligatory radical approach to this tumour. Also the staged match 5-year survival rates for invasive IPNB is 44% compared to 63% in invasive IPMN of pancreas, further warrants towards a radical approach [12,3]. However, they have better prognosis compared to conventional CCA [13].

The other more unusual feature of this case is the direct extension of the mucinous lesion on to the body of the pancreas. The presumed preoperative benign nature, patient's age, background cirrhosis and tolerability of the procedure would justify a more conservative approach, the cauterization of the premalignant epithelium, on the cyst wall of the pancreas. Retrospectively, considering the prolonged postop recovery and intrahepatic cholestatsis, decision to decline from distal pancreatectomy that would have potentiated the possibility of pancreatic leak otherwise, undoubtedly benefitted the patient's outcome. Estimated median survival being a Child A cirrhotic in the background of PSC, was between 12-18 years [14,15] in the beginning. However, detection of an IPNB with a Invasive component compromised his prognostication towards a maximal 5 year survival rateto around 44% [12] and deprived the opportunity for liver transplantation in case of decompensation. Under these circumstances it further justifies our conservative approach on the pancreas but obviously mandates a close follow up.

In conclusion, we describe a mucinous IPNB with an invasive component in the background of PSC, causing a diagnostic dilemma, showing possible lineage and synergy towards a bad prognostic disease.

Figures

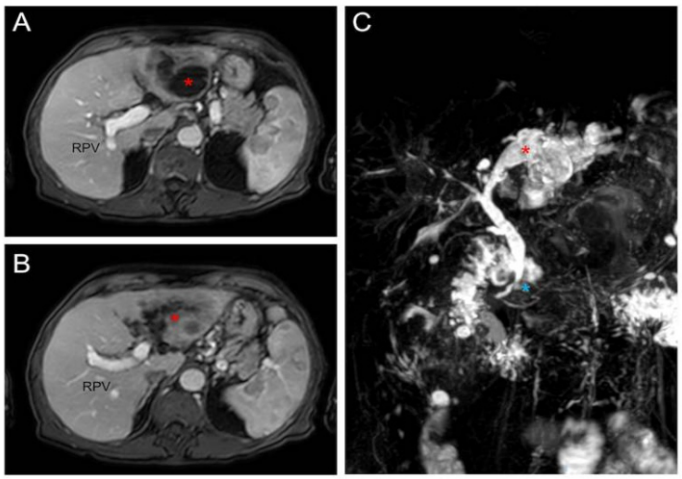

Figure 1: MRI Images from 2016 March A) Showing the cystic lesion (red asterisk) and occluded left Portal veinB) Dilated left intrahepatic ducts (red asterisk)C) cystic lesion communicating with left biliary ducts (red asterisk) and distal CBD stricture (blue asterisk).
RPV: Right portal vein

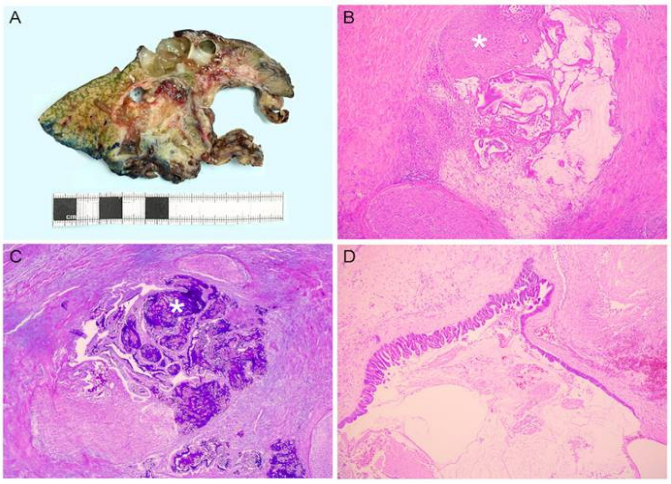

Figure 2: Histopathology of the resection specimen.

A) Photograph of a representative slice from the specimen, showing liver tissue with a multicystic subcapsular lesion (70 x 45 x 30 mm). Some mucinous material can be seen within the cystic spaces.

B) Photomicrograph of the lesion, H&E stain, 100x magnification. The invasive component of the lesion is composed of islands of atypical epithelium lying in abundant extracellular mucin. Tumour is seen infiltrating a nerve trunk in this field.

C) Photomicrograph of the lesion, Alcian blue/periodic acid Schiff stain, 100x magnification. The mucin within the area in figure 2b is highlighted in purple.

D) Photomicrograph of the lesion, H&E stain, 100x magnification. The background liver contains numerous dilated ducts with inspissated mucus, lined by variably dysplastic epithelium.

Contributor ship statement

Niroshan Samantha Atulugama contributed to the original concept, planning, writing and revision of manuscript, interpretation of findings and approval of the final version.

Peter Mark Ellery contributed to the planning, writing and revision of manuscript, interpretation of findings and approval of the final version.

Jennifer Watkins contributed to the planning, writing and revision of manuscript, interpretation of findings and approval of the final version.

Brian Davidson contributed to the original concept, planning, writing and revision of manuscript, interpretation of findings and approval of the final version.

All authors unanimously agree on the terms of licence of publication by open Journal of Clinical & Medical case reports. Informed written consent was taken from the patient for publication.

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