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Adenomyomatous Hyperplasia of the Vaterian System Peculiar by the Association with a Concomitant Low Grade Pancreatic Intraepithelial Neoplasia - A Rare Case Report

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Abstract: ***Adenomyomas are rare benign lesions that have been observed in different sites throughout the gastrointestinal tract, most frequently in the gallbladder. Few cases have been described in the stomach, small bowel, bile ducts, and the ampullary region. Adenomyomas of the Vaterian system (ampulla and common bile duct) have important clinical consequences, since most lesions present with biliary tract obstruction and mimic malignancy. As a consequence, considering the diagnostic difficulty of these lesions, patients are often treated with extensive surgery (pancreaticoduodenectomy). We present a rare case of adenomyomatous hyperplasia of the ampulla of Vater peculiar by the association with a concomitant low grade pancreatic intraepithelial neoplasia (Pan - IN).***

Keywords: Adenomyomatous hyperplasia, Ampulla of Vater, Common bile duct (CBD), Low grade pancreatic intraepithelial neoplasia

1. Introduction

Benign tumors constitute about 6% of all extrahepatic biliary tree neoplasms and are responsible for 0.1% of all biliary surgical procedures [1]. Adenomyomatous hyperplasia / adenomyomas are rare benign lesions of the gastrointestinal and hepatobiliary tract. Adenomyomatous hyperplasia of the Vaterian system is extremely rare [2]. The adenomyomas/ adenomyomatous hyperplasia of the ampulla of Vater has clinical importance due to its strategic location, unlike in other locations of the gastrointestinal tract that are usually asymptomatic [3]. We report a case of adenomyomatous hyperplasia of the ampulla of Vater associated with a concomitant low grade Pan - IN lesion. This lesion in association with Pan - IN is the first case reported in the medical English literature.

2. Case Presentation

A 64 year old male patient presented with intermittent epigastric pain and loss of appetite for a month. Jaundice was observed a week before presenting to our hospital. There was no history of fever or chills. Abdominal examination revealed mild epigastric tenderness. Laboratory work up showed mildly elevated WBC count. Liver function tests showed raised total and direct bilirubin levels (9.68 mg/dL & 9.67 mg/dL, respectively), decreased serum albumin (2.38g/dl), AST 96 U/dL, ALT 91 U/dL, alkaline phosphatase 146 U/dL and GGT 600u/dL and normal prothrombin values.

Abdominal ultrasound examination revealed a dilated common bile duct with a diameter of 10.9 mm (normal diameter of CBD ranges from 1.8 to 5.9 mm in adults) in the head of pancreas. Gall bladder showed some sludge. There were no stones or mass lesions in the gall bladder. A CT scan examination of the abdomen revealed a dilated CBD with a maximum calibre of 15mm. At the distal CBD/ Periampullary region, heterogenous wall enhancement with a suspected small soft tissue mass was seen measuring 15 x 10mm (Figure 1).

Endoscopic ultrasound (EUS) revealed a lobulated periampullary mass. There was an indistinct margin with the head of the pancreas. The EUS examination was performed at another medical center, detailed data were not available. A biopsy was attempted but was unsuccessful owing to its difficult location.

The multidisciplinary meeting concluded to the diagnosis of ampullary mass of uncertain behaviour/ possibly malignant with possible clinical/ biological complication/ cholestasis. A surgical treatment (Whipple's Pancreaticoduodenectomy) was proposed to the patient. He consented for the procedure and the surgical procedure was planned.

We received a specimen of Pancreaticoduodenectomy. On cutting open the duodenum, the mucosa covering the ampulla was smooth and appeared to bulge into the duodenal lumen. The ampullary opening could not be identified. On cut section, a grey white, soft to firm well circumscribed and lobulated peri and sub ampullary lesion

was identified measuring 1.2x1x0.6cm. The lesion was well limited and non - encapsulated. The lesion appeared firm in consistency on comparison to the adjacent pancreatic tissue. The dilated part of the common bile duct (10 mm in diameter) was detected 10 mm away from ampulla of Vater over a length of 30 mm traversing into the head of pancreas. The pancreatic duct showed stenosis of the lumen (2 mm in diameter) over a length 25 mm. On tracing the duct further, the duct was completely stenosed beyond this length. No intraductal papillary growth or mass lesion was identified. The entire resected pancreas was evaluated for microscopic examination. The rest of the duodenal and gastric mucosa was unremarkable.

Histopathological examination revealed an adenomyomatous hyperplasia of the ampulla of Vater (Figure 2) showing hyperplastic lobules of small glands surrounding the larger duct embedded within the proliferating myofibroblasts and smooth muscle cells (Figure 3) highlighted by SMA and desmin. Cytologic atypia and mitotic figures were not seen. On immunohistochemistry, the epithelial component expressed CK7 and CK19 similar to that of the normal pancreatico - biliary system. MUC5AC was not expressed. P53 showed wild type expression.

The p53 staining pattern is described as wild type (normal) expression and aberrant (mutant) type expression. The mutant type expression can be seen in high grade pancreatic intraepithelial neoplasia (PanIN - 3).

In our case, the dilated pancreatic duct showed a low grade pancreatic intraepithelial neoplasia (PanIN - 2, Figure 4). The duct revealed a papillary pattern lined by pseudostratified tall columnar mucinous epithelial cells with mild nuclear atypia (Figure 5). Skip foci of PanIN was identified only in the pancreatic duct located at a distance of 2mm from the stenosis, secondary to pseudotumoral adenomyomatous hyperplasia over a length of 15mm. The CBD showed inflammatory changes secondary to obstruction. No tumor or intraepithelial neoplasia was identified in the CBD. The ki67 proliferation index was not performed.

Micropapillary pattern, cribriform glands, marked nuclear atypia, significant mitotic activity and adenocarcinoma was not seen.

The rest of the pancreas showed features of acute pancreatitis with fat necrosis.

3. Discussion

Adenomyomatous hyperplasia is an extremely rare lesion encountered in the ampulla of Vater and can be misdiagnosed as an ampullary adenoma or carcinoma. According to the WHO classification [4], adenomyoma and adenomyomatous hyperplasia are defined as ductlike structures accompanied by hyperplasia of smooth muscle cells. To our knowledge, by 2021, less than 50 cases have been described in the indexed English literature [5]. Higher frequency was noted in a post - mortem specimen's study, in which 54% of 100 unselected patients had this lesion, with no clinical significance [6].

The histogenesis of adenomyoma and adenomyomatous hyperplasia is still a subject of controversy. The most widely accepted hypothesis is that these lesions may represent a form of incomplete heterotopic pancreas (type III), as described by von Heinrich in 1909 [7]. Martin et al. compared adenomyoma of the Vaterian system to its gallbladder counterpart and claimed that the former is a lesion developed in diverticula. Fernandez - Cruz and Pera [8] considered adenomyoma as part of an involutive process of fibroadenomatous type due to increasing age. Other authors, such as Narita and Yokoyama [9], stress the possible inflammatory nature of this lesion.

In one case series of 13 patients reported by Handra - Luca et al, from France, the average age of presentation was 63 years (ranging from 38 to 78 years), consistent with the age of our patient at 64 years. In the same case series, the male - to - female ratio was 6: 7. The clinical presentation is usually variable depending on the location of the lesion. It can be asymptomatic or may present with jaundice, epigastric pain, right upper quadrant pain or non - icteric cholangitis. Our patient was symptomatic and presented with abdominal pain and jaundice due to obstruction of the ampulla of Vater.

Kwon et al [10] reported the first case of adenomyoma of the ampulla of Vater presenting as acute recurrent pancreatitis, which is extremely rare. Our patient also presented with histological features of acute pancreatitis.

The diagnosis of adenomyoma of the Vaterian system is challenging. The overall accuracy for preoperative histopathological diagnosis with endoscopic forceps biopsies in patients with ampullary tumors was reported as 62% by Menzel et al [11]. The potential roles of intraductal ultrasound, magnifying endoscopy, capsule endoscopy and narrow - band imaging endoscopy in diagnosing ampullary adenoma are still under investigation [12 - 15]. There is no widely accepted approach to managing these patients. Ampullectomy, local resections with endoscopic snare excisions, or simply biliary tree drainage with sphincterotomy have been offered when a preoperative diagnosis is possible, avoiding postoperative morbidity and mortality. However, pancreaticoduodenectomy is the traditional surgical approach [16]. Extensive surgeries have also been recommended by some authors taking into account a recurrence rate of 22% for local resection of benign tumors of extrahepatic biliary duct or ampulla of Vater [17].

PanINs have been reported in 16% to 45% of pancreas that do not harbor an invasive cancer [18]. Autopsy studies indicate that low - grade PanINs are found in the pancreas of most adults once they reach middle age [19]. High - grade PanINs, however, are rarely found, unless there is an associated invasive pancreatic cancer or the patient has a strong family history of pancreatic cancer. Paralleling this histologic progression is a genetic progression. The lower grade lesions (PanIN - 1 and PanIN - 2) often harbor genetic alterations in the KRAS and p16/CDKN2A genes, whereas the higher grade PanIN - 3 lesions and invasive adenocarcinomas, in addition to genetic alterations in KRAS and p16/CDKN2A, also often harbor mutations in TP53 and SMAD4 [20]. However, no correlation was found with adenomyomatous hyperplasia and PanINs. To the best of our

knowledge during literature search this is the only reported case of coincidence of adenomyomatous hyperplasia of ampulla of Vater and low grade pancreatic intraepithelial neoplasia.

Our patient underwent a pancreaticoduodenectomy procedure and a histopathological diagnosis of adenomyomatous hyperplasia of the ampulla of Vater with a low grade pancreatic intraepithelial neoplasia was diagnosed. The patient was reviewed at OPD 3 months post surgery and her progress is uneventful.

4. Conclusion

Adenomyomatous hyperplasias are rare benign lesions involving the ampulla of Vater often presenting with biliary obstruction mimicking a malignant neoplasm. They often pose a diagnostic challenge as imaging and endoscopy findings are non - conclusive. As a consequence, in most cases, patients are treated with extensive surgery despite its benign nature. In our case, we found a concomitant low grade pancreatic intraepithelial neoplasia involving the pancreatic duct along with adenomyomatous hyperplasia of the Vaterian system.

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Figures:

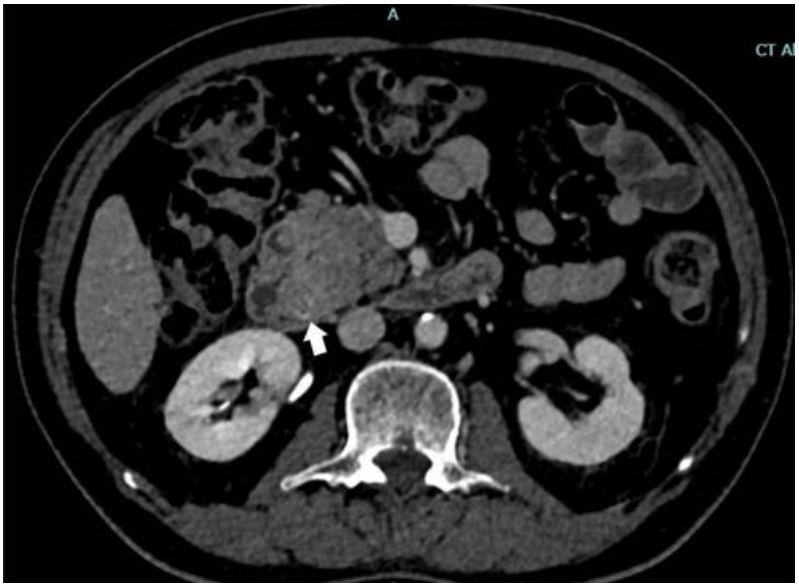

Figure 1

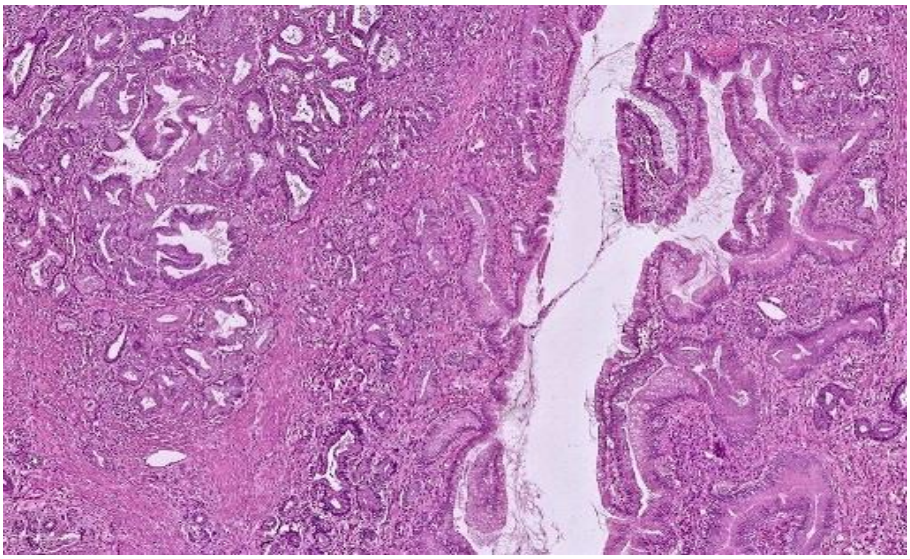

Figure 2

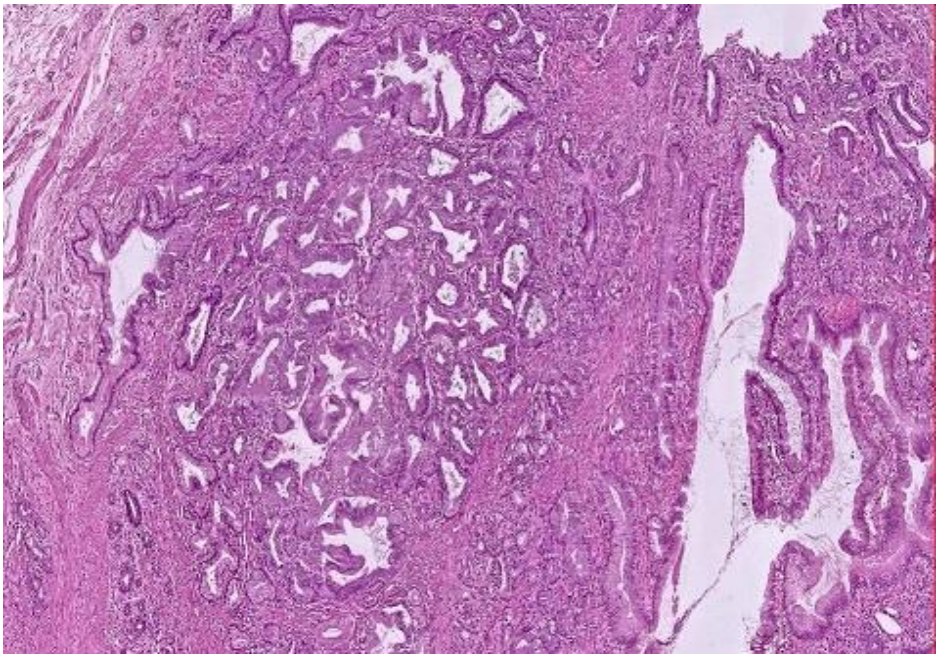

Figure 3

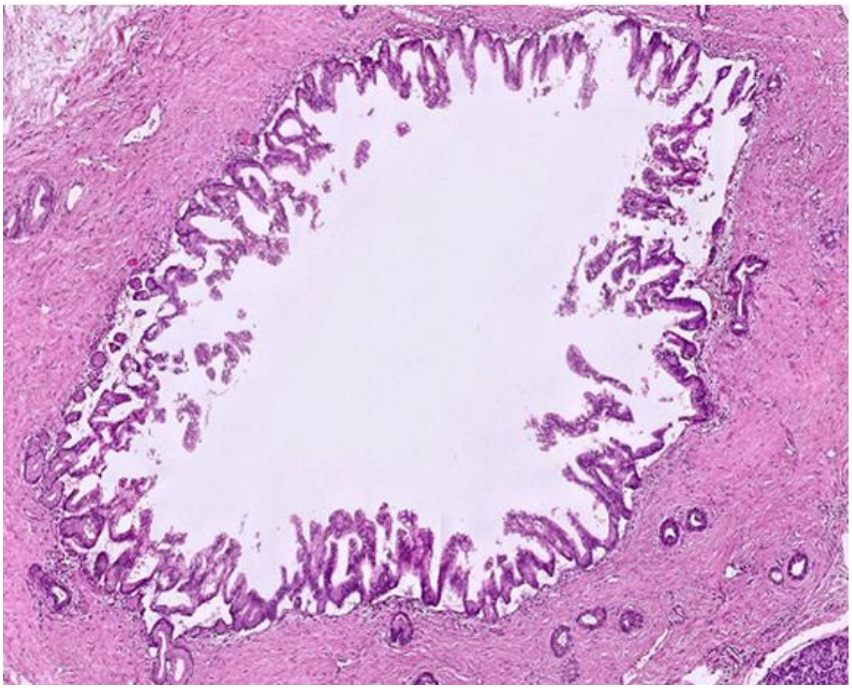

Figure 4

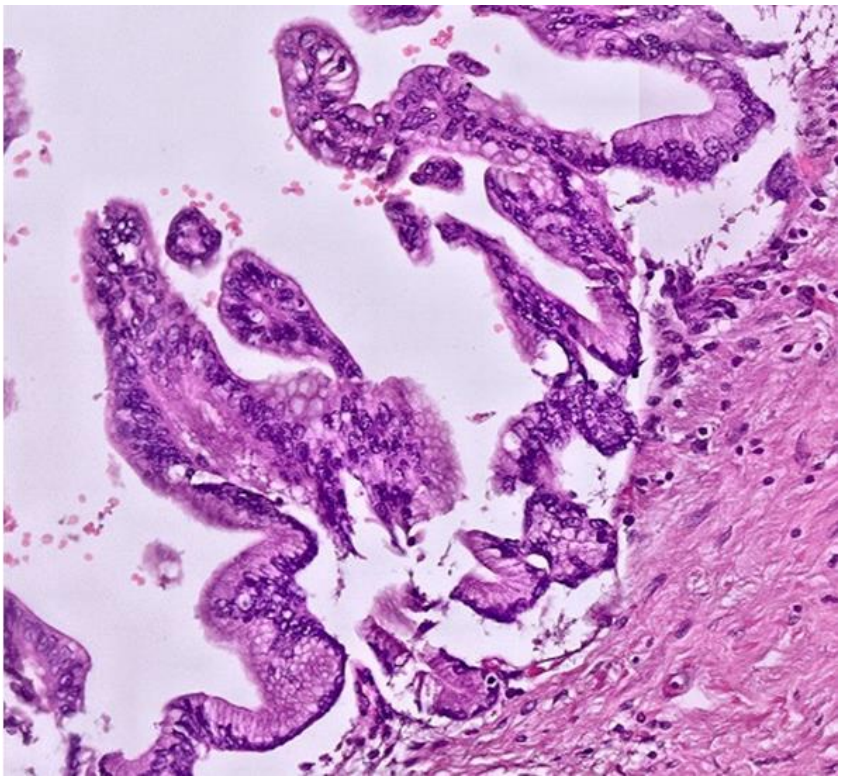

Figure 5

Keys:
Figure 1: Axial view of CECT scan showing arterial enhancing lesion in the head of pancreas (white arrow).
Figure 2: Adenomyomatous hyperplasia of ampulla of Vater [10X field, H and E stain].
Figure 3: Hyperplastic lobules of small glands surrounding a larger duct embedded in a myofibroblastic stroma and smooth muscles - Adenomyomatous hyperplasia of ampulla of Vater [10X field, H and E stain].
Figure 4: Low grade pancreatic intraepithelial neoplasia, Pan - IN lesion [10X field, H and E stain].
Figure 5: Low grade cytologic atypia/ dysplasia in a Low grade pancreatic intraepithelial neoplasia, Pan - IN lesion [40X field, H and E stain].