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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/19255
DOI URL: http://dx.doi.org/10.21474/IJAR01/19255

RESEARCH ARTICLE

PERIBILIARY GLANDULAR HYPERPLASIA AS A MIMICKER OF MALIGNANCY

Aishwarya Prasad Nair[1], Sai Sudha Muddha[2], Thanka J.[3] and Rajendran Shanmugasundaram[4]

1. Postgraduate, Department of Pathology, Sree Balaji Medical College and Hospital, 600044.
2. Associate Professor, Department of Pathology, Sree Balaji Medical College and Hospital, 600044.
3. Director and Professor, Department of Pathology, Sree Balaji Medical College and Hospital, 600044.
4. Professor, Department of Surgical Gastroenterology, Sree Balaji Medical College and Hospital, 600044.

Manuscript Info

Manuscript History
Received: 09 June 2024
Final Accepted: 11 July 2024
Published: August 2024

Key words:-
Peribiliary Glands, Glandular Hyperplasia, Hepatolithiasis, Cholangiocarcinoma

Abstract

Peribiliary glands are a group of tiny glandular structures located along the intrahepatic and extrahepatic bile ducts, and cystic duct. Their major function is to regulate enzyme secretion and turn over, and regeneration of the bile duct epithelium. They are closely associated with conditions like Primary sclerosing cholangitis, Hepatolithiasis and neoplasms like Cholangiocarcinoma. If the hyperplasia is severe enough to cause bile duct obstruction, it will closely mimic biliary neoplasms like cholangiocarcinoma. Unfamiliarity of this rare condition can create false positive diagnosis of malignancy. Hence careful and thorough histopathological examination of the specimen is essential in such cases. Here we report a rare case of extensive peribiliary glandular hyperplasia in association with hepatolithiasis in which a 57-year-old woman with colicky abdominal pain, fever, vomiting, and abdominal distention was diagnosed with multiple strictures of the left hepatic duct and recurrent pyogenic cholangitis. MRI and liver function tests indicated obstruction for which she underwent surgery. Histopathology revealed benign glandular hyperplasia with no malignancy.

Introduction:-

Peribiliary glands (Beale glands) are small tubulo-alveolar structures located along the intrahepatic and extrahepatic bile ducts, and cystic duct[1]. Major physiological function of PBGs is enzyme secretion similar to that of pancreatic exocrine tissue [2]. Recent experimental studies have revealed that they harbor biliary tree stem cell/progenitor cells which are involved in epithelial cell turnover and regeneration. Hence peribiliary gland cells plays an important role in conditions like primary sclerosing cholangitis and hepatolithiasis to replace the epithelial cell loss [3].

In addition to the sclerosing lesions, PBGs also closely associated with several neoplasms like cholangiocarcinoma, intraductal papillary neoplasm and cystic micropapillary neoplasm [2]. Recent histopathological research studies revealed that PBGs are the cell of origin of cholangiocarcinoma, especially inflammation induced biliary tract cancer[4].

Corresponding Author:- Aishwarya Prasad Nair
Address:- Postgraduate, Department of Pathology, Sree Balaji Medical College and Hospital, 600044.

The pathological spectrum of these peribiliary glands includes peribiliary cysts, glandular hyperplasia, benign and malignant neoplasms. Peribiliary glandular hyperplasia is a rare condition in which there is increased proliferation of these glands causing mucosal elevation and in severe cases, obstructing the Common bile duct lumen. Hence it should be differentiated from other glandular tumors like adenomyoma and adenocarcinoma [5,6]. Peribiliary glandular hyperplasia is seen in hepatolithiasis, sub-massive hepatic necrosis and other biliary tract infections [3].

Case Report:

A 57-year-old female patient presented with the complaints of intermittent, colicky abdominal pain for 2 months and on and off fever for 1 month. Abdominal pain radiates to the right shoulder and back and also associated with vomiting and abdominal distention. Liver function tests reveal increased GGT (Gamma glutamyl transferase) levels – 67IU/L suggesting obstruction. MRI upper abdomen and MRCP revealed moderate hepatomegaly and mild intrahepatic biliary radicals' dilatation in left lobe of liver segments 2&3 with internal hypointense calcific shadows with secondary to stricture of proximal bile duct leading to segment 2-3. A clinical diagnosis of left hepatic duct multiple strictures with stones and Recurrent pyogenic cholangitis was made out and patient underwent lateral segmentectomy of left lobe of the liver and cholecystectomy with choledocho-duodenostomy procedure (Fig 1). Intra-operative findings were atrophic left lateral lobe of the liver, dilated CBD distal to biliary stricture and gall bladder sludge. After the surgery patient recovered well. Histopathological examination of the specimen revealed Extensive Peribiliary glandular hyperplasia with microliths in the dilated hepatic duct (Fig 2&3). In order to rule out the malignancy, specimen was carefully examined and thoroughly sampled and additional sections were taken from the dilated hepatic duct and its adjacent area. Final and detailed examination revealed no cellular atypia in the glands (Fig 4) suggesting it of Benign glandular hyperplasia in association with hepatolithiasis.

Figure 1:- Segmentectomy specimen of left lobe of the liver.

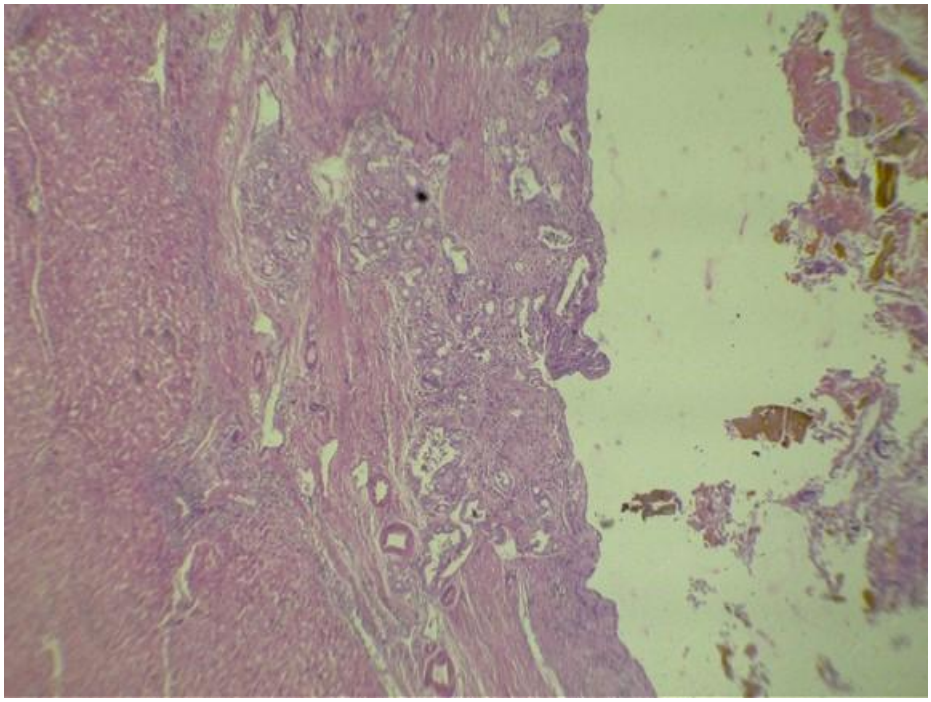

Figure 2:- Hyperplastic peribiliary glands around the dilated duct with microlith (H&E 10X).

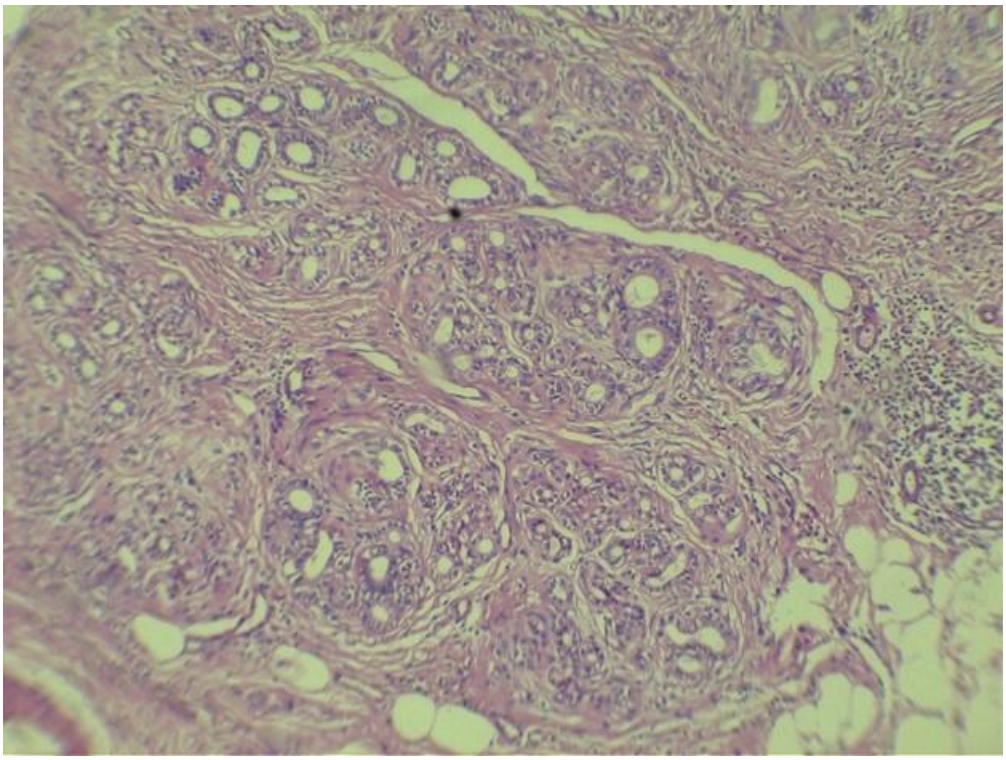

Figure 3:- Benign peribiliary glands maintaining lobular architecture (H&E 40X).

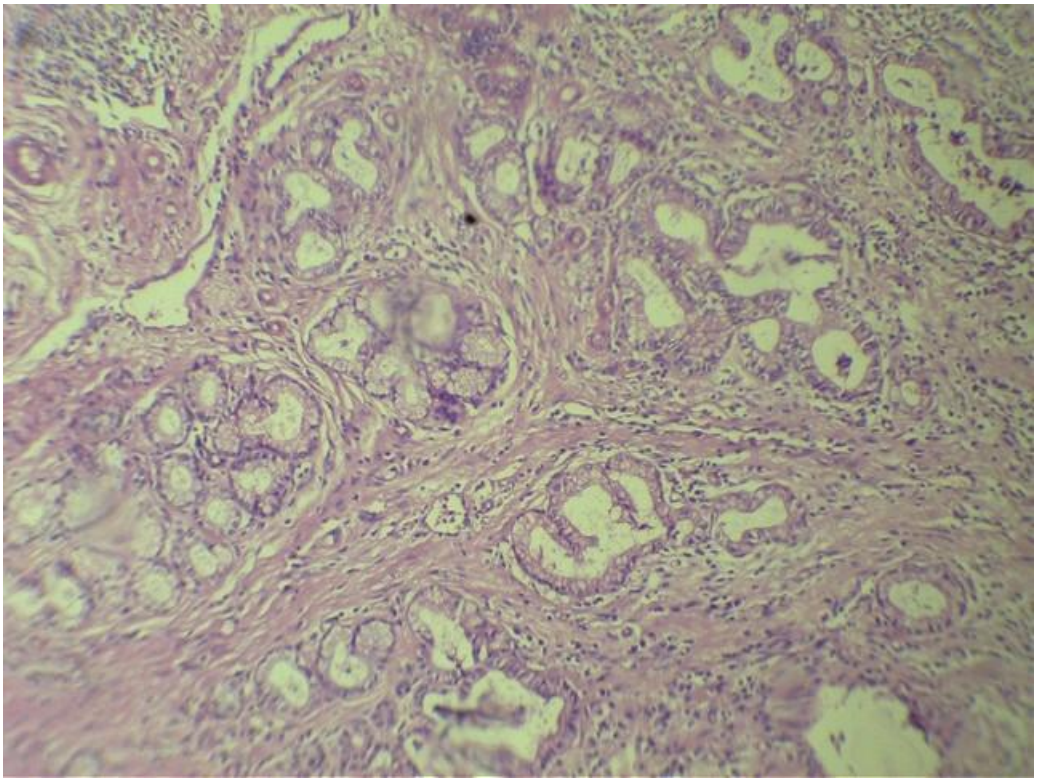

Figure 4:- Benign peribiliary glands without cellular atypia (H&E 40X).

Discussion:-

Peribiliary glands are tiny structures distributed densely in the hilar bile duct, cystic duct and in the periampullary region. Developmentally, these glands share the same origin of the intrahepatic ducts, that is from the ductal plate. Anatomically, based on their location in the biliary wall, they are classified into two types: Intramural and Extramural glands. Intramural glands are seen within the bile duct walls and are primarily of mucinous type, whereas extramural type is located in the periductal connective tissue and histologically, these are tubulo-alveolar acini composed of serous, mucinous and mixed types [2,7]. PBGs along with intermingled vascular system, lymphatic vessels and nerve fibers form a complex called peribiliary glandular network, which has a pivotal role in the spread of inflammation and neoplasm [8]. Their physiological functions include enzymatic secretion, secretion of mucin, preservation of immunity and regeneration and repair of bile tract [1,2].

Peribiliary glandular hyperplasia is a rare condition, commonly associated with hepatolithiasis and other conditions like cholangitis, hepatic necrosis, cirrhosis and systemic infections.

Association with hepatolithiasis:

Hepatolithiasis is the presence of calculi in the bile ducts proximal to the joining of right and left hepatic ducts [9]. It is of two types, based on the etiology: Primary and Secondary [10]. Primary hepatolithiasis is a rare disease, usually asymptomatic or presents with the symptoms of cholangitis [11]. A patient with hepatolithiasis usually has a history of recurrent episodes of cholangitis, which is similar to the case presented here.

The most common calculi are calcium bilirubinate type, whereas cholesterol stones are less common in primary hepatolithiasis. The common causes for stone formation include bacterial infection of bile with bile stasis and mucin hypersecretion [10,12]. Histological examination reveals bile duct inflammation, fibrosis of bile duct walls and peribiliary glandular hyperplasia. Proliferation of PBGs, both intramural and extramural, in and around the bile duct wall is consistently seen in the primary hepatolithiasis. Increased mucin secretion into the biliary ducts by these glands will promote the stone formation by causing bile stasis, which favors bacterial proliferation, and increased mucin itself acts as nidus for the aggregation of calcium bilirubinate crystals. Hence it is very clear that PBGs play an important role in the pathogenesis of hepatolithiasis [12].

In few cases, PBGs can be a precursor for the cholangiocarcinoma in hepatolithiasis, because of their harbored biliary progenitor stem cells [13]. So detailed and thorough histopathological examination is a must to rule out a malignant lesion in the specimen, as well as to distinguish the benign peribiliary glandular hyperplasia from cholangiocarcinoma

Peribiliary glandular hyperplasia, especially if it is diffuse, should be differentiated from the malignant hyperplasia. A rare case of diffuse and severe hyperplasia of PBGs of both intrahepatic and extrahepatic bile ducts was reported by Dumas et al [14], in which they encountered diffuse peribiliary glandular hyperplasia, in association with massive hepatic necrosis. Another case report by Durairaj Segamalai et al [15], was a case of benign Beale gland hyperplasia mimicking a periampullary carcinoma. Histological features like normal lobular architecture of glands, lack of cellular atypia, necrosis and invasion favors benign peribiliary glandular hyperplasia. Since PBG lesions lack particular diagnostic IHC markers, histomorphological traits play a major role in making the final diagnosis.

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