DOI: http://doi.org/10.4038/jdp.v15i2.7790 *Journal of Diagnostic Pathology 2020;15(2):10-15*

Case Report

Mucinous Cystic Neoplasm of the Liver- Three Rare Cases with Different Clinical Impressions

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Abstract

Mucinous Cystic Neoplasm of the Liver (MCN-L) is a rare cystic epithelial tumour that does not communicate with bile ducts and comprising ovarian-type mesenchymal stroma and mucinous epithelium. Though it is a benign tumour it may be associated with invasive carcinoma. Therefore, complete surgical excision and extensive sampling is important to prevent recurrence and detect associated malignancy. Its rarity precludes its recognition as it can mimic other cystic liver lesions. Awareness of this rare entity is essential as it lacks well-defined characteristics and poses a considerable diagnostic challenge preoperatively. Here we present three cases of MCN-L with different clinical impressions preoperatively. All three were women who presented with abdominal pain or discomfort and were found to have cystic lesions in the liver which subsequently underwent excision. The preoperative diagnoses were hydaticd cyst, hepatic abscess and simple liver cyst in case 1 ,2 and 3 respectively. Histopathology of all three cysts were MCN-L with no high grade dysplasia or invasive carcinoma.

Key words: Mucinous Cystic Neoplasm of the Liver, differential diagnosis liver cysts

Introduction

MCN-L is a rare cystic neoplasm of the liver affecting 5-10% of the world population. According to the recent world health organization (WHO) classification, the cystic neoplasms of the liver are classified into mucinous cystic neoplasm of the liver (MCN-L) and intraductal papillary neoplasm of the bile duct [IPN-B], similar to the classification used in pancreas [1]. MCN-L comprise less than 5% of all cystic liver diseases [1, 2] and is characterized by the presence of ovarian stroma and absence of bile duct communication. The presence of bile duct communication excludes MCN-L according to the current WHO classification.

MCN-L occurs almost exclusively in women [1]. It commonly occurs in left hepatic lobe and occasionally involves in extra hepatic biliary system [1,2]. In majority of the cases, it is an incidental finding on imaging and liver function tests are usually within normal limits. However, serum levels of CA-19-9 can be elevated, particularly in cases associated with carcinoma [1,3]. Generally, it is an incidental finding in Ultrasound Scan (USS) in asymptomatic patients with small lesions. However. larger lesions can present with abdominal pain and discomfort [4,5].

Radiological appearance of MCN-L can be varied with different imaging modalities. Mostly, they are seen as a multilocular cystic mass with smaller cysts in the cyst wall [4]. The management of choice is complete surgical resection as there is a risk of malignant transformation and recurrence.

Here we present three cases of MCN- L presented to us, with different radiological and clinical impressions highlighting the preoperative diagnostic difficulty of this rare entity.

Case report

Case 1: A 36-year-old woman who was previously well, presented to a peripheral hospital with features of intestinal obstruction. She was afebrile and anicteric. The only available radiological investigation was USS, which showed a large cystic mass obstructing the bowel. She was transferred to North Colombo Teaching Hospital and an emergency laparotomy was performed. Intraoperatively a large cystic mass arising from the liver was evident which had ruptured during the surgery revealing straw coloured cyst contents and multiple daughter cysts. As the gross appearance was highly suggestive of a hydatid cyst, empirical antibiotics were started postoperatively and the completely resected cyst was sent to the parasitology laboratory for assessment. The specimen was later handed over to the histopathology laboratory for further evaluation. We received a previously cut opened multilocular cyst measuring 150 x 90 mm with a smooth outer surface. The inner surface contained cystic areas filled with straw coloured thin fluid. The wall thickness ranged from 4 to 10mm. Solid areas and papillary projections were not evident in the lumen (Figure 1A).

Microscopy revealed an encapsulated multiloculated cystic lesion (Figure 3A), predominantly lined by a single layer of mucinous epithelial cells resting on a basement membrane (Figure 3C). Subjacent to the basement membrane was a cellular compact ovarian like mesenchymal stroma (Figure 3B) which was surrounded by a loose fibrous tissue. There were scattered and collections of hemosiderin laden macrophages in the wall. There was no evidence of nuclear enlargement, hyperchromasia, multilayering or mitoses in the lining epithelium. An invasive component was not seen following extensive sampling. Adjacent liver parenchyma showed reactive changes. This cyst was diagnosed as a MCN-L with no dysplasia or invasive carcinoma.

Case 2: A 23- year- old woman, presented with on and off abdominal pain for one year duration. The USS showed a hepatic cyst measuring 5.8 x 6.5 x 7.1 cm with sedimental material within it. Magnetic Resonance Cholangiopancreatography (MRCP) showed a normal sized liver with a cyst in segment IV, measuring 9.5 x 8.1 x7.1 cm with a large exophytic component. There was no demonstratable communication with the dilated biliary system. Cyst contents were hyperintense. The radiological impression was of a benign cyst. As the patient developed sustained fever, the possibility of a pyogenic abscess was considered. Hence the cyst was aspirated and a drain inserted. Culture of the cyst fluid was negative and cytology showed no malignant cells. As there was no improvement of symptoms following aspiration and insertion of the drain, enucleation of the liver cyst was performed and sent for histology. We received a brown coloured nodular piece of tissue measuring 75x70x50mm. The outer surface was smooth. The cut surface showed an encapsulated multilocular cystic lesion measuring 40x30x20mm. The cyst wall was thick, fibrous and the thickness ranged from 2mm to 4mm. There were no abnormally thickened areas or papillary projections. The cyst was empty with no solid areas. (Figure 1B)

Microscopy showed a multilocular cyst with a thick fibrous capsule containing smooth muscle fibres. The cyst was lined by a single layer of flattened to columnar mucus secreting epithelium with no nuclear stratification, enlargement or hyperchromasia (Figure 4B). Subepithelial stroma showed ovarian like stroma comprising densely packed spindle cells (Figure 4A). The epithelial cells were positive for EMA (Figure 4C). and the ovarian like stroma showed nuclear positivity with ER and PR (Figure 4 D & E). This case was concluded as a MCN- L with no high grade dysplasia or invasive carcinoma.

Case 3: A 40- year old woman presented with gradually worsening abdominal discomfort for 4 years. Contrast enhanced computed tomography (CECT) of abdomen showed a large cystic lesion involving segment II, III, IV, V, and VIII measuring 17x14x13 cm in size with enhancing septations and calcifications. The radiological impression was of a large cyst with

enhancing septations and daughter cysts (Figure 2) and the differential diagnosis were hydatid cyst and a simple cyst. As she had a previous history of laparoscopic excision of a simple liver cyst 13 years ago, the main clinical diagnosis was of a recurrence of a benign cyst. Aspirated cyst fluid was negative for malignant cells. Cystectomy was performed and sent for histology. Gross appearance was of a partly opened cystic lesion with a smooth outer surface measuring 170x130x 40 mm. Cut surface showed a multilocular cyst with loculi ranging from 80-10 mm in diameter. They were filled with clear fluid. No solid or papillary areas were noted in the inner surface and the maximum cyst wall thickness was 3mm. Extensively sampled cyst showed a collapsed cyst wall with extensive surface ulcerations. The cyst was focally lined by single layer of biliary type epithelium showing oncocytic differentiation. No papillary tufting, multilayering, nuclear atypia, mitoses or evidence of invasion seen. The subepithelial stroma showed densely packed spindle shaped cells suggestive of ovarian type stroma with focal haemorrhages. moderate chronic inflammation, and bile ductular proliferation (Figure 5 A &B).

The post operative period was uneventful in all three patients and they are currently being followed up at the surgical clinic.

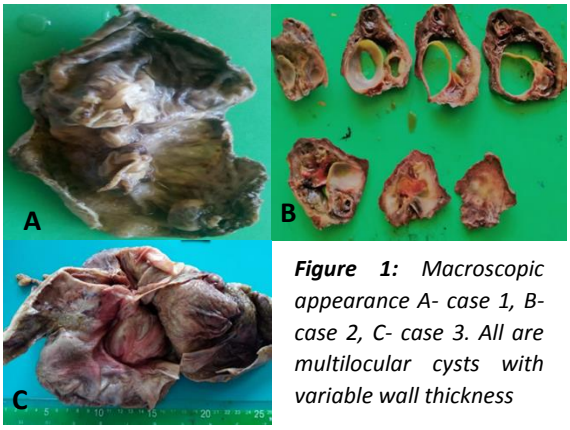

Figure 1: *Macroscopic appearance A- case 1, B- case 2, C- case 3. All are multilocular cysts with variable wall thickness*

Discussion

Cystic liver lesions are common and may represent a myriad of disorders in adults [2,6]. Most liver cysts are incidental findings on imaging and are benign in nature. Liver cysts could be simple or complex lesions. Radiologically simple hepatic cysts appear as fluid-filled structures with smooth thin walls, whereas complex liver cysts have additional elements including wall thickening, irregularity, septations, internal nodularity, enhancement, calcification, or hemorrhagic/ proteinaceous contents.

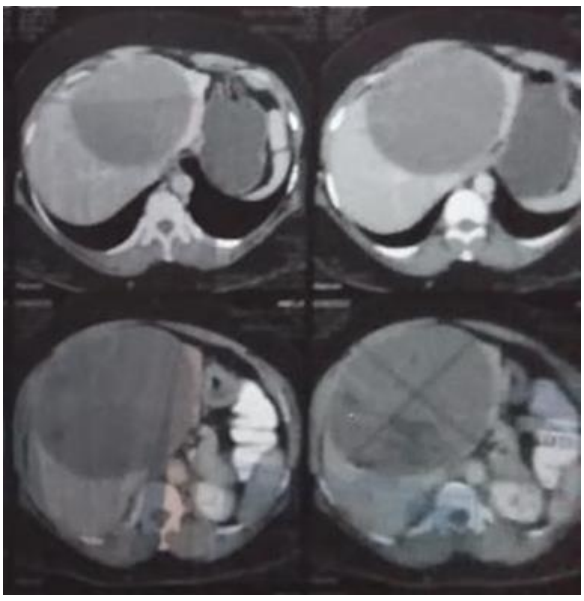

Figure 2: Case 3 CECT abdomen showing a large cyst with thin septation.

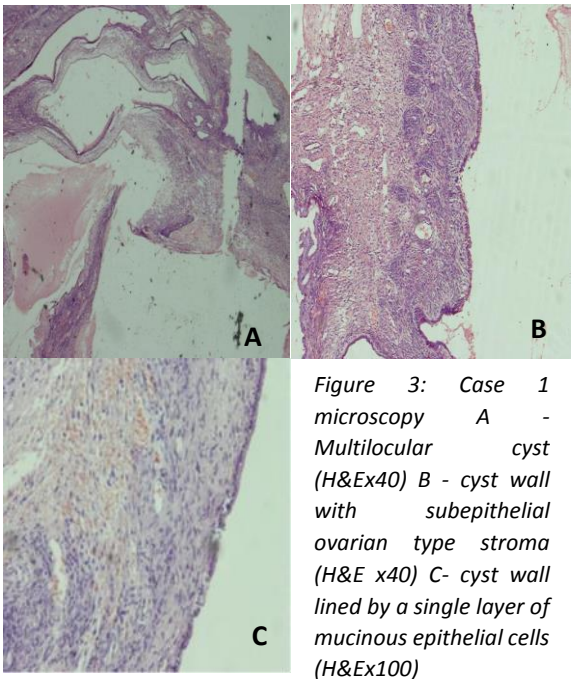

Figure 3: Case 1 microscopy A - Multilocular cyst (H&Ex40) B - cyst wall with subepithelial ovarian type stroma (H&E x40) C- cyst wall lined by a single layer of mucinous epithelial cells (H&Ex100)

Solitary simple liver cysts are mostly asymptomatic, rarely require treatment and can be confidently diagnosed by either CT or MRI.

The aetiology of complex cystic liver lesions vary and includes neoplastic, infectious, inflammatory and some miscellaneous pathologic entities. Neoplastic lesions include IPN-B, MCN-L, primary hepatic neoplasms with hypervascularity leading to cystic degeneration such as cystic hepatocellular carcinoma (HCC) and giant cavernous hemangioma. Metastasis from the ovaries, colon, and some neuroendocrine tumours may occasionally appear as cystic liver lesions [7]. These often need MRI for proper evaluation. Echinococcal and Entamoeba histolytica cysts are parasitic causes of cystic liver lesions while pyogenic abscesses and fungal abscesses are other infectious causes. Caroli disease, adult poly cystic liver disease and traumatic causes are other miscellaneous pathologic entities [6,8].

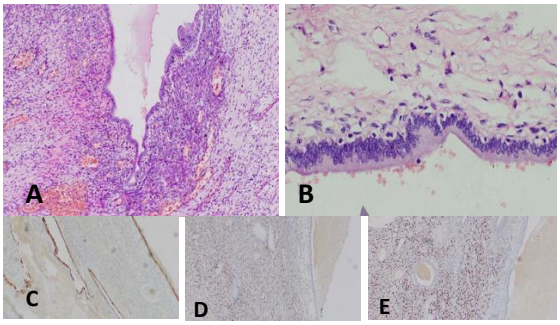

Figure 4: *Case 2 microscopy. A- cyst wall lined by a single layer of mucinous epithelium with subepithelial ovarian type stroma (H&E x40). B-cyst wall lined by mucinous epithelium devoid of dysplasia (H&Ex100). Immunohistochemistry C- EMA positive in the epithelial cells, D- PR and E-ER staining subepithelial stromal cells.*

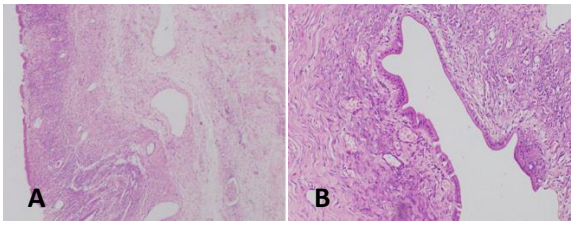

Figure 5: *Case 3 microscopy. A- cyst wall lined by epithelium with subepithelial ovarian type stroma (H&E x40). B-cyst wall lined by single layer of tall columnar mucinous epithelium devoid of dysplasia (H&Ex100).*

MCN-L is a rare cyst-forming epithelial neoplasm, usually showing no communication with the bile ducts. It is lined by cuboidal to columnar, variably mucin-producing epithelium associated with ovarian-type stroma. Rare instances of communicating with the biliary system due to erosion of the expanding cyst wall into the ducts to form a fistula and polypoid intra luminal extensions into bile ducts have been reported [2]. Grossly they are well demarcated, multilocular cystic lesions ranging from 5 to 29 cm. The inner surface of the cyst wall is smooth or trabeculated. Tiny papillary projections are a rare occurrence. The cyst may contain a clear, haemorrhagic or mucinous fluid. A solid area of greyish white tumour may represent an associated invasive carcinoma. Hence these areas should be extensively sampled for histological evaluation. The inner surface is lined by columnar, cuboidal to flattened epithelial cells with pale, eosinophilic to mucinous cytoplasm and basally located nuclei. In around 50% of the cases, the lining epithelium can be non- mucinous. The epithelial cells may undergo gastric or squamous metaplasia. The subepithelial stroma is hypercellular and spindly, resembling ovarian stroma. This stroma is diffusely (>75%) seen in half of the cases while it is focal in the rest [1]. The stroma can be luteinized, focally hyalinized, inflamed or undergo degenerative changes. The epithelial cells express CK7, CK8, CK 18, CK 19, EMA, CEA and MUC5AC. The stromal cells are positive for ER, PR and alpha-inhibin [1].

The majority of MCN- L exhibit low grade dysplasia while high grade dysplasia is rarely seen [1]. High grade dysplasia is characterized by considerable architectural atypia, nuclear pleomorphism and increased mitotic activity. Some cases may harbour invasive carcinoma specially in large tumours with intracystic papillary like projections. As invasive areas can be very focal, extensive sampling is recommended. About 20% of MCN-L, mostly in cases with high grade dysplasia are found to have KRAS mutation [1].

Many other non-neoplastic and neoplastic lesions can mimic MCN-L clinically and radiologically. There are reported cases of hydatic cysts and liver metastases mimicking MCN-L [9]. However, histopathological diagnosis MCN-L is undemanding and the presence of ovarian- like stroma is essential. ER, PR and alpha-inhibin immuno stains are helpful in demonstrating ovarian stroma when it is focal or in the presence of inflammation and degenerative change.

MCN-L has an excellent prognosis if complete resection is possible and incomplete excision can lead to recurrences. Invasive carcinoma, arising from the MCN-L have better prognosis compared to conventional intrahepatic cholangiocarcinoma [1].

All three patients of ours were women and presented with very non-specific symptoms. In case 1 and 3 both patients were middle aged females and the radiological impression was of hydatid cysts of the liver. In case 1 it was a large cyst obstructing the bowel and compressing the adjacent organs. Complete resection was performed and this large cyst was suspicious for Hydatid cysts intraoperatively. In case 3 though the imaging findings were highly suggestive of a hydatid cyst, recurrence of a benign cyst was also considered as the patient had a past history of laparoscopic excision of a simple liver cyst.

Hydatid cyst is caused by the larval form of *Echinococcus* species, generally affects middle aged people and present with pain in the right upper quadrant and jaundice. Eosinophilia and positive serology are key laboratory findings in hydatid cyst and they appear as a hypo-attenuating large unilocular or multilocular liver cyst on CT imaging. Approximately one half of them present with crescentic mural calcifications. Daughter cysts appear different from the mother cyst because they have lower attenuation than fluid and are round peripheral structures within the mother cyst [10]. Hydatid cyst can cause complications like bile duct compression, cholangitis, portal hypertension and rupture. It is treated with albendazole or mebendazole and the cyst has to be drained or surgically resected. Rarely liver transplantation may be needed in very large and complicated cysts [10].

There are several reports where MCN-Ls are misinterpreted as hydatid cyst in CT imaging [8, 10].

In case 2, the radiological impression was that of a benign cyst which did not have any communication with the dilated biliary system. Though this appearance is compatible with a MCN-L, patient had persistent fever which raised the suspicion of an infective etiology. Therefore, a hepatic abscess was considered as an alternative diagnosis. Initially cyst was aspirated under USS guidance, a drain was inserted and the patient treated with antibiotics. Surgical enucleation of the cyst was performed as symptoms persisted in spite of the treatment. This case highlights an unusual presentation of MCN-L mimicking a liver abscess clinically.

Though the MCN-L are rare benign cystic lesions of the liver, they can be associated with high grade dysplasia or invasive carcinoma and hence considered as premalignant lesions. Therefore, extensive sampling is of utmost importance to find out the presence of invasive carcinoma or high grade dysplasia. As highlighted in these three cases, MCN-L can present with nonspecific symptoms and imaging findings mimicking non-neoplastic cystic lesions of the liver. Therefore, awareness of this rare neoplasm is very important, as these lesions can harbour high grade dysplasia and invasive carcinoma.

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