

A Rare Association of Multiple Hepatic Lesions: Case Report and Literature Review

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Abstract

Biliary hamartomas or von Meyenburg complexes are uncommon benign biliary malformations, which are considered as part of the spectrum of fibrocystic diseases of the liver due to ductal plate malformation. Development of intrahepatic cholangiocarcinoma is well described in these complexes. However, only 10 cases of hepatocellular carcinoma arising in association with von Meyenburg complexes have been described in the English-language literature to date. In this paper, the authors report a peculiar case of hepatocellular carcinoma occurring on a background of von-Meyenburg's complexes and solitary unilocular bile duct cyst. It is not clear whether development of hepatocellular carcinomas is an epiphenomenon unrelated to the precursor lesion or biliary hamartomas may progress to liver cancers. Further studies are mandatory so as to elucidate and consolidate this very rare association.

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INTRODUCTION

Biliary hamartomas or von Meyenburg complexes (VMCs) are uncommon benign malformations of the liver, composed of disorganized bile ducts and ductules within a fibrocollagenous stroma [1]. Although VMCs are largely considered to be innocuous, their association with malignancy has been reported in literature. Malignant tumours that develop in the background of VMCs are usually cholangiocarcinomas. [2]. Rarely, hepatocellular carcinomas (HCCs) have been seen in association with bile duct hamartomas. To the best of our knowledge, only 10 cases of HCC arising in a background of VMCs have been described in the English-language literature to date (Table 1). In this paper, the authors report a peculiar case of several coexisting hepatic lesions including multiple VMCs, HCC and solitary unilocular bile duct cyst. Through this case and literature review, they discuss the pathogenesis of this exceedingly rare association.

CLINICAL HISTORY:

A 70-year-old male patient with a medical history of prostate adenoma, presented with right upper abdominal pain of approximately two months' duration. Upon admission, the patient was well and the vital

signs were stable. Physical examination revealed hepatomegaly. Serum laboratory work was remarkable for elevated alpha-fetoprotein (70.8 ng/ml). Liver transaminases were mildly elevated with a normal total bilirubin. Albumin and coagulation factors were within normal limits. Serology for hepatitis C and hepatitis B virus was negative. Chest X-ray was within normal limits. Abdominal ultrasonography revealed a hyperechoic heterogeneous lesion in the right lobe of the liver. Computed tomography scan demonstrated a solitary hypodense tumour measuring 12 cm in diameter that was located in the right lobe of the liver. Both kidneys were within normal limits and there was no evidence of renal cysts. The patient underwent right hepatectomy of the liver with cholecystectomy.

Macroscopically, the right hepatectomy specimen measured 17x14x6 cm and on sectioning of the surgical specimen, a yellowish lesion measuring about 11,5x9,5x7 cm with a granular cut surface was identified (Figure 1). There was also a subcapsular unilocular cyst measuring 1 cm in diameter and several whitish nodules measuring less than 1cm scattered throughout the liver. The surrounding liver parenchyma was unremarkable without cirrhotic changes. Resection margins were free from the tumour. Histologically, this

lesion was made of tumour cells simulating hepatocytes that were arranged in plates and pseudoglandular structures (Figure 2). The neoplastic cells had round nuclei with mild size variation and hyperchromasia as well as increased nucleocytoplasmic ratio. Focally, bile plugs were noticed in pseudoglandular structures. Tumour cells showed positive immunostaining with Hepar-1 (Figure 3).

In the adjacent liver parenchyma which was not cirrhotic, there were several irregular and branching ductular structures, some of which are dilated with inspissated bile, embedded in a sclerotic stroma

(Figures 4 and 5). There was no evidence of histologic transition between HCC and VMCs. A subcapsular solitary unilocular cyst lined by flattened epithelium was identified (Figure 6). The final pathological diagnosis was moderately differentiated hepatocellular carcinoma concomitant with von Meyenburg complexes and a unilocular bile duct cyst. Postoperative course was uneventful. During the one-year follow-up period, thoraco-abdominal CT scan demonstrated bilateral pulmonary lesions and a hyperdense lesion of the right adrenal gland suspicious of being metastatic.

Table 1: Reported cases of HCC associated with VMCs [2,4, 8,9,10,11]

Author/year	Age/sex	Size (cm)	Location	Associated lesions	VMCs	Histology	FU
Kim et al, 1999 [8]	74/M	2 and 5	NA	HBV	Multiple	HCC, CC with cirrhosis	Alive at 2.5 y
Jain et al, 2000	63/M	1.5	Left lobe	Alcohol	Multiple	HCC, CC	Died at 1 y
Blanc et al, 2000	61/M	2 and 4	Right lobe	Hemochromatosis	Multiple	Moderately differentiated HCC,CC	NA
Song et al, 2008	75/M	4.5	Right lobe	HCV	Multiple	HCC, CC with cirrhosis	Alive at 10 mo
Heinke et al, 2008	19/F	20.5	Right lobe	None	Multiple	Well-differentiated HCC	NA
Heinke et al, 2008	39/M	3.2	Right lobe	None	Multiple	Moderately differentiated HCC	NA
Jain et al, 2010	55/M	3.5	Right lobe	HCV	Multiple	Well to Moderately differentiated HCC	Well after 4 y
	59/M	3, 2.2 and 2	Right lobe	HCV	Multiple	Moderately differentiated HCC	Well after 3 y
	60/M	3.5	Right lobe	Alcohol	Multiple	Moderately differentiated HCC	Well after 3 y
	56/M	1	Right lobe	NAFLD	Multiple	Moderately differentiated HCC	Well after 4 y
Limaïem et al 2012	73/M	11.5	Right lobe	Solitary unilocular bile duct cyst.	Multiple	Moderately differentiated HCC Solitary unilocular bile duct cyst	Alive at 1 y

CC: Cholangiocarcinoma; **F:** Female; **FU:** Follow-up; **HBV:** Hepatitis B virus; **HCV:** Hepatitis C virus; **M:** Male; **mo:** month; **NA:** Not available; **NAFLD:** Non-alcoholic fatty liver disease; **VMCs:** von Meyenburg complexes; **y:** year.



Figure 1. Macroscopic findings: On sectioning of the right hepatectomy specimen, a yellowish lesion measuring about 11.5x9.5x7 cm with a granular cut surface was identified.

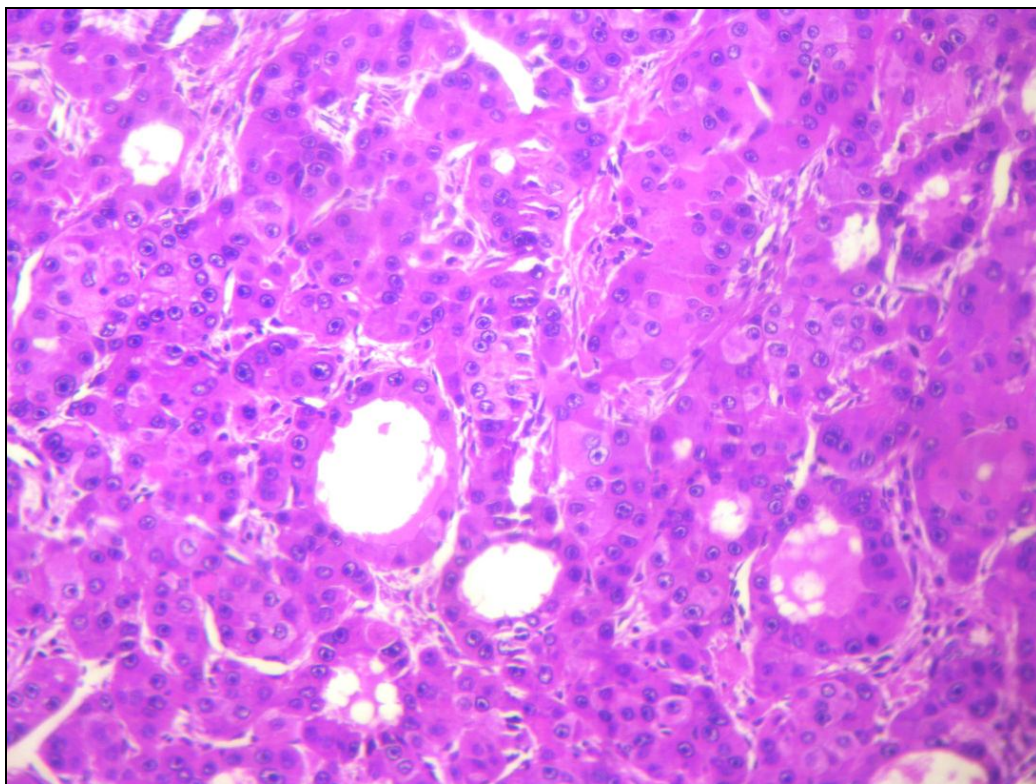


Figure 2. Moderately differentiated hepatocellular carcinoma. The neoplastic cells were arranged in plates and pseudoglandular structures (H & E, original magnification x 10).

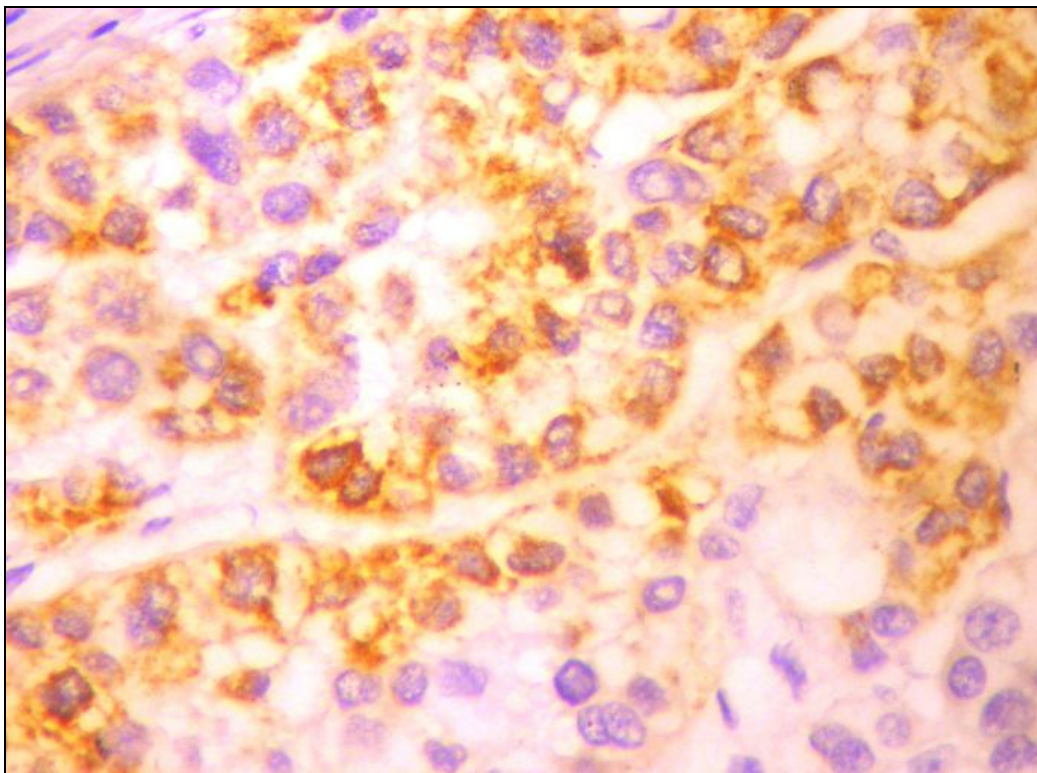


Figure 3: Tumour cells showed positive immunostaining for Hepar-1 (immunohistochemistry, original magnification x 40).

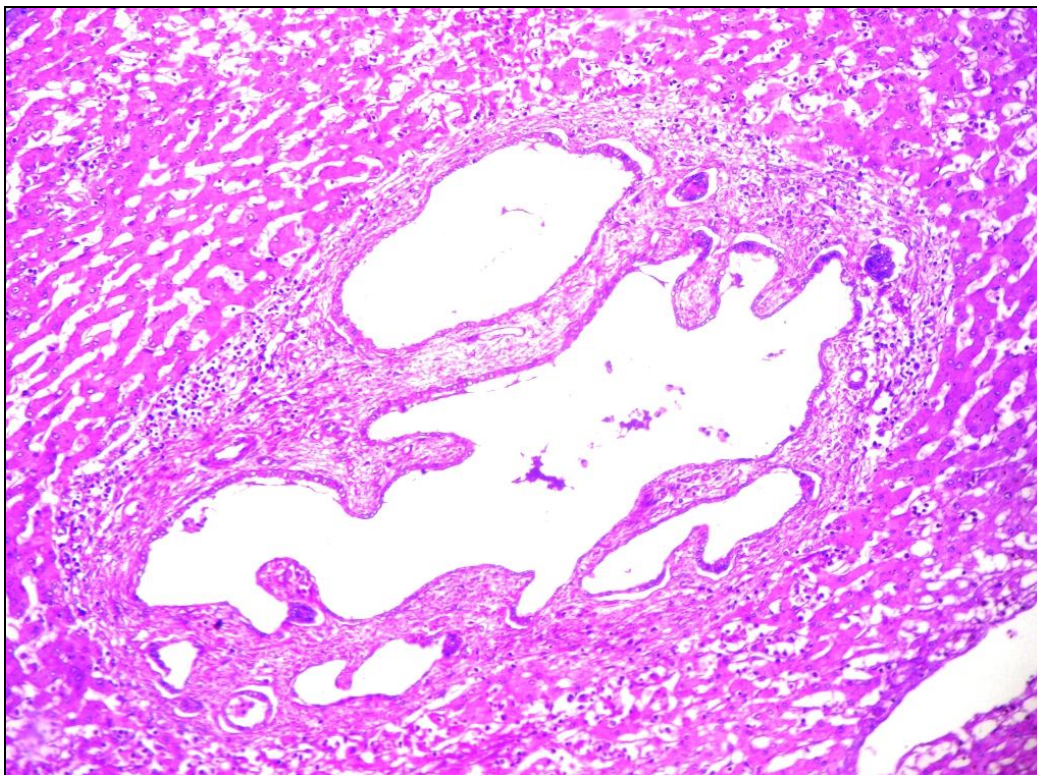


Figure 4: Von Meyenburg complex: small irregular dilated bile ducts embedded within a fibrous stroma (H&E, original magnification x 20).

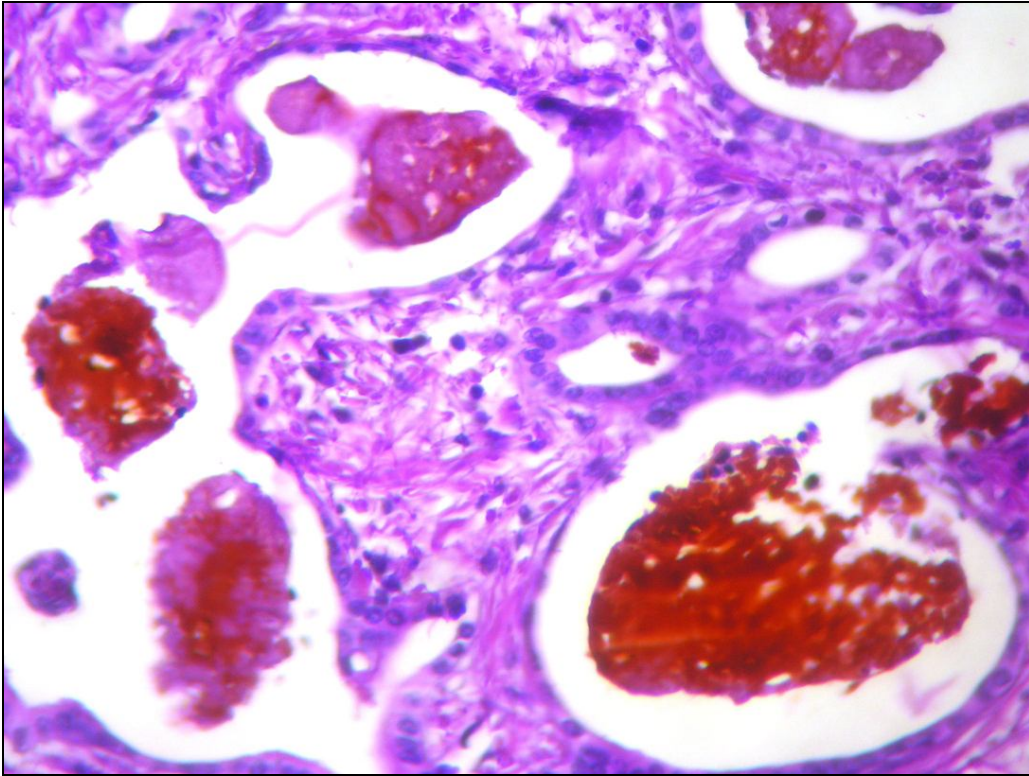


Figure 5: Some ductular structures contain inspissated bile (H & E, original magnification x 40).

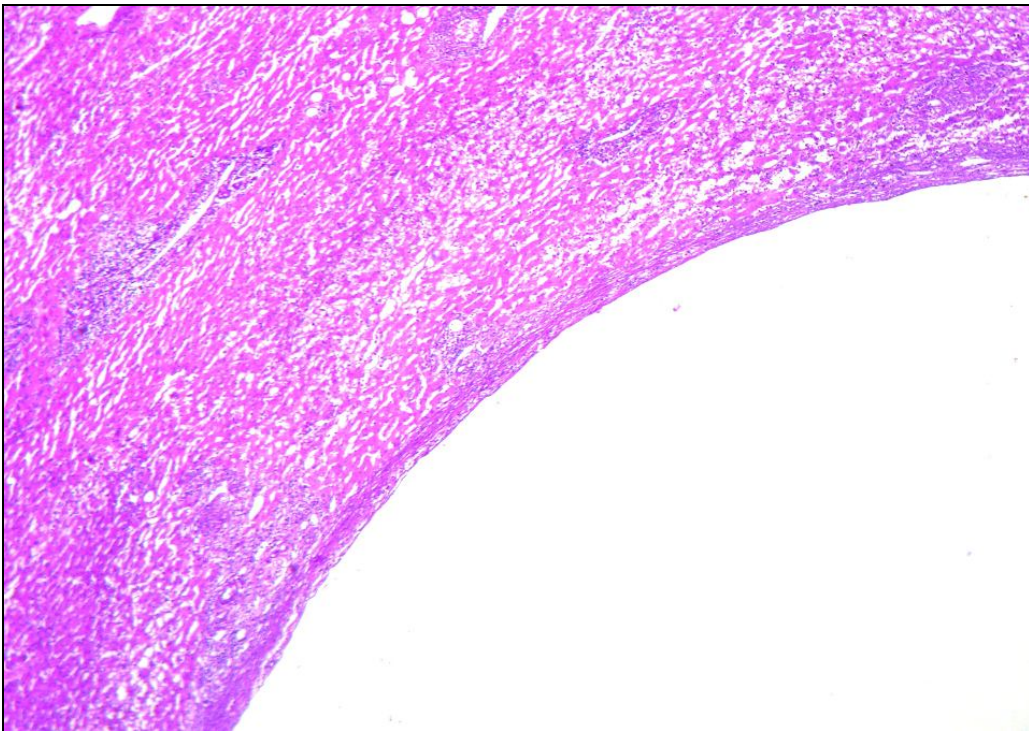


Figure 6: Solitary unilocular bile duct cyst (H & E, original magnification x 4) lined by flattened epithelium with bland cytological features.

DISCUSSION

Prevalence of VMCs is age-dependent and varies from 1% in children to 5.6% in adults in a large autopsy series [3]. Macroscopically, grayish-whitish nodules measuring less than 1 cm in diameter are seen scattered throughout the liver [4, 5]. Microscopically, VMCs consist of dilated intrahepatic bile ducts with flattened or cubic bile duct epithelium, embedded in fibrovascular stroma. Neoplastic progression of VMCs is clearly described in the literature. These have been postulated to be the origin of cholangiocarcinoma, although HCCs, adenocarcinoid of the liver, as well as neuroendocrine carcinoma of the pancreas in association with bile duct hamartomas have been reported [6-10]. There are now 18 case reports and series that link cholangiocarcinoma to a background of multiple VMCs [11]. However, association with HCC is rarely described. Only 10 cases of HCC arising in association with VMCs have been described in the English-language literature to date (Table 1). There was a male predominance in these cases with a male to female ratio of 9:1. Our case was a male patient. The association of HCC and VMCs has been diagnosed at a wide range of ages from 19 to 75 years, with a mean age at diagnosis of 56.1 years. The tumour size ranged from 1 to 20.5 cm. In all cases except two, (including one case in which the exact site of the lesions was not available), HCC and VMCs involved the right hepatic lobe as it was the case in our patient. In reviewing the literature, it is apparent that all cases except two were associated with either viral hepatitis or other etiologic factors such as alcohol and hemochromatosis [7]. It may be argued that HCC in these patients might have developed because of underlying precancerous etiologic factor, and VMCs are just incidental. The recently reported 2 cases as well as our patient did not have any causative agent and there was no evidence of histologic transition between HCC and VMCs and no background of cirrhosis. Now, it is a matter of debate whether VMCs are truly precursors of HCC or these are just an incidental finding. It needs to be explored in the future with further studies.

CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

REFERENCES

1. Ohta W, Ushio H. Histological reconstruction of a von Meyenburg's complex on the liver surface. *Endoscopy* 1984; 16: 71-4.
2. Jain D, Nayak NC, Saigal S. Hepatocellular carcinoma arising in association with von-Meyenburg's complexes: an incidental finding or precursor lesions? A clinicopathologic study of 4 cases. *Ann Diag Pathol* 2010; 14: 317-320.
3. Redston MS, Wanless IR. The hepatic von Meyenburg complex: prevalence and association with hepatic and renal cysts among 2843 autopsies. *Mod Pathol* 1996; 9: 233-7.
4. van Baardewijk LJ, Idenburg FJ, Clahsen PC, Mollers MJ. [Von Meyenburg complexes in the liver: not metastases]. *Ned Tijdschr Geneesk* 2010; 154: A1674.
5. Singhal A, Kanagala R, Wright HI, Kohli V. Multiple bile duct hamartomas mimicking diffuse hepatic metastasis: GI image. *J Gastrointest Surg* 2010; 14: 1629-1631.
6. Rocken C, Pross M, Brucks U, Ridwelski K, Roessner A. Cholangiocarcinoma occurring in a liver with multiple bile duct hamartomas (von Meyenburg complexes). *Arch Pathol Lab Med* 2000; 124: 1704-1706.
7. Heinke T, Pellacani L, de Oliveira Costa H, Fuziy R, Franco M. Hepatocellular carcinoma in association with bile duct hamartomas: Report on 2 cases and review of the literature. *Ann Diag Pathol* 2008; 12: 208-211.
8. Papadogiannakis N, Gad A, Sjostedt S, Tour R, Thorne A, Seensalu R. Adenocarcinoid of the liver arising within an area of hamartoma with predominant bile duct component. *J Clin Gastroenterol* 1996; 23: 145-151.
9. Bruegel M, Rummeny EJ, Gaa J. Image of the month. Multiple biliary hamartomas as an incidental finding in a patient with neuroendocrine carcinoma of the pancreas. *Gastroenterology* 2005; 128: 259.
10. Xu AM, Xian ZH, Zhang SH, Chen XF. Intrahepatic cholangiocarcinoma arising in multiple bile duct hamartomas: Report of two cases and review of the literature. *Eur J Gastroenterol Hepatol* 2009; 21: 580-584.
11. Song JS, Lee YJ, Kim KW, Huh J, Jang SJ, Yu E. Cholangiocarcinoma arising in von Meyenburg complexes: Report of four cases. *Pathol Int* 2008; 58: 503-512.

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