Letters to the Editor

Hepatic von Meyenburg complex: a trigger of severe portal hypertension

DOI: 10.1111/j.1478-3231.2008.01903.x

To the Editor:

Multiple bile duct hamartoma [von Meyenburg complex (VMC)] is a benign liver malformation that includes biliary cystic lesions with congenital hepatic fibrosis causing ductal plate malformations (1–7). It is generally asymptomatic and tends to be identified either at autopsy or during histological examinations (1). We report a very rare case of severe portal hypertension caused by VMC diagnosed by magnetic resonance cholangiopancreatography (MRCP) and histopathology.

Case report

An 88-year-old female was hospitalized with hypoxic orthopnoea, abdominal fullness and leg oedema. Arterial blood gas analysis revealed 88% oxygen saturation. A chest X-ray revealed a widespread right pleural effusion. Past history was unremarkable. Laboratory tests showed normal liver chemistry except for mild elevations of alkaline phosphatase and γ-glutamyl transpeptidase. Antinuclear antibody and antimitochondrial-2 antibody were negative. Serology for hepatitis B virus, hepatitis C virus and HIV were negative. Tumour markers showed: α-fetoprotein, 2.4 ng/ml (0–20 ng/ml); carbohydrate antigen 19-9, 56.6 U/ml (0–37 U/ml); and carcinoembryonic antigen, 9.0 ng/ml (0–5.0 ng/ml). Endoscopy revealed large oesophageal varices in the mid-oesophagus. Abdominal computed tomography revealed multiple cystic images in the whole liver and both kidneys, some ascites and mild splenomegaly (Fig. 1A). The intrahepatic and extrahepatic bile ducts were not dilated. No evidence of cirrhosis, heart failure or renal dysfunction was observed. Especially, brain natriuretic peptide, human atrial natriuretic peptide and cardiac ejection fraction were normal. Furthermore, no malignant lesion or vessel thrombus was seen. MRCP T2-weighted sequences showed multiple small hyperintense lesions < 1 cm diameter and normal intrahepatic and extrahepatic bile ducts (Fig. 1B). Inferior vena cavaography and hepatic venography showed no angiostenosis or thrombus in the major blood vessels. Hepatic venous pressure gradient was 14 mmHg. Therefore, VMC or multiple liver cysts were strongly suspected. A liver biopsy revealed diffuse bile duct hamartomas arising in the portal region. Haematoxylin–eosin staining showed bile duct microhamartomas consisting of circumscribed fibrous areas containing many irregularly dilated bile duct structures and only a few narrowed vessels in the portal region (Fig. 1C). A narrowing of the portal vein might have occurred. Therefore, a diagnosis of VMC with portal hypertension was confirmed. We believe that the displacement of the portal vein triggered portal hypertension. Furosemide therapy rapidly improved the patient’s condition. One year later, the patient’s condition has remained stable on diuretic treatment. However, a follow-up endoscopy showed mid-oesophageal varices unchanged from the previous.

Discussion

This is the first report of a VMC patient with severe symptoms due to portal hypertension. Magnetic resonance imaging is generally useful for the diagnosis of VMC (2, 3). This condition is incidentally detected in from 0.5 to 5.6% of autopsies (1) and is generally asymptomatic. In contrast, our patient presented with severe portal hypertension. It was thought that portal hypertension was due to displacement of the portal vein by the presence of VMC. As a result, severe pleural effusion, ascites and oesophageal varices developed. Previous reports described VMC cases with epigastric pain (4, 5). However, those were not pure VMC cases.

In contrast, there are only a few published VMC reports supporting the current findings (5–7). Brancatelli et al. (7) described portal hypertension that occurred from fibropolycystic liver disease. Their observations are helpful for our clinical perspective. Despite furosemide treatment, oesophageal varices remained unchanged, indicating the presence of persisting portal hypertension in the setting of VMC.

In conclusion, VMC can trigger severe symptoms requiring urgent and continuous treatment. The present case therefore fell outside of the traditional diagnostic criteria and management guidelines for VMC. These findings suggest that the concept of VMC may require modification because it does not apply to all cases. In addition, the clinicopathological and
radiological features of VMC, as well as the pathogenesis need further study and clarification.

Shuhei Yoshida1,2, Kazutaka Kurokohchi2, Takuya Ueno3, Morihiko Yoshino1, Masahiko Shimada1 and Tsutomu Masaki2

1 Department of Gastroenterology, Internal Medicine, TMG Asakadai Central General Hospital, Saitama, Japan
2 Division of Gastroenterology and Hepatology, Internal Medicine, Kagawa University School of Medicine, Kagawa, Japan
3 Critical Care Medicine, Hachioji Medical Center, Tokyo Medical University, Tokyo, Japan

References

1. 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.
2. Zheng RQ, Zhang B, Kudo M, Onda H, Inoue T. Imaging findings of biliary hamartomas. World J Gastroenterol 2005; 11: 6354–9.
3. Ye BB, Hu B, Wang L, et al. Mesenchymal hamartoma of liver: magnetic resonance imaging and histopathologic correlation. World J Gastroenterol 2005; 11: 5807–10.
4. Röcken 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: 1704–6.
5. Karahan OI, Kahriman G, Soyuer I, Ok E. Hepatic von Meyenburg complex simulating biliary cystadenocarcinoma. Clin Imaging 2007; 31: 50–3.
6. Jain D, Sarode VR, Abdul-Karim FW, et al. Evidence for the neoplastic transformation of Von-Meyenburg complexes. Am J Surg Pathol 2000; 24: 1131–9.
7. Brancatelli G, Federle MP, Vilgrain V, et al. Fibropolycystic liver disease: CT and MR imaging findings. Radiographics 2005; 25: 659–70.

Fig. 1. (A) Axial computed tomography 42 × 42 mm (300 × 300 DPI). (B) T2-weighted magnetic resonance cholangiogram shows numerous high-signal-intensity liver lesions and no communication between these and the normal-sized intra- and extrahepatic biliary system. 42 × 42 mm (300 × 300 DPI). (C) Photomicrograph (original magnification, × 40; H&E stain) shows a portal region (arrowheads) containing several cystic spaces, which are interspersed with fibrous stroma and lined by a layer of biliary epithelium (arrows). 84 × 63 mm (300 × 300 DPI).
To the Editor:

We thank Paulette Bioulac-Sage and colleagues for their interesting comments concerning our paper on liver adenomatosis (1, 2). We are aware of the important work this group has published with regard to the subclassification of hepatocellular adenomas (HCA) according to mutations in HNF1α or β-catenin and to inflammatory changes. In view of their findings, we agree that the term adenomatosis to indicate patients with >10 HCA does not necessarily imply a specific entity in terms of aetiology and management. To ascertain HCA and the specific subtypes, however, remains a crucial point and may give rise to a diagnostic dilemma. Accurate diagnosis depends on a representative tissue sample of the lesion for immunohistochemical or molecular pathological analysis. In most cases, we rely on percutaneous needle biopsies of the tumour, which are prone to sampling errors or are of such quality that even experienced pathologists find it difficult to make the right diagnosis or distinguish HCA from a highly differentiated hepatocellular carcinoma (HCC). Until we have better (imaging) methods to diagnose HCA and to differentiate HCA from other lesions such as focal nodular hyperplasia and HCC, establishing the correct diagnosis and subtype classification remains a challenge. The use of magnetic resonance imaging holds great promise in this regard (3).

In patients with adenomatosis (HCA >10), we advise to excise lesions >5 cm as is our national policy in the management of solitary HCA. The advantage of surgery is, in addition, the opportunity to acquire ample lesional tissue to establish the diagnosis of HCA and to further analyse the subtypes. As smaller, superficial lesions are readily excised, sampling of additional lesions during surgery is also possible. Because liver resections for benign tumours are nowadays performed with a low risk, we find more patients referred for resection, especially those patients with upper abdominal complaints related to the tumour (4). It should be emphasized at this point that non-suspicious lesions can be surgically enucleated instead of undertaking (non)anatomical liver resections with a sufficient safety margin as one would do with malignant lesions. Hence, the surgical trauma is less and assuming that adenomatous tissue does not contribute to the overall liver function, the risk of postresectional liver failure is negligible.

It would be of great benefit if we could identify those patients with a high risk of developing HCC out of HCA on the basis of assessment of β-catenin mutations. The question is whether in patients with multiple HCA and a proven transformation to HCC, liver transplantation is not an option, similar to patients with limited HCC in cirrhosis. As yet, we would monitor patients after resection of a malignant HCA/HCC and aggressively resect any lesion increasing in size or changing in appearance. The relative scarcity of the condition and the lack of a large series reported in literature hamper insight in the natural history of multiple HCA.

There is indeed a correlation between the size of HCA and the risk of bleeding. Intra-abdominal rupture of a bleeding HCA is a life-threatening complication of large HCA. To which extent the risk of bleeding increases with size is uncertain as in patients who have bled, it is difficult to define the size of the original lesion. The use of selective arterial embolization has proven to be effective in arresting major bleeding and has contributed to a more conservative approach in the management of patients presenting with a bleed from HCA (5). In patients who did undergo delayed resection after bleeding of HCA, the finding of viable (remnants of) adenomatous tissue on microscopical examination of the specimen was disappointing in our experience (6).

The spectrum of single HCA to multiple HCA is complex and is intriguing. Its association with liver steatosis or steatohepatitis and the metabolic syndrome are unresolved and require further investigation in the light of what seems to be an increasing incidence of HCA in the western European population. We fully support Paulette Bioulac-Sage and colleagues in their call for a multicentric collaboration and long-term studies.

Thomas M. van Gulik, Jacomina W. van den Esschert, Deha Erdogan and Reeta Vetelainen

Department of Surgery, Academic Medical Center, Amsterdam, the Netherlands

References

1. Bioulac-Sage P, Laumonier H, Sa Cunha A, Balabaud C. Hepatocellular adenomas. Liver Int 2009; 29: 142 (published online 1 October 2008).
2. Vetelainen R, Erdogan D, de Graaf W, et al. Liver adenomatosis: re-evaluation of aetiology and management. Liver Int 2008; 28: 499–508.
3. Laumonier H, Bioulac-Sage P, Laurent C, et al. Hepatocellular adenomas: MRI features as a function of molecular pathological classification. Hepatology 2008; 48: 808–18.
4. Erdogan D, van Delden OM, Busch ORC, Gouma DJ, van Gulik TM. Morbidity and mortality after liver resection for benign and malignant hepatobiliary lesions. Liver Int 2009; 29: 175–80. Epub 2008 Jun 18.
5. Erdogan D, van Delden OM, Busch ORC, Gouma DJ, van Gulik TM. Selective transcatheter arterial embolization for treatment of bleeding complications or reduction of tumor mass of hepatocellular adenomas. Cardiovasc Intervent Radiol 2007; 30: 1252–8.
6. Erdogan D, Busch ORC, van Delden OM, et al. Management of spontaneous haemorrhage and rupture of hepatocellular adenomas. A single centre experience. Liver Int 2006; 26: 433–8.