CASE REPORT

Exophytic cystic liver lesion: an unusual presentation of a hepatocellular carcinoma in a young female

Thomas Gardiner,¹ David Nasralla,² Eve Fryer,³ Helen Bungay,⁴ Michael Silva²

¹Medical Sciences Division, University of Oxford, Oxford, UK
²Hepatobiliary Surgery, Churchill Hospital, Oxford, UK

³Cellular Pathology, John Radcliffe Hospital, Oxford, UK

⁴Department of Radiology, John Radcliffe Hospital, Oxford, UK

Correspondence to

Thomas Gardiner,
 thomas.gardiner@worc.ox.ac.uk

Accepted 7 November 2017

SUMMARY

Hepatocellular carcinoma (HCC) is one of the most common malignant primary liver tumours. However, primary hepatic carcinomas are rare in young adults, accounting for approximately 1% of tumours in people below the age of 20. Hepatitis B virus (HBV) and hepatitis C virus (HCV) infection are the two most important aetiological agents of HCC. The average age at onset of HBV-related HCC (~50 years old) is 10 years younger than that of HCV-related HCC (61–64 years). Evidence for an association between the oral contraceptive pill (OCP) and development of HCC remains inconclusive. Here, we describe a case of a 28-year-old woman with normal background liver, who presented with a large palpable abdominal mass due to a bilobar, exophytic, cystic lesion arising from the right lobe of the liver, later diagnosed as HCC on histological analysis. We highlight the need for considering HCC even in the unusual setting of a cystic, exophytic lesion.

BACKGROUND

Hepatocellular carcinoma (HCC) accounts for approximately 75% of all primary hepatic cancers.¹ It is the fifth most common malignancy worldwide and is the third largest contributor to cancer mortality, with global incidence on the rise.¹ HCC is most commonly associated with alcohol-induced cirrhosis and infection with the hepatitis B virus (HBV) and hepatitis C virus (HCV).² It is primarily a cancer of the elderly, rarely occurring in the first four decades of life (except in HBV-endemic populations) and occurs more frequently in men than women.² It is usually diagnosed following radiological imaging, although in recent years we have begun to understand that HCC can present atypically, mimicking other benign or malignant

Figure 2 Intraoperative photograph of the large, bilobar solid-cystic lesion which, along with segments V and VI of the liver, was subsequently resected.

pathologies. We present the case of a 28-year-old woman with a rare presentation of an exophytic cystic HCC but without a history of established risk factors for development of this malignancy.

CASE PRESENTATION

A 28-year-old woman with no medical history presented with early satiety and a painless mass in the right side of her abdomen. The patient's medical, family and social history were unremarkable and her only medication was the oral contraceptive pill (OCP), which she had taken regularly for the past 10 years. She had a body mass index (BMI) of 20, did not smoke and consumed little alcohol.

INVESTIGATIONS

Blood test results were unremarkable: full blood count, liver biochemistry and alpha fetoprotein (AFP) levels were all normal.

A CT scan showed two large solid-cystic lesions with discrete but thin walls (**figure 1**). One was pedunculated and attached to segments 5 and 6 of the liver, measuring 96×66×115 mm. The other extended to the right lower quadrant, measuring 76×117×106 mm and impinging on and compressing the small bowel and central retroperitoneal structures. The liver appeared smooth with no biliary dilatation, and the remaining chest, abdominal and pelvic organs appeared normal.

DIFFERENTIAL DIAGNOSIS

Hydatid disease was ruled out following negative serology, and of the remaining differential

Figure 1 Abdominal CT scans show two large lesions emerging from the right lobe of the liver (A) which are cystic/solid in nature (B). The rest of the liver and abdominal viscera appear normal.

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To cite: Gardiner T, Nasralla D, Fryer E, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-222076

Figure 3 Representative sections from the tumour at the point closest to the hepatic resection margin. (A) H&E staining illustrates some of the aforementioned microscopic irregularities of the nodular tissue; (B) reduced and irregular reticulin staining shows loss of the normal cell plate architecture and (C) diffuse positive immunostaining for glypican-3. Together, these histological investigations favour well-differentiated hepatocellular carcinoma over adenoma.

diagnoses, an exophytic benign cystic lesion was considered the most likely. HCC was not considered in the preoperation differential diagnosis due to the appearance of the tumour and the absence of risk factors.

TREATMENT

Segments V and VI liver resection was planned on the basis that it would be both diagnostic and potentially therapeutic. At surgery, a bilobar solid-cystic lesion originating from segments V and VI and extending to the pelvic brim was resected (figure 2).

OUTCOME AND FOLLOW-UP

The patient made an unremarkable recovery and was discharged after 6 days. An MRI scan 1 month postsurgery was performed as a baseline for follow-up; there was no indication of recurrence or abnormality.

Histological examination of the resected specimen demonstrated a multinodular, solid appearance of the lesions with areas of cystic degeneration and haemorrhage. Sections from the two tumour masses showed sheets of hepatocyte-like cells, many of which showed ballooning, Mallory's hyaline formation and megamitochondria (figure 3). There was no lymphovascular invasion. They were immunonegative for AFP. The small amount of background liver present was normal, with no evidence of cirrhosis. Intact beta-catenin staining indicated that this carcinoma was not an evolution from previous adenoma, consistent with the absence of multicystic presentation in this patient. There were no features to suggest fibrolamellar carcinoma. The overall features were consistent with a well-differentiated HCC.

Although this was an unexpected finding, several factors indicate a favourable prognosis for this patient: complete resection of the lesions, no evidence of metastasis or lymphatic and venous invasion, the well-differentiated nature of the lesions and a clear postsurgical baseline MRI. The patient remains well approaching 1 year postoperation, with no evidence of local or distant disease.

This patient had no risk factors for HCC. However, cessation of the OCP has been advised based on the known association between the OCP and formation of liver adenomas, which harbour a small risk of transformation into HCCs. However, given the histological findings, this change is unlikely to have played a part in the pathogenesis of this patient's HCC.

DISCUSSION

The diagnosis of HCC is typically made following ultrasound imaging and investigation of AFP levels, with further

Patient's perspective

- ▶ As far as I am concerned, the reason why I developed this hepatocellular carcinoma (HCC) is a mystery. I never eat precooked or processed meals, do drugs or smoke. I knew I drank a little too much alcohol (approximately 17 units/week before the operation).
- ▶ Looking back, learning that it was an HCC after the analysis may have been the best scenario, as I would have panicked if I knew before the operation. Ignorance is bliss sometimes; I am glad it could be removed.
- ▶ I am back doing sport at least four times a week, although I like to do it every day if I can. I did not gain back the 4 kg I lost during my time in hospital and am happy with that. The muscles under the scar complain more than the other side when I do abs, which I expect comes from the fact that they were cut.
- ▶ I reconsidered my lifestyle and diet, though without finding satisfactory answers. My friends and family all said it is because I work too hard and am too stressed, but I am not sure what I can do about that during the end of my PhD, or ever.
- ▶ I looked into nutrition and decided to try and buy organic food whenever possible. It may not do anything, but at least it cannot hurt and reduces the amount of chemicals in my food. I drink less, trying to never go above the recommended 14 units/week.

Learning points

- The finding of such a large exophytic lesion in a young female that was hepatocellular carcinoma (HCC) is rare but significant.
- It indicates that hepatic cystic masses should raise the possibility of HCC as part of a differential diagnosis, even if there are neither systemic or peripheral signs of malignancy (tumour markers, AFP, etc) nor the presence of clear risk factors for HCC development.

characterisation of the tumour using CT or MRI scans. Cystic HCC on a background of non-cirrhotic liver—as with our patient—is a very rare presentation. Although cystic degeneration of large HCCs have been described, to the best of our knowledge, this is the first description of such a large cystic and exophytic lesion.³

Various factors contributed to the initial diagnosis of a benign cystic mass in our patient: no apparent risk factors for malignancy or parasitic disease, the radiological features of the tumour and a lack of positive laboratory investigations (AFP levels).

Understanding the possible risk factors and mechanisms of hepatocarcinogenesis in these atypical presentations of HCC represents a significant challenge. A retrospective analysis by Bralet *et al*⁴ helped define the epidemiology of non-cirrhotic HCC cases, the minority of HCC.⁵ Patients with non-cirrhotic HCC were younger than those with cirrhosis (43 ± 9 vs 57 ± 13) and, conducive with well-established male dominance in HCC cases,¹ the male to female ratio in patients with cirrhosis was 5:1. However, this ratio fell to 1.96:1 in patients without cirrhosis. These findings show that in the non-cirrhotic HCC subgroup, patients are more likely to be female and young than in the cirrhotic HCC subgroup. Serological and histological analysis of each group showed that AFP is more likely to be normal, and tumours larger, in patients without cirrhosis compared with patients with cirrhosis.

The association between the OCP and benign hepatocellular adenoma has been well established for several decades,⁶ although both gross and histological features of this patient's lesion were inconsistent with HCC evolved from hepatocellular adenoma. Evidence for an association between HCC and the OCP remains inconclusive.⁷ The Liver Cancer Pooling Project showed no significant association between OCP use and duration of OCP use and HCC incidence (HR=1.12, 95% CI 0.82 to 1.55).⁸ However, the majority of women in this study were over 50 years old; further analysis of the association between OCP use and HCC incidence in younger women is needed.

Contributors TG and DN contributed equally to research and writing the paper. EF reviewed the manuscript and advised from histopathology view point. HB reviewed the manuscript and advised from radiology view point. MS did the overall supervision and reviewed the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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