CASE REPORT

Spontaneous regression of a biopsy confirmed hepatocellular carcinoma

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SUMMARY

A 74-year-old woman was diagnosed with histologically proven multiple bilobar hepatocellular carcinomas (HCC) in 2012. The lesions were inoperable and a repeat CT scan prior to starting chemotherapy revealed spontaneous regression of these lesions. Subsequent repeat scans have revealed continued regression of these lesions despite no active treatment. The case is presented with a literature review and discussion summarising the possible aetiologies of this phenomenon.

BACKGROUND

Spontaneously regressing hepatocellular carcinomas (HCC) are extremely rare and this case was the first we have seen in a professorial liver unit where approximately 200 patients with liver lesions are discussed in multidisciplinary meetings every year. There are several important messages to be learnt from this case.

CASE PRESENTATION

A 74-year-old woman presented to her general practitioner in June 2012 with a vague back pain and was found to have microscopic haematuria. A renal ultrasound scan and subsequent abdominal CT scan in July 2012 demonstrated at least 20 hypervascular lesions in her liver with the largest measuring 7 cm×9 cm, located in the inferior left lobe. There was no extended history of alcohol misuse and she had history of hypertension, cholecystectomy and tubal ligation. Blood test showed deranged liver enzymes with normal alkaline phosphatase and bilirubin. Her tumour markers (α -fetoprotein (AFP), CA 19.9 and CA 125) were negative as were viral hepatitis serologies. The lesions were deemed inoperable and after discussion in our hepatobiliary multidisciplinary meeting, biopsy of one of these liver lesions was organised and it confirmed the diagnosis of a well-differentiated hepatocellular carcinoma.

She was reviewed by the oncologist in September 2012, who arranged a restaging CT as her liver function tests had returned to normal and her past CT was over 2 months old. This scan, in September 2012, showed a dramatic reduction in the number and size of the lesions. An independent pathologist, who was blinded to the initial result, reviewed the biopsy results and the diagnosis of well-differentiated HCC was reconfirmed. She continues to remain asymptomatic and serial CT scans (April and December 2013) have continued to show

either regression or resolution of all lesions (figure 1—arterial phase, figure 2—venous phase).

INVESTIGATIONS

Tumour markers, liver function tests and CT scans as above.

DIFFERENTIAL DIAGNOSIS

Benign adenoma and focal nodular hyperplasia can have similar histological appearances to well-differentiated HCC. However immunostains help distinguish benign from malignant lesions.

TREATMENT

Watch and wait with serial CT scans.

OUTCOME AND FOLLOW-UP

Latest scans show continued regression of lesions.

DISCUSSION

Globally, liver cancer is the second leading cause of cancer-related death in men and sixth in women with poor 5 year survival if inoperable and 50% if operable. Over 1300 new cases per year are diagnosed in Australia, which account for 1.1% of all new cancers.^{1–3} Partial or spontaneous regression of HCC has been described before; however the majority of cases are described in the East and on the background of liver disease and/or raised AFP.^{4–13} Although rare, this phenomenon draws attention and provides hope to clinicians to find cure of HCC by understanding the underlying mechanism of spontaneous regression. Although no definitive mechanism has been elucidated, the two most popular theories are related to induction of ischaemia and the body's immunological response.¹⁴

A systemic review estimated the rate of partial objective regression to be around 0.5%⁴ and a literature review conducted by Huz *et al*¹⁵ in 2012 suggested that at least one-third of the cases with spontaneously regressing HCC were related to the systemic immune response. T-cell activation by antigen-presenting dendritic cells allows the body to mount a specific and long-lasting antitumour response as demonstrated in animal models of HCC that received vaccination of AFP as an antigen.¹⁶ Other potential antigens in HCC include the melanoma antigen gene family and glypican-3.¹⁶ The same theory is used to explain regressions after rupture of the tumour or seeding of malignant cells via biopsy or surgery.¹⁷ Elevation of cytokines IL-18¹⁸ and TNF α ^{19 20} in cases of spontaneously regressing HCC suggest that a systemic immune response may be responsible for this rare phenomenon.

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Figure 1 Serial arterial scans.

Necrosis resulting from ischaemia or tumour hypoxia via variable mechanisms is a potential cause for regression of HCCs. In Huz's report, 28% of spontaneous regressions of HCC were as

a result of tumour ischaemia.¹⁵ Disruption of blood supply, either due to the local effect of vascular injury,²¹ arterioportal shunt²² or portal vein thrombosis²³ or due to the systemic

Figure 2 Serial venous scans.

hypoperfusion from bleeding,²⁴ can lead to necrosis and regression of hepatocellular carcinoma. This mechanism is exploited artificially by hepatic artery embolisation and antiangiogenic agents such as sorafenib, which are well-known therapeutic manoeuvres that induce tumour hypoxia and subsequent regression.¹⁵

Learning points

- This case adds to the world literature on spontaneously regressing hepatocellular carcinomas (HCC).
- Unlike the vast majority of cases, this HCC developed on a background of a normal liver and α -fetoprotein.
- It is imperative to restage the patient if the presenting symptoms subside or the patient's blood tests improve (as it was the case here).
- A rebiopsy is not necessary, however the original pathology should always be reviewed if there is any doubt regarding the diagnosis.

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Competing interests None.

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