CASE REPORT

Ruptured hepatocellular carcinoma disguising as heterotopic pregnancy

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SUMMARY

The incidence of hepatocellular carcinoma (HCC) in pregnancy is rare but is typically aggressive, with a 1-year survival rate of 23%. One of the complications of HCC is spontaneous rupture, resulting in haemoperitoneum. A 36-year-old pregnant Chinese immigrant who was positive for hepatitis B virus and in her first trimester presented to the emergency department of Wyong Hospital, Hamlyn Terrace, New South Wales, Australia, with severe epigastric and right upper quadrant pain and haemodynamic instability. Spontaneous rupture of a heterotopic pregnancy was initially suspected. However, histopathological staining of the lesions excised during surgery revealed HCC. To our knowledge, this is the first case of spontaneous rupture of HCC with haemoperitoneum during pregnancy in Australia. As developed countries receive global migrants, similar cases may be seen in the future. Epidemiological studies suggest that immigrants from China and Vietnam have the highest incidence of chronic hepatitis B virus carrier status.

CASE PRESENTATION

A 36-year-old woman of Chinese ethnicity in her sixth week of gestation presented with severe epigastric and right shoulder tip pain, associated with vomiting. Her obstetric history was significant for being a gravida 5, para 5 with a twin pregnancy. Her only risk factor for hepatocellular carcinoma (HCC) was known hepatitis B virus (HBV) positivity. She denied a history of peptic ulcer disease, pancreatitis or biliary colic.

On arrival at the emergency department of Wyong Hospital, she was triaged as category 1 according to the Australasian Triage Scale¹ and was immediately transferred to the resuscitation room. On examination, she looked unwell, pale and clammy. Her airway was patent, with a respiratory rate of 22/min, normal breath sounds and an oxygen saturation of 97% on room air. She was haemodynamically unstable with a blood pressure of 65/46 mm Hg. Her abdomen was full, with severe tenderness in the epigastric and right upper quadrant regions. Her Glasgow Coma Scale score was 14 out of 15. Her blood glucose level was normal. A bedside ultrasonography revealed fluid in Morison's pouch, splenorenal space and pouch of Douglas. The liver looked abnormal within the limits of a bedside ultrasonography.

It was also noted that her routine pelvic ultrasound prior to presentation showed an intrauterine

pregnancy with a fetal heartbeat. Our first impression was therefore of a ruptured heterotopic pregnancy, with a differential diagnosis of a haemorrhagic corpus luteum. She was initially managed according to the protocol for hypotensive resuscitation and was transferred to the theatre. Laboratory investigations revealed a white cell count of $9.4 \times 10^9/L$ and haemoglobin of 112 g/L. Her liver function tests were normal.

Laparoscopy revealed 2 L of haemoperitoneum and a liver tumour located left of the falciform ligament with a necrotic area at the inferior aspect of the tumour, which was considered the likely source of bleeding. However, no active bleeding was noted at the time. Her liver did not appear to be cirrhotic. A biopsy of the liver mass was sent for histopathological assessment (figure 1).

She was transferred to the care of the liver surgery unit, where she had further imaging with a three-phase contrast CT scan of the abdomen (figure 2). This revealed a 6.2 cm primarily hypodense, minimally enhancing lesion in the hepatic segment 2/3 with internal high density and an arterial enhancing component in segment 3 medially. These appearances were thought to favour a hepatic adenoma with evidence of internal haemorrhage. However, the histology showed HCC.

She was subsequently taken to the theatre for a second surgery, where she had excision of the lesions in segments 2/3 and 4.

Seven days following her initial presentation, her pregnancy was terminated, after an informed consent was obtained. Six months after her initial presentation, she is alive and well and receiving chemotherapy.

The tumour was assigned American Joint Committee on Cancer stage pT4, stage IIIc.²

Immunohistochemistry: CD10 focally positive.

Hepar 1: focally positive.

Arginase 1: focally positive.

Glypican 3: diffusely positive.

GLOBAL HEALTH PROBLEM LIST

1. There is increasing migration of people across the world, especially from low-income/middle-income countries to developed countries.
2. With this increase in global migration comes the attendant risk of transfer of medical conditions, especially chronic infections such as hepatitis B infection and their complications.
3. There is a need for increased awareness of the above, especially regarding hepatitis B, and of

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Figure 1 Slides demonstrating predominantly moderately differentiated hepatocellular cancer.

what needs to be done to reduce morbidity and mortality, both in and out of the hospital.

4. Bedside ultrasonography has a role in making a timely diagnosis, to salvage a potentially life-threatening clinical problem that may occur anywhere in the world.

GLOBAL HEALTH PROBLEM ANALYSIS

HCC in pregnancy is very rare, and HCC complicated by spontaneous rupture and haemoperitoneum is even more so. HCC is associated with infertility, and its incidence is lower in women, especially those of reproductive age.³ HCC in pregnancy is typically aggressive, with a 1-year maternal survival rate of 23%.⁴ The standard management is early delivery or pregnancy termination, depending on the gestational age of the fetus, to facilitate treatment of the cancer.^{3 4} Twenty of the 33 reported cases in pregnancy died within days to weeks of their initial presentation, secondary to complications that included lung metastasis, failure to resuscitate, liver failure and hypovolaemic shock.^{3 5 6}

HCC rupture usually involves larger tumours protruding beyond the original liver margin. In the acute phase, patients present with haemodynamic instability and acute abdominal

pain, mimicking a ruptured ectopic in a heterotopic pregnancy or uterine rupture.

To our knowledge, five cases have been reported (4 in 1991 and 1 in 1995^{3 7}) and were described by Lau *et al.*³ Four of the cases were identified from their literature search, while the fifth was from their case series of five patients.

It was not until 2016 that a report of another case of ruptured HCC in pregnancy was published, in which the authors claimed it was the first reported case of haemoperitoneum associated with HCC in pregnancy.⁸ The authors described a 32-year-old woman who developed haemoperitoneum at the 19th week of gestation, with intrauterine fetal demise confirmed by ultrasound. The mother survived post hepatectomy, and there were no signs of HCC recurrence during follow-up. Since these six reports, we are not aware of any other similar reports in the English literature.

On clinical presentation, it may be difficult to distinguish a ruptured heterotopic pregnancy from a spontaneous rupture of HCC in pregnancy.

The diagnosis of HCC in pregnancy can be challenging, as pregnancy itself limits the use of diagnostic modalities such as CT scan and liver biopsy because these interventions may be associated with greater risks.

Impact of immigrants who are hepatitis B virus carriers on the Australian population

As of 2010, liver cancer is in the top 10 leading causes of death from cancer in Australia, with 1778 new cases diagnosed in 2013 and 1732 deaths in 2014.⁹ HCC is the most common form of liver cancer, and 80% of the cases are related to chronic hepatitis B and hepatitis C infections,¹⁰ with chronic HBV carriers having 10-fold to 25-fold increased lifetime risk of developing HCC compared with non-carriers.¹¹ Although the overall prevalence of chronic hepatitis B infection in the Australian population is 1.0%, according to The Kirby Institute,¹² it is estimated that in Australia, 100 000 people are living with undiagnosed hepatitis B, and less than 20% of those needing treatment are receiving it.¹³ It is unclear why such a large number of people are living with undiagnosed hepatitis B, despite a good immunisation programme from birth and detailed pre-employment checks for hepatitis B. With increased global migration, the number of undiagnosed people with hepatitis B may increase, especially considering migrants that come from countries with less comparable immunisation programmes and pre-employment checks. This was the situation with our case report, where the patient emigrated from China to Australia less than a decade ago. It is very likely that a similar picture is emerging in other developed countries similar to Australia. Despite this concern on the transfer of infections between countries, the prevalence of hepatitis B is considered low at 1%. This low prevalence in Australia is likely due to the implementation of effective awareness and intervention campaigns such as education, vaccination and screening programmes, which are targeted at the local level.

As Australia and other developed countries receive immigrants from different parts of the world, it is inevitable that migrants may arrive with chronic hepatitis B infection and its attendant risks, especially HCC.

It has also been suggested that women with high parity may have an increased risk of developing HCC, which is consistent with our case.³ This could be due to the acceleration of tumour growth from high oestrogen levels and the immunosuppressive status associated with pregnancy.³ Unfortunately, from conversations with the patient and her partner, it appeared that she did

Figure 2 Axial and coronal slices of CT of the abdomen of the patient demonstrating the liver tumour as described.

not receive any treatment, despite being aware of her positive HBV status. Twenty-one out of 28 cases described by Lau *et al*³ were found to have HCC progression in multigravidas, with 14 of them having four or more children, a story similar to that of our patient.

Learning points

- Global migration of people is on the increase, as there are multiple means of travelling easier, quicker and less expensive across the world and between countries.
- The increase in global migration implies that infective conditions such as hepatitis B and the associated complications may be transferred from one country to another. Therefore, health practitioners need to be aware of this and similar global problems to deliver best practice, enhance established preventive modalities and improve the morbidity and mortality of patients.
- For patients who present to the emergency department haemodynamically unstable with a similar story, a bedside ultrasonography is invaluable in achieving timely management and good outcome.

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