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Case Report

Pathology Section

A Rare Case of Haemoperitoneum in Pregnancy

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ABSTRACT

Haemoperitoneum in pregnancy is a rare, but potentially fatal condition. Primary hepatocellular carcinoma (HCC) in pregnancy is also very uncommon. Primary hepatocellular carcinoma occuring in a pregnant lady and presenting with massive haemoperitoneum is, to the best of our knowledge, the first case to be reported in world literature. Here we present a case of 32-year-old female who had no typical risk factors for HCC; was in nineteenth week of gestation presented with abdominal pain. Following a spontaneous expulsion of a dead and macerated foetus, she developed massive haemoperitoneum due to rupture of a liver mass. This caused a great diagnostic challenge for us to differentiate between the benign Hepatocellular Adenoma (HA) and well differentiated HCC because of the age and typical clinical presentation favouring HA and the histopathological features favouring more for HCC. Diagnosis of HCC was confirmed based on the immunohistochemical findings. The differential diagnosis between HA and well differentiated HCC is very difficult and sometimes impossible especially when it occurs in young females and in pregnancy.

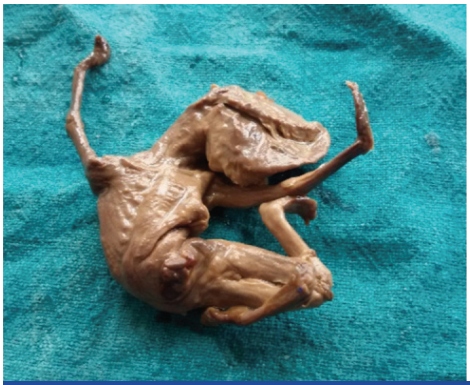
Keywords: Hepatocellular carcinoma, Hepatocellular adenoma, Young female

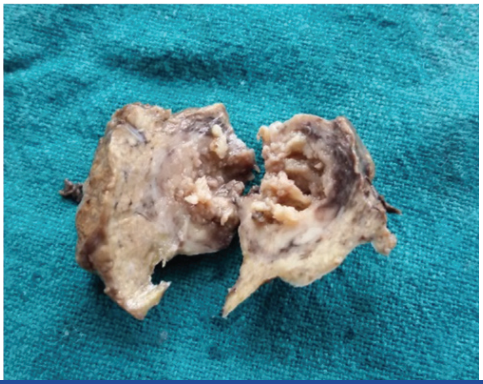
CASE HISTORY

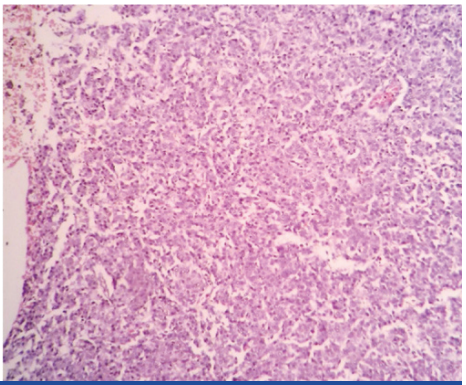
A 32-year-old female in her nineteenth week of gestation was referred to our institute with ultrasound diagnosis of intrauterine foetal demise. She presented with pain in epigastrium and lower abdomen and bleeding per vaginum. She has been married since six years and had a bad obstetric history with one spontaneous abortion at three months of gestation, four years back and a ruptured ectopic gestation for which salpingectomy was done three years back. She was diagnosed to have hypothyroidism two weeks back and was started on Thyroxine. On presentation she was pale with pulse rate 94/min, blood pressure 90/50mm of mercury. Per vaginal examination showed uterus of 16 weeks size. Os was open and products of conception were felt through the os. Ultrasound revealed a single foetus with absent cardiac activity.

About four hours later she spontaneously expelled a dead and macerated foetus [Table/Fig-1]. Placenta was not expelled. Her giddiness and pallor worsened and there was increasing abdominal distension with guarding and rigidity. Her pulse rate at that time was 120/min and blood pressure 80/50mm of mercury. Per vaginal examination showed umbilical cord protruding through the os. There was no undue bleeding per vaginum. Ultrasound was repeated which revealed haemoperitoneum. Suspecting a uterine rupture, emergency laparotomy was done. About two litres of blood collected in the peritoneal cavity was drained. Uterus, cervix, both fallopian tubes and ovaries were found to be normal. The origin of bleeding was detected to be from a space occupying lesion in segment three of liver. Clinical diagnosis of HA that has undergone rupture was made and anatomical liver resection was done. Manual removal of placenta and check curettage was done subsequently.

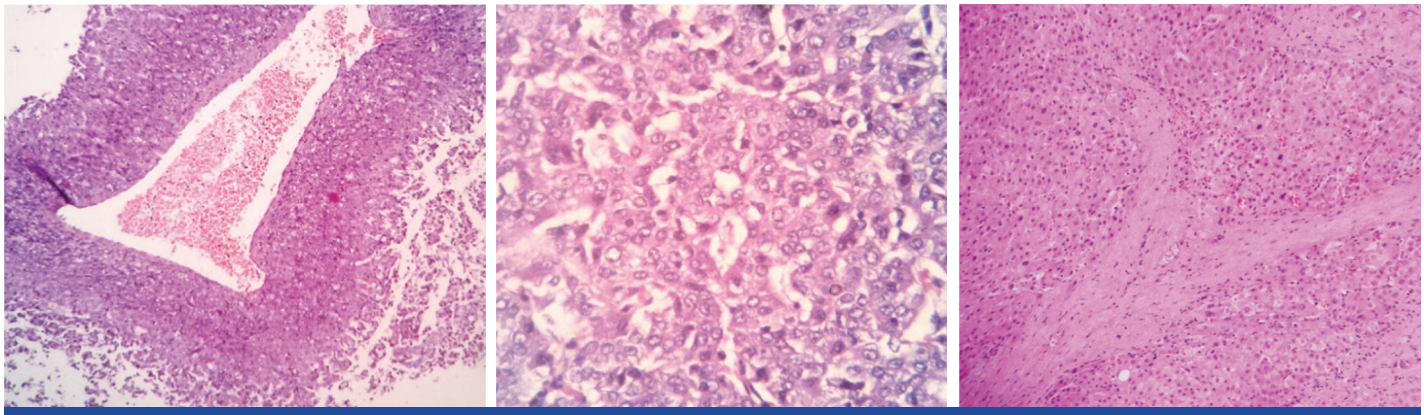
Grossly [Table/Fig-2] the tumour measured 2.5 x 2 x 2 cm with external surface showing a rupture site measuring 1cm. Microscopically [Table/Fig-3,4] the lesion showed liver parenchyma with partially encapsulated neoplasm composed of round to polygonal cells with scant eosinophilic cytoplasm and vesicular nucleus which were arranged in trabecular pattern of more than four cell plate thickness. The cells showed atypia and a few mitotic figures were seen [Table/Fig-5]. Background liver showed features of cirrhosis [Table/Fig-6]. Resected margins showed tumour tissue extending into the surrounding hepatic parenchyma. The diagnosis of HCC with positive resected margin was made. Immunohistochemistry (IHC) showed Alphafetoprotein (AFP) positivity in tumour cells [Table/Fig-7] and CD34 positivity in the capillaries within tumour tissue [Table/Fig-8]. Ki-67 (MIB-I index) was 30% [Table/Fig-9]. IHC features confirmed the diagnosis of HCC. Postoperatively, ultrasound abdomen showed cirrhotic liver and splenomegaly. Portal venous Doppler showed portal venous hypertension. Serum AFP level was 64.7IU/ml (increased). Patient underwent radiofrequency ablation. Currently the patient is on regular follow up. Her last follow up showed a normal liver function test and no evidence of tumour recurrence or metastasis were detected in computerised tomography of abdomen.



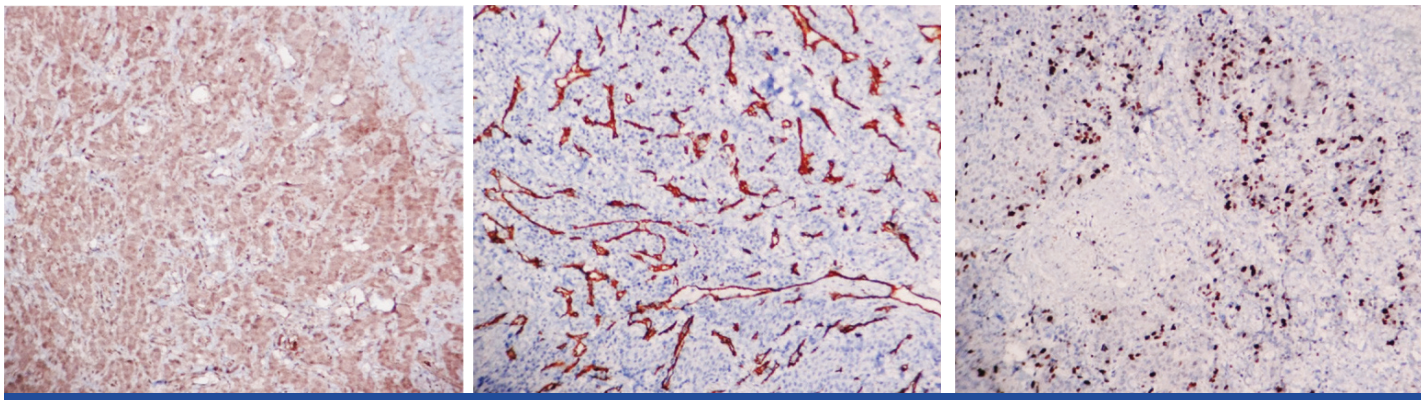




[Table/Fig-1]: Macerated foetus that was expelled spontaneously. **[Table/Fig-2]:** Tumor showing rupture site. **[Table/Fig-3]:** Tumor cells in sheets and trabecule 10x, H&E.



[Table/Fig-4]: Perivascular aggregation of tumor cells 10x, H&E. **[Table/Fig-5]:** Tumor cells showing mild atypia and a few mitotic figures 40x, H&E. **[Table/Fig-6]:** Adjacent liver showing cirrhosis 10x, H&E.



[Table/Fig-7]: Alpha feto protein positivity in tumor cells, 10x. **[Table/Fig-8]:** Positvity in capillaries within tumor tissue, 10x. **[Table/Fig-9]:** Ki 67 more than 30% positivity.

DISCUSSION

Haemoperitoneum in pregnancy is a rare, but potentially fatal condition. The causes for haemoperitoneum in pregnancy [1] are rupture of ectopic pregnancy, uterine rupture due to placenta accrete, placenta increta [2], or previous surgical scar, rupture of corpus luteum, superficial uterine vessel rupture, HELLP syndrome. The non-obstetric causes are rare and include rupture of an arterial aneurysm, rupture of haemangioma or space occupying lesion of liver.

Hepatocellular Carcinoma (HCC) is the fifth most common carcinoma worldwide and is more common in men. HCC is exceptionally rare in pregnancy and was first reported by Roddie in 1957 [3]. There are only very few reported cases of HCC presenting in pregnancy [4-6]. Primary HCC is a very rare disease in females, especially in association with pregnancy. The clinical presentation of HCC in pregnancy is similar to that of HCC in non-pregnant patients, like abdominal pain, abdominal mass or jaundice. Another uncommon liver tumour occurring in women of child bearing age group is Hepatocellular Adenoma (HA). It presents as abdominal pain, abdominal mass, or as haemoperitoneum due to rupture of the adenoma.

The largest review of HCC in pregnancy was reported by Lau et al., in 1995 [7]. According to this study, the rarity of this condition was due to lower incidence of HCC in females, especially of reproductive age group and frequent occurrence of liver cirrhosis in HCC patients, which can cause infertility.

In this case the greatest challenge during the diagnosis was to differentiate it from HA. HA occurs more commonly in young females of reproductive age group. It is a hormone dependent tumour and increase in size during pregnancy with a high chance of rupture and intraperitoneal bleed, which was exactly the mode of presentation in our case [8]. Microscopically round to polygonal cells with minimal atypia, absence of bile ducts within the tumour cells and absence of vascular invasion favoured HA. The features against HA was absence of history of OCP intake and the presence of a cirrhotic liver.

Grossly the presence of background of cirrhotic liver was suggestive of HCC. Microscopic features favouring HCC were presence of wide cell plates (more than three cell thickness), presence of focal areas of cytological atypia, mitotic figures, and presence of infiltration to adjacent liver parenchyma [8]. IHC markers that supported the diagnosis of HCC were positivity of tumour cells for AFP, CD34 positivity in capillaries within tumour mass and a high Ki-67 (MIB-1 index).

HCC in pregnancy is associated with worse prognosis. Many studies showed high maternal mortality rates suggesting adverse effect of pregnancy on the outcome of HCC [6]. Many authors have reported more aggressive behaviour of HCC during pregnancy. It is suggested that oestrogen may accelerate evolution of HCC as in many other liver tumours [9]. In addition, gestational immune suppression may be an enabling factor in tumour progression [9]. In several reports however foetal outcome was satisfactory [6].

Regarding the treatment of HCC in pregnancy there is no well defined protocol because of rarity of this condition [10]. With available studies it can be concluded that in cases diagnosed early, termination of pregnancy is more appropriate. In cases which are diagnosed later, initiating therapy after induced delivery or caesarean section may be preferable.

CONCLUSION

To conclude, distinguishing HA from well differentiated HCC may become impossible on clinical and histopathological grounds alone, and in such situations IHC can aid in arriving at a definite diagnosis.

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