

Case reports

Non-fatal acute fatty liver of pregnancy

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SUMMARY Four patients are described, admitted during a three-year period, who recovered from acute fatty liver of pregnancy; vomiting and jaundice were the main manifestations of the disease; coma and anuria were absent. During the same period, we observed one patient who died of acute fatty liver of pregnancy. This experience suggests that the non-fatal form of the disorder may be much commoner than the fatal form.

It is generally admitted that recovery from acute fatty liver of pregnancy is uncommon. The main purpose of this paper is to describe four patients who recovered from this disease and to suggest that the non-fatal form is much more commonly encountered than the fatal form of the disease. An additional aim of this paper is to show that portal hypertension is a common consequence of acute fatty liver of pregnancy.

Case reports

During a three-year period (1978-80), five patients with histologically proven acute fatty liver of pregnancy were admitted to Hôpital Beaujon. None of them had received tetracycline. Four patients recovered and one died. Only the four non-fatal cases of acute fatty liver of pregnancy are reported in this paper. Biochemical and coagulation disorders are set out in Tables 1 and 2. Serum hepatitis B surface antigen, detected by radioimmunoassay, and IgM anti-hepatitis A antibody were absent in all these patients. Specific details are given in the following case reports.

CASE 1

A 20-year old woman had a first normal pregnancy in 1976. From 20 May, 1978, at the 36th week of her second pregnancy, to 10 June, she complained of abdominal pain, anorexia, and vomiting. At

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admission, on 28 May, jaundice was noted; liver span was 8 cm on the right midclavicular line. On 9 June, labour was induced by oxytocin infusion and a normal infant was delivered. From 10 to 14 June, dextrose infusion, 200 g per day, was required to maintain blood glucose above 3.3 mmol/l (0.6 g/l). On 16 June, transperietal liver biopsy was performed. On 1 July, the patient was discharged.

CASE 2

A 30-year old woman had been treated for systemic hypertension with beta-blocking agents from 1973 to 1978. In 1978, she had a first normal pregnancy. On 1 February, 1979, at the 26th week of her second pregnancy, she complained of headache; arterial blood pressure was 170-120 mm Hg and she received a thiazide diuretic and alphamethyldopa for 15 days. From 13 to 19 February, she vomited repeatedly. Jaundice developed on 14 February. At admission, on 16 February, liver span was 8 cm on the right midclavicular line; arterial blood pressure was 120-80 mm Hg; fetal heart tones were present. Diurnal somnolence was noted during the following three days. On 19 February, fetal heart tones disappeared and a stillborn fetus was delivered by caesarean section. On 20 February, ascites developed; infection of ascitic fluid and septicaemia due to Gram-negative bacteria required antibiotics for 10 days. On 23 February, transvenous liver biopsy² was performed; the gradient between wedged and free hepatic venous pressures was 12 mm Hg (normal: 1-4). Ascites disappeared on 28 February. The patient was discharged on 3 March.

Table 1 *Biochemical disorders**

| | Normal value in early puerperium | Case | | | |
|--|--|------|-----|-----|-----|
| | | 1 | 2 | 3 | 4 |
| Serum bilirubin ($\mu\text{mol/l}$; $\text{mg/l} \times 1.71$) | 6-17 | 253 | 265 | 78 | 215 |
| Serum aspartate aminotransferase (IU) | 5-25 | 120 | 45 | 38 | 74 |
| Serum albumin (g/l) | 25-35 | 26 | 24 | 21 | 21 |
| Plasma ammonia ($\mu\text{mol/l}$; $\text{mg/l} \times 58.8$) | 17-59 | 82 | 76 | 65 | 53 |
| Plasma glucose (mmol/l; $\text{g/l} \times 5.56$) | 2.7-5.0 | 1.6 | 1.6 | 3.2 | 8.3 |
| Serum creatinine ($\mu\text{mol/l}$; $\text{mg/l} \times 8.85$) | 26-53 | 115 | 203 | 168 | 194 |

* Most abnormal values noted during the course of the disease.

CASE 3

A 33-year old woman had a first normal pregnancy in 1971. From 29 May, 1980, at the 32nd week of her second pregnancy, to 29 June, she complained of epigastric pain and vomiting. At admission, on 25 June, arterial blood pressure was 150-90 mm Hg and moderate ankle oedema was noted. Jaundice appeared on 27 June. On 29 June, live twins were delivered by caesarean section. Diurnal somnolence was present for two days. Heparin was administered from 30 June to 7 July. From 1 to 8 July, mild ascites was noted. On 4 July, transvenous liver biopsy was performed; the gradient between wedged and free hepatic venous pressures was 9 mm Hg. The patient was discharged on 11 July.

CASE 4

A 25-year old woman had a first pregnancy, interrupted at the eighth week, in 1976. On 26 October 1980, at the 34th week of her second pregnancy, jaundice occurred. From 2 to 12 November, she complained of abdominal pain and vomiting. At admission, on 8 November, liver span was 8 cm on the right midclavicular line. On 9 November, labour developed spontaneously and a live infant was delivered; episiotomy was required. Diurnal somnolence was repeatedly noted for the following three days. From 10 to 18 November, mild ascites was noted. From 10 to 16 November,

oxytocin and heparin were administered. On 10 and 11 November, copious bleeding due to episiotomy required blood transfusion of 4 l of blood. On 16 November, transvenous liver biopsy was performed; the gradient between wedged and free hepatic venous pressures was 10 mm Hg. The patient was discharged on 30 November.

LIVER HISTOLOGICAL STUDIES

Liver specimens were obtained 19, nine, seven, and 21 days after the onset of jaundice in cases 1, 2, 3, and 4, respectively. On haematoxylin-eosin stained sections from patients 2 and 3, numerous centrilobular swollen hepatocytes, with nuclei in a central position, containing abundant cytoplasmic microvacuoles, were seen (Fig. 1); in patients 1 and 4, only a few centrilobular swollen hepatocytes, with sparse cytoplasmic microvacuoles, were observed (Fig. 2). On frozen sections stained with oil-red O, fat-filled cytoplasmic microvacuoles were demonstrated in all our patients (Figs. 1 and 2). Additional lesions were rare necrotic hepatocytes, surrounded by mononuclear cells, and bile pigment deposits within the hepatocytes and canaliculi.

Discussion

In the four cases reported above, acute fatty liver of pregnancy was documented by the demonstration of

Table 2 *Coagulations disorders**

| | Normal value in early puerperium† | Case | | | |
|---------------------------------------|---|---------|--------|--------|---------|
| | | 1‡ | 2 | 3‡ | 4‡ |
| Platelet count ($10^5/\mu\text{l}$) | 2.0-5.0 | 1.5 | 1.9 | 0.7 | 0.5 |
| Plasma fibrinogen (g/l) | 4.0-6.0 | 1.0 | 2.0 | 0.8 | 0.9 |
| Factor V (% of normal) | 100-150 | 55 | 50 | 32 | 28 |
| Soluble fibrin complexes | May be present | Present | Absent | Absent | Present |

* Values on the day after delivery.

† From Hathaway and Bonnar.¹

‡ Patients in whom disseminated intravascular coagulation was present (cases 1 and 4) or probable (case 3).

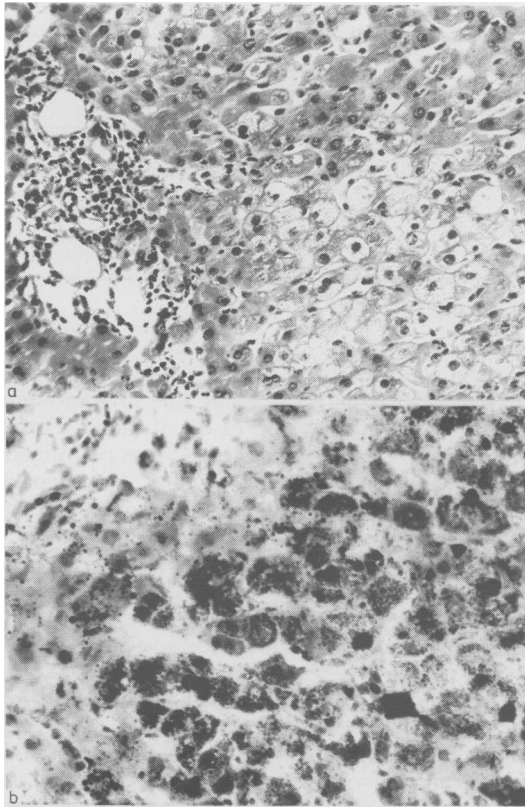


Fig. 1 Case 2. Liver specimen taken nine days after the onset of jaundice. Numerous centrilobular hepatocytes contain cytoplasmic fat-filled microvacuoles clearly visible on both the haematoxylin-eosin stained section (A) and the frozen section stained with oil-red O (B). $\times 240$ (original magnification).

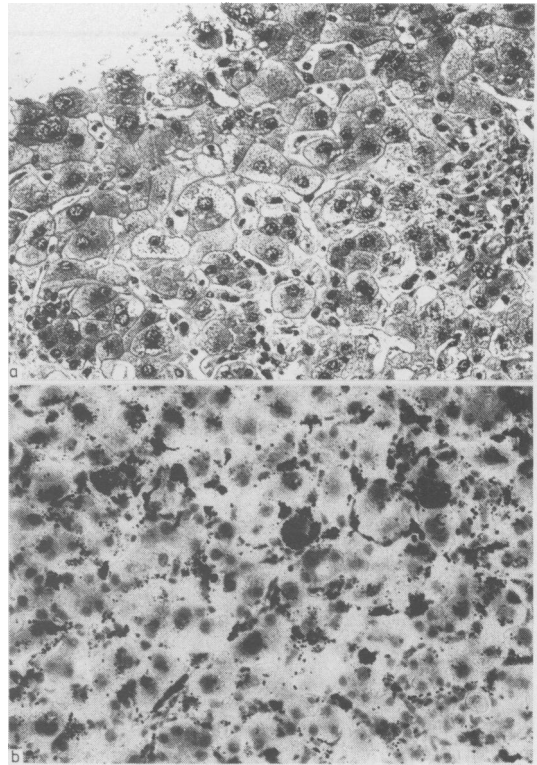


Fig. 2 Case 4. Liver specimen taken 21 days after the onset of jaundice. Cytoplasmic microvacuoles, which could be only suspected in few centrilobular pale hepatocytes on the haematoxylin-eosin stained section (A), are conspicuous in several hepatocytes on the frozen section stained with oil-red O (B). $\times 240$ (original magnification).

typical liver lesions:³ fat-filled microvacuoles were present in the cytoplasm of swollen hepatocytes; the nuclei of affected hepatocytes remained in a central position; the lesions were mainly seen in the centrilobular areas. In the specimens taken about 10 days after the onset of jaundice (cases 2 and 3), the liver lesions were conspicuous in preparations stained with haematoxylin-eosin. In contrast, in the specimens taken about 20 days after the onset of jaundice (cases 1 and 4), the liver changes were mild and the cytoplasmic fat-filled microvacuoles were clearly recognised only on the frozen sections stained with oil-red O. Thus, histological diagnosis of non-fatal acute fatty liver of pregnancy may be overlooked if the liver specimens are taken late after the onset of jaundice or if specific staining for fat is not available. The mild liver changes in the non-fatal

form of the disease are likely to be related to the rapid improvement and/or the moderate intensity of the lesions.

In the four cases reported above, not only was the outcome favourable, but also the entire course of the disease remained remarkably benign. Although all our patients complained of somnolence none suffered from loss of consciousness, whereas coma is a nearly constant feature of fatal acute fatty liver of pregnancy.^{4,5} Renal failure remained mild in all our patients, whereas severe renal failure with anuria is a common complication of the disease.^{4,5} Hypoglycaemia was noted in two of our four patients, but did not give rise to symptoms. Disseminated intravascular coagulation was absent in one of our patients, asymptomatic in two, and might have been a factor in persistent bleeding after episiotomy in

our fourth patient (Table 2), whereas severe disseminated intravascular coagulation frequently occurs in fatal acute fatty liver of pregnancy.⁶

Hepatic vein catheterisation was performed for transvenous liver biopsy² in three of our patients in whom transparietal liver biopsy was contraindicated because of coagulation disorders. Hepatic vein catheterisation has permitted the measurement of the gradient between wedged and free hepatic venous pressures, which was found to be abnormally high in these three patients. As the gradient between wedged and free hepatic venous pressures closely reflects portal venous pressure in the absence of blockade on the portal vein or its intrahepatic branches, the increased gradient indicates that portal hypertension was present in these three patients. Portal hypertension is likely to be the consequence of sinusoidal compression by the diseased hepatocytes. Portal hypertension may play a part in the development of ascites, which was noted in three of our patients and is a well-recognised feature of acute fatty liver of pregnancy.⁷

Although at least 29 histologically documented non-fatal cases have been reported so far,⁷⁻²⁷ the view that the maternal mortality rate in acute fatty liver of pregnancy is high,⁴ amounting to 80%,^{5,6} is generally accepted. In contrast, our experience of four non-fatal cases and only one fatal case observed during the same period suggests that recovery might be a much commoner issue than a fatal outcome in acute fatty liver of pregnancy. The discrepancy between that view and our experience – both, admittedly, based on retrospective analysis of a limited number of cases – could be attributed to the fact that some non-fatal cases of acute fatty liver of pregnancy go unrecognised. This lack of recognition of non-fatal cases of the disorder could be explained as follows: (a) diagnosis of acute fatty liver of pregnancy may not have been considered because of the benign clinical course of the disease; (b) transparietal liver biopsy may not have been performed in the course of the disease because of coagulation disorders; (c) liver biopsy may not have seemed to be justified because of complete recovery; (d) the liver specimen may have been taken too late when the histological lesions had already disappeared; (e) staining for fat, which is essential for recognising acute fatty liver of pregnancy with mild histological lesions, may not have been available.

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