Acute fatty liver of pregnancy in a woman with ulcerative colitis and familial hidradenitis suppurativa

Adam Morton

Abstract

Acute fatty liver of pregnancy is a heterogeneous disorder which may occur in the absence of a detectable gene mutation for the enzyme long-chain L-3-hydroxyacyl-CoA dehydrogenase. Acute fatty liver of pregnancy has been reported to complicate several gastrointestinal disorders including viral hepatitis, chronic active hepatitis and intrahepatic cholestasis of pregnancy. A case of acute fatty liver of pregnancy in a woman with ulcerative colitis and familial hidradenitis suppurativa without a detectable gene mutation is presented. The potential role of inflammatory cytokines in precipitating acute fatty liver of pregnancy is discussed.

Keywords

Acute fatty liver of pregnancy, ulcerative colitis, tumour necrosis factor-alpha

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Introduction

Acute fatty liver of pregnancy (AFLP) is a rare mitochondrial hepatopathy estimated to complicate 5–30 per 100,000 pregnancies. The disorder is attributed to a defect in mitochondrial β -oxidation and characterised by hepatic microvesicular steatosis. It shares clinical and histologic features with Reye's syndrome and sodium valproate hepatotoxicity, other microvesicular fat diseases secondary to impaired fatty acid oxidation. It is increasingly recognised that AFLP is a heterogeneous disorder. In addition to the association with mutations in the gene for the enzyme long-chain L-3-hydroxyacyl-CoA dehydrogenase (LCHAD), cases of AFLP have been associated with fetal deficiency of carnitine palmitoyl transferase I or short or medium chain acyl-CoA dehydrogenase. There have also been many case reports and series where AFLP was not associated with a detectable gene mutation.

Case report

A 34-year-old Fijian Indian woman, Gravida 2 Para 1, presented at 37 weeks' gestation because of reduced fetal movements. The patient's history was significant for ulcerative colitis (UC) and familial hidradenitis suppurativa (HS). UC had flared at 6 weeks' gestation, with the disease being adequately controlled for the remainder of her pregnancy while taking sulphasalazine 4 g per day. HS had been active throughout the pregnancy with axillary and inframammary skin lesions. An emergency Caesarean section was performed because of fetal bradycardia (rate 60 beats per minute); a live male birthweight 3210 g with meconium-stained liquor was delivered. Venous cord blood estimation revealed a combined respiratory and metabolic acidosis with pH 7.11, pO_2 16 mmHg, pCO_2 50 mmHg, base excess -14 mmol/L and bicarbonate 15 mmol/L. Following delivery, the patient complained of dizziness. Maternal blood pressure was 130/70 mmHg having been 110/70 mmHg on presentation. Maternal investigations revealed hyponatraemia, hyperbilirubinaemia, hypoalbuminaemia, elevated hepatic transaminases, hypoglycaemia, acute renal failure, coagulopathy, severely depressed antithrombin III and burr cells on blood film consistent with AFLP (Table 1). Urine protein:creatinine ratio was normal. Serological testing for viral and autoimmune hepatitis and leptospirosis was negative. Serum paracetamol, ammonia, ceruloplasmin and alpha1-antitrypsin were normal. Budd-Chiari syndrome was excluded by maternal Doppler ultrasound. The mother gradually

improved over a period of 14 days with supportive treatment. Other than transient unexplained hypoglycaemia, the neonatal course was uncomplicated. Neonatal metabolic screen was unremarkable. Molecular analysis for mutations in LCHAD gene was negative. The mother was adamant she did not want any further pregnancies and her husband had committed to sterilisation.

Discussion

Although hyponatraemia due to transient diabetes insipidus may occur with AFLP as a result of reduced hepatic breakdown of vasopressinase, severe hyponatraemia has been reported in three previous cases of AFLP.^{1–3} A review of 17 cases of AFLP at the author's institution revealed a median serum sodium level of 130 mmol/L (range: 122–137) on presentation. Hyponatraemia in hepatic failure is likely due to limitation of free water clearance as a result of enhanced release of antidiuretic hormone (ADH) with tissue hypoperfusion together with reduced renal function.⁴ Hypothalamic–pituitary–adrenal axis insufficiency in acute hepatic failure may be an additional factor.⁵

Liver disease occurs in approximately 10–20% of patients with inflammatory bowel disease (IBD).⁶ Non-alcoholic fatty liver disease is the most common hepatic complication and primary sclerosing cholangitis is the most specific for IBD. Other hepatic complications include cholelithiasis, IgG 4 cholangitis, PSC-autoimmune hepatitis, hepatic amyloid, granulomatous hepatitis and portal vein thrombosis.

HS is estimated to occur in 17.3% of patients with Crohn's disease and 8.5% of patients with UC.⁷ HS is associated with earlier onset and more severe IBD, more frequent requirement for anti-tumour necrosis factor-alpha (TNF- α) therapy and surgery. T-helper 17 cells and TNF- α are involved in both IBD and HS, and both conditions respond to anti-TNF- α therapy. Pro-inflammatory cytokines TNF- α and interleukin-1 beta are significantly elevated in HS skin.⁸

Obstetric Medicine, University of Queensland, Queensland, Australia

Corresponding author:

Adam Morton, Mater Hospital Raymond Tce, South Brisbane, Queensland 4101, Australia.

Email: adam.morton@mater.org.au

Table 1. Laboratory investigations.

Days post-partum	0	1	3	5	10	Normal
Sodium (mmol/L)	122	127	130	136	137	135–145
Creatinine (mmol/L)	129	166	139	79	64	30–90
Glucose (mmol/L)	2.4	5.6	3.4	4.2	5.6	3.6–7.7
Albumin (g/L)	20	18	17	24	28	33–47
Bilirubin (μ mol/L)	96	89	118	137	98	<20
Aspartate transaminase (U/L)	318	202	103	104	104	10–45
Alanine transaminase (U/L)	305	229	116	93	72	5–45
Urate (mmol/L)	0.36					0.15–0.45
Prothrombin time (s)	29.2	30.6	22.9	16.1	14.1	11–14
APTT (s)	45.7	48.2	44.2	35.2	29.2	23–28
Fibrinogen (g/L)	1.6	1.5	2.1	3.7	5.5	3.7–6.2
Antithrombin III	12%					
Haemoglobin (g/L)	106	88	82	98	96	115–160
White cell count ($\times 10^9$ /L)	24	34	30	21	12.4	4–15
Platelets ($\times 10^9$ /L)	233	187	200	220	210	150–450

APTT: activated partial thromboplastin time.

TNF- α is one of the key factors in the pathophysiology of alcoholic liver disease and non-alcoholic fatty liver disease. TNF- α transgenic mice are characterised by reduced mitochondrial β -oxidation of fatty acids and altered hepatic fatty acid composition. Hepatic mitochondrial β -oxidation is increased following administration of tetrade-cylthioacetic acid, an anti-inflammatory bioactive fatty acid. Similarly, anti-TNF- α antibody treatment improves mitochondrial function in ob/ob mice.⁹

AFLP has been reported to occur following acute viral hepatitis with hepatitis B, influenza A and herpes simplex type 2 viruses, as well as two patients with chronic active hepatitis.¹⁰ Infection with PR8 influenza results in Kupffer cells releasing inflammatory cytokines which mediate reduced hepatic fatty acid oxidation. Reye's syndrome has been reported in adults as well as children following influenza A viral infection.¹¹ A review of 30 fatal cases of proven influenza A virus infection and encephalopathy noted liver dysfunction in 57% and fatty degeneration in 40%.¹¹

Conclusion

The association between AFLP in the mother and fetal deficiency of LCHAD was first reported in 1993. AFLP is a heterogeneous disorder; however, mutations causing paediatric LCHAD were found in only 19% of families with a maternal history of AFLP.¹² In one study of 10 women with AFLP, none were found to have the common G1528C LCHAD gene mutation.¹³ To the best of the author's knowledge, this is the first report of AFLP in a patient with UC and HS and may simply represent a coincidental occurrence. A potential mechanism linking the development of AFLP in a woman with UC and HS may be impaired hepatic mitochondrial fatty acid β -oxidation secondary to increased cytokine release. Physicians caring for pregnant women with IBD and HS should be aware of AFLP as a potential complication.

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Ethical approval

The patient provided signed informed consent for publication of this case report.

Guarantor

AM.

Contributorship

AM cared for the patient and wrote the manuscript.

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