

A rare presentation of acute fatty liver disease in pregnancy in the background of T-cell non-Hodgkin lymphoma

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Introduction

Lymphoma is the fourth most frequently diagnosed malignancy during pregnancy after melanoma, breast cancer and cervical cancer. The commonest type of lymphoma in pregnant women is Hodgkin lymphoma with a reported incidence ranging from 1 per 1,000 to 1 per 6,000 births¹. Non-Hodgkin lymphoma (NHL) in pregnancy is rare and T-cell Non-Hodgkin lymphoma (T-NHL) is a rarer form of NHL with only a few reported cases to our knowledge. NHL in pregnancy is usually diagnosed during the second or third trimester and commonly associated with aggressive histology and disseminated disease. A rapid tumour growth is thought to occur in early pregnancy, puerperium and especially during lactation and reproductive organ involvement is common^{2,3}.

Acute fatty liver disease (AFLD) in pregnancy is a rare condition and occurs in approximately one in 7,000 to one in 15,000 pregnancies⁴. The cause is a deficiency

of LCHAD (3-hydroxyacyl-CoA dehydrogenase) enzyme and the condition has an autosomal recessive inheritance pattern. The condition used to be universally fatal a couple of decades ago. However, due to the advancement in medicine, the case fatality rate has come down in recent years to 18% for the mother and 23% for the fetus^{4,5}. Acute Fatty Liver Disease in Pregnancy in the background of NHL is an extremely rare occurrence and this is possibly the first-ever case reported to the best of our knowledge.

Case

A 35 year old woman with three healthy children, presented to the hospital at 27 weeks of gestation with nonspecific abdominal pain, vomiting and generalised weakness for 3 days. At 20 weeks she had a tonsillectomy due to chronic tonsillitis refractory to medical management and the histology was highly suspicious of T-NHL. She also had cervical lymphadenopathy and had been planned for a biopsy for

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confirmation of the diagnosis. However, she defaulted follow up and was not seen until she presented with the acute illness. On examination, there were no localising signs or overt features of sepsis. Her liver enzymes were slightly elevated with aspartate transaminase (AST) and alanine transaminase (ALT) in 200s. Other initial blood investigations including bilirubin level, white cell count, inflammatory markers and renal function test were normal. The patient became agitated and confused within a few hours and deteriorated quickly. Therefore, she was admitted to the Intensive Care Unit (ICU) for monitoring and further care. She had a CT brain done due to acute confusion, which was also normal. On the repeated blood work, her AST and ALT had risen to 400s with a marginally elevated bilirubin level. Inputs were sought from multiple disciplines including general medicine, oncology and haematology for her management.

Despite the efforts, she continued to deteriorate and required three inotropes to maintain circulation by the end of the day. A collective decision was made to deliver the foetus hoping it would improve maternal circulation as well it would give a fair chance to the baby to survive. A 1.2 kg live baby was delivered by hysterotomy in the ICU. The procedure was uncomplicated and the patient managed to barely survive with intense support for another 2 days and succumbed. The baby required ventilator support at first, but discharged in good condition after 4 weeks.

Postmortem examination of the liver revealed microvesicular steatosis and intracellular cholestasis, which are suggestive of AFLD in pregnancy (Figure 1). Histology of cervical lymph nodes confirmed the presence of a T-NHL, which was supplemented by immunohistochemistry (Figure 2).

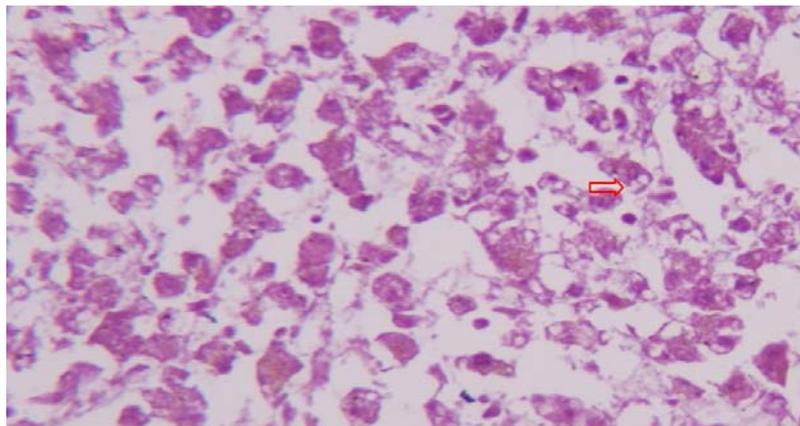


Figure 1. **Microvesicular steatosis (red arrow) and cholestasis present in hepatocytes.**

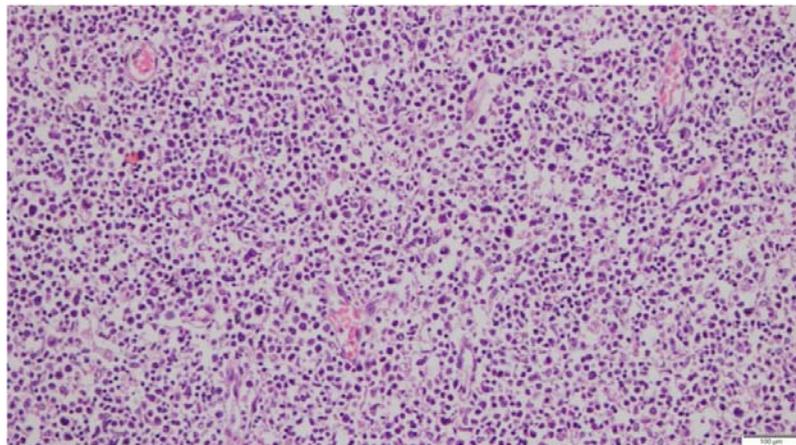


Figure 2. **High grade T-NHL of a cervical lymph node.**

Discussion

Acute fatty liver disease in pregnancy usually presents in the third trimester and rarely can present in the postpartum period or the late second trimester like in this case. Diagnosis is made on clinical features, biochemistry, radiological and histological features using Swansea criteria (Table 1).

Presence of six or more features listed, in the absence of other explanation, increases the likelihood of AFLD in pregnancy⁶. With AFLD, typically liver enzymes are elevated, with AST and ALT enzymes ranging from a minimal elevation to 1000 IU/L, but usually staying in the 300-500 range. Bilirubin is almost universally elevated⁷. In retrospect, this patient had abdominal pain, vomiting, encephalopathy (manifested by agitation), elevated liver enzymes and bilirubin. During the hysterotomy, she was noted to have mild ascites and the postmortem revealed microvesicular steatohepatosis in the liver. Acute fatty liver disease in pregnancy was not considered as a differential diagnosis when managing this patient because she had an incompletely worked-out, aggressive form of NHL in the background, which may produce a similar clinical

picture in its disseminated form. Furthermore, the fact that she had 3 uncomplicated pregnancies in the past, would have contributed to hinder AFLD from the list of possibilities.

On literature search, we could not find any relationship between AFLD in pregnancy and T-NHL.

It's difficult to say at this point if the T-NHL contributed to the unfavourable outcome and rapid course of the disease in this particular case.

Patients with AFLD in pregnancy may present with non-specific symptoms and their background clinical conditions may mask the diagnosis. However, some form of liver involvement is always seen from the beginning with AFLD. The maternal outcome in AFLD in pregnancy largely depends on prompt diagnosis and timely delivery of the fetus. Therefore, it is imperative for the clinicians to take a minute and see if the patients fulfill Swansea criteria for AFLD in pregnancy when they present with such symptoms, even if they have other diagnoses in their background, which may produce a similar clinical picture.

Table 1. Swansea criteria for AFLD in pregnancy

Feature	Definition
Clinical	Vomiting Abdominal pain Polydipsia/ Polyuria Encephalopathy
Laboratory	
Bilirubin	> 0.8 mg/dl (14 kmol/l)
Hypoglycemia	< 72 mg/dl (4 mmol/l)
Uric acid	> 5.7 mg/dl (340 kmol/l)
Leukocytosis	> 11 *10 ⁶ /l
Renal impairment	Ammonia > 27.5 mg/dl (47 kmol/l), Creatinine > 1.7mg/dl (150 kmol/l)
Coagulopathy	Prothrombin time (PT) >14s or activated partial thromboplastin time (APTT) > 34s
AST and ALT	> 42 IU/l
Bilirubin	> 0.8 mg/dl (14 kmol/l)
Ultrasonography	Ascites or bright liver
Liver biopsy	Microvesicular steatosis

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