Acute Liver Failure in a Primiparous Female

A case report and update on the literature

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Introduction

Acute liver failure (ALF) is an obstetric emergency. It complicates the minority of pregnancies however has an associated mortality rate of 40% (1). Aetiologies can range from pregnancy specific causes such as Haemolysis Elevated Liver Enzymes Low Platelets (HELLP), Preclampsia Toxaemia (PET) and Acute Fatty Liver of Pregnancy (AFLP) (1). Other conditions affecting the general populations are additionally prevalent, including Viral Hepatitis, Budd-Chiari and other thromboses, trauma and direct toxic effects (1). Arguably the most dangerous cause is AFLP, which has historically been associated with a near 100 % mortality rate. Prevalence is stable, affecting 1 in 7 500 pregnancies (2, 3).

Risk factors include; Multigravida status, Male foetus, other liver conditions, diabetes and previous pregnancies complicated by AFLP (2). Acute liver failure diagnoses are not mutually exclusive (2). The most common differential diagnosis to AFLP is HELLP. AFLP is significant more serious, being associated with increased maternal mortality, stillbirth, transfusion requirement and length of stay in hospital (4). Mortality from obstetric specific causes, such as AFLP is decreasing, with most recent estimates showing AFLP mortality down trending from historical estimates of 80-100% to current estimates in developed countries of 10-15% (2). The pathogenesis of AFLP is poorly understood. It is known that fatty acid oxidation is decreased with increasing gestation secondary to known hormonal changes (5). The diagnostic criteria is included in Figure 1.

There is a genetic role with known mutations in cellular metabolic enzymes in the mother or foetus resulting abnormal fatty acid oxidation defects (FAOD's). This can be an attributable in 62% of ccases, but the lack of its presence in all cases highlights the limited understanding of this diseases pathogenic process (5, 6).

Six or more of the criteria below should be considered diagnostic of AFLP in a woman with no other liver conditions of pregnancy (PE or HELLP)

- Vomiting
- Encephalopathy
- Polydipsia/polyuria
- Abdominal pain
- Bilirubin more than 0.8 mg/dL
- Elevated urea above 950 mg/dL
- Hypoglycemia less than 72 mg/dL
- Leukocytosis more than 11,000/mL
- Ascites
- ALT values above 42 U/L
- Ammonia values above 66/µmol
- Coagulation function or prothrombin time more than 14 seconds
- Acute kidney injury or creatinine more than 1.7 mg/dL
- Intense liver on ultrasound image
- Microvesicular steatosis on liver biopsy

Figure 1 – Swansea Criteria: the diagnostic criteria for Acute Fatty Liver in pregnancy (7)

Result

Proposed Criteria

References

Case Presentation

This case involves a primiparous female presenting to a tertiary referral hospital with 24 hours gastrointestinal symptoms at 38 weeks gestation. On the surface, symptomatically it resembled gastroenteritis. The patient had normal observations. 24 hours prior she had presented to the same hospital with her first presentation of decreased foetal movements. Antenatally, her only complicating factors were GDM and an LGA foetus. Foetal wellbeing assessment was normal. Pre-gestation, she he had no other past medical or family history. Physical examination demonstrated hepatic tenderness and otherwise contained no other features of preeclampsia or fulminant liver failure at presentation. She was of an Indian subcontinental background with a caucasian partner and was well engaged with antenatal care.

The patient was admitted to hospital and a multidisciplinary team was engaged. A joint decision made for urgent delivery with attempted coagulopathy reversal followed by medical optimisation postnatally. Coagulopathy was significant suggesting DIC. Delivery of a live male infant was expedited by caesarean section with minimal complications within hours of presentation.

Following delivery, her condition continued to deteriorate. The same evening, new hypoxia required non-invasive ventilation in Intensive Care. Clinical signs of hepatopathy worsened with a new asterixis and confusion. Cross sectional Imaging (CT Abdomen & pelvis with intravenous contrast) revealed no structural cause of the illness such as thromboses. A new high anion gap metabolic acidosis with raised lactate developed. She was given prophylactic antifungal therapy and an insulin dextrose infusion. In the setting of this she was referred to the Liver Transplant service for urgent consideration.

Fortunately, her condition began to improve at 24 hour postnatally with a stabilisation of both the clinical and biochemical situation, with the latter being demonstrated via the below QR code. Her coagulopathy began improving despite no change in her clinical management. Her acute confusion and hypoxia reversed. After 9 days she was discharged home.

In terms of outpatient follow up; 2 months post presentation she was symptomatically and biochemically at status quo and at 1 year the only ongoing issue was microalbuminuria. Susceptibility investigations into genetic abnormalities were negative with both long-chain 3-hydroxyl coenzyme A dehydrogenase (LCHAD) testing and Long Chain Fatty Acids revealing normal results.

Discussion

This case demonstrates a favourable outcome in a critical presentation.

Regarding the diagnosis, multiple investigations cemented the diagnosis as Acute Fatty Liver of Pregnancy. Multiple tests, both maternal serology and cross sectional imaging excluded the majority of widespread common causes of ALF (1, 2, 6). The additional fulfillment of the Swansea criteria further consolidated diagnosis. A liver biopsy would be required to make the diagnosis more certain but was not required as it does not change management and is associated with some morbidity especially in the context of coagulopathy (2, 7). It is interesting the choice of mode of delivery . No strong data identifying normal vaginal as opposed to lower segment caesarean section as favorable from a bleeding or maternofoetal outcome point of view , although 65% are delivered via caesarean (5).

Regarding risk factor identification, it is interesting that biochemical investigations revealed no known defect in fatty acid oxidation illness, which is usually present in the majority of cases (2, 8). In fact, the only discernable risk factor was the male sex of the foetus (2). Currently there are no validated risk stratification models or methods for early modification. Neither are there proven methods for risk factor modification. Nothwishtanding this, significant advances are being made for early case identification beyond the standardized Swansea Criteria model (8). Recent cohort studies and case series have demonstrated that expanded biochemical testing and selected use of specific patters can create a diagnostic model with a sensitivity and specificity of 97% (8). Although this remains to be proven beyond these small studies (4, 8). Suggested criteria are included in the below QR code.

This case has complied with known standards of both presentation, biochemistry and complications of AFLP literature (3, 9, 10). The main deviation of this case was their advanced gestation (38 weeks) compared to the established mean presentation gestational age (35 weeks) (3). Importantly, there were almost no prodromal warning signs or risk factors in this patient, of an impending life threatening condition (3, 7).

This case report serves to both remind the medical community of this insidious and potentially fatal problem, and the great improvements needed in its primary prevention. As with any health problem, prevention is key which is underpinned by aetiological understanding. Whilst there is a proven correlation between inborn errors of fatty acid metabolism and AFLP, this is not mutually exclusive. Screening tests based on such have been studied in the United states, but not proven feasible secondary to poor sensitivity (2). Given the non-modifiable nature of known risk factors, prevention of AFLP has no proven methods (7). Acute diagnosis is one of the regions making improvements in the domain of AFLP. Multiple recent studies have purposed mixed variable probabilistic models to improve the accuracy of AFLP diagnosis using blood, history and examination based findings to yield better sensitivities and specificities than the classical Swansea Criteria (3, 8). Finally, management has remained unchanged since the disease was defined – urgent delivery. There have not been any proven treatments for the extension of gestation or antenatal management (5). Additionally, there is no strong data regarding preferred intrapartum management (5). Luckily there is significant data regarding the acute management of hepatic consequences from similar hepatic conditions affecting the general populous (5).

In summary, case report serves to highlight the presence of this rare an life threaning condition. It demonstrates the excellent management available to patients, but unfortunately shows the absence of any predictive or preventative tools for this potentially fatal condition.