DIAGNOSTIC DILEMMAS WITH DIAGNOSING HELLP SYNDROME IN PREGNANCY A CASE REPORT AND REVIEW OF LITERATURE

Dr Lynette Ngothanh[1], Dr Swetha Rao[1] & Dr Jolene Ng[2]
1. Department of Obstetrics and Gynaecology, Liverpool Hospital, NSW, Australia 2. Department of Obstetrics Medicine, Liverpool Hospital, Sydney, NSW, Australia

INTRODUCTION

HELLP syndrome describes a disorder of haemolysis, elevated liver enzymes and low platelet count. It may be a complication of severe preeclampsia (PET). HELLP syndrome is generally thought to be the extreme spectrum of preeclampsia, however around 15-20% of patients with HELLP syndrome do not present with preceding hypertension or proteinuria.[1] The prevalence of HELLP syndrome is 0.5-0.9% with 70% of cases occurring in the 3rd trimester of pregnancy.[1]

AIM

To highlight the diagnostic challenges of HELLP syndrome and its impact on pregnancy outcomes.

CASE REPORT

A 38-year-old nulliparous woman of Nepalese background with an IVF pregnancy, diet-controlled gestational diabetes and longstanding mild thrombocytopenia (baseline platelet count 157) presented at 36 weeks gestation with pruritus of her hands and arms without a rash. Initial investigations demonstrated mildly elevated bile acids of 12.6, deranged liver transaminases with AST of 97 and ALT of 200, and platelets of 138. Repeat testing three days later showed worsening transaminitis, thrombocytopenia to 92, a sFlt-1/PlGF ratio of 117 (normal range is <38) and normal renal function. An elevated sFLT/PlGF ratio suggests a degree of placental dysfunction. Blood pressure was mildly elevated at 136/81 mmHg. She was not on aspirin during the pregnancy. She was admitted for investigation of suspected evolving intrahepatic cholestasis of pregnancy and preterm pre-eclampsia. Ursodeoxycholic acid was commenced.

Haemolysis screening demonstrated low but detectable haptoglobin, reticulocytosis and mild anaemia, although blood film showed no schistocytes. A liver ultrasound identified two small lesions consistent with haemangiomas.
Following a multidisciplinary review with obstetric medicine and haematology, the overall impression was evolving HELLP syndrome, with differentials including immune thrombocytopenia and gestational thrombocytopenia, alongside mild intrahepatic cholestasis of pregnancy. An induction of labour was commenced at 36+6 weeks. Following prostaglandin cervical ripening, the CTG became abnormal with reduced variability and recurrent deep decelerations. Despite terbutaline administration, the CTG remained abnormal and she proceeded to an emergency caesarean section, delivering a 3 kg male infant without intraoperative complications and an estimated blood loss of 700 mL.
Postnatally, platelet counts improved, although liver function tests remained abnormal initially. A liver screen was otherwise unremarkable apart from elevated cholesterol and triglyceride levels. By day six postpartum, liver enzymes had improved and she was discharged home with outpatient follow-up. Placental histopathology demonstrated a placenta of size in the 5th–10th centile with villous agglutination, consistent with maternal vascular malperfusion associated with pre-eclampsia.

DISCUSSION

HELLP syndrome is considered part of the spectrum of pre-eclampsia, but it is a distinct clinical entity within that spectrum. Diagnosis can be challenging as hypertension and proteinuria may be absent or develop late, leading to delayed recognition.[3] Many patients present meeting only some laboratory criteria for HELLP syndrome, creating uncertainty regarding diagnosis, escalation of care and timing of delivery.

HELLP may also present or worsen postpartum, and failure of thrombocytopenia or haemolysis to improve after delivery should prompt consideration of alternative thrombotic microangiopathies (TMA).[5] Diagnostic classification commonly uses the Tennessee criteria, requiring haemolysis, elevated liver enzymes and platelets <100 $\times 10^9$/L, or the Mississippi system, which grades severity by platelet levels.

Tennessee System	Mississippi System
AST > 70 IU/L LDH > 600 IU/L Plt < 100 x 10^9/L	AST > 40 IU/L and LDH > 600 IU/L and • Class I: platelets: < 50 x 10^9/L • Class II: platelets: 50 -100 x 10^9/L • Class I: platelets: 100 - 150 x 10^9/L

Table 1: Diagnostic frameworks for HELLP syndrome

However, laboratory variability and evolving disease mean patients may deteriorate despite not fully meeting thresholds. Haemolysis markers may also be inconsistent, with biochemical evidence preceding blood film changes.[5]
The most important diagnostic dilemma is distinguishing HELLP from conditions where delivery alone is insufficient, particularly thrombotic thrombocytopenic purpura (TTP) and pregnancy-associated atypical haemolytic uraemic syndrome (a-HUS), which may mimic or coexist with HELLP and require urgent disease-specific therapy.[6] Increasingly, angiogenic biomarkers such as the sFlt-1/PlGF ratio are used to support diagnosis when features of pre-eclampsia are evolving or atypical. Overall, the literature emphasises that HELLP is frequently atypical, incomplete or postpartum, and careful differentiation from other TMAs is critical to avoid delayed treatment.

1. Khalid F, Mahendraker N, Tonismae T. HELLP Syndrome. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Updated 2023. PMID:32809450.
2. Jebbink J, Tabbers M, Arink G, Beuers U, Ellerkmann RO, Rio-Stalpers C, van der Post J. HELLP syndrome preceded by intrahepatic cholestasis of pregnancy: one serious itch. BMJ Case Rep. 2014 Apr 7;2014:bcr2013203208. doi: 10.1136/bcr-2013-203208. PMID: 24711473; PMCID: PMC3987518.
3. He, Y-D. and Yang, H-X., 2022. Clinical diagnosis and treatment of "atypical" HELLP syndrome. Gynecology and Obstetrics Clinical Medicine, 2(3), pp.105-109.
4. Magee LA, Brown MA, Hall DR, Gupte S, Hennessy A, Karumanchi SA, Kenny LC, McCarthy F, Myers J, Poon LC, Rana S, Saito S, Staff AC, Tsigas E, von Dadelszen P. The 2021 International Society for the Study of Hypertension in Pregnancy classification, diagnosis & management recommendations for international practice. Pregnancy Hypertens. 2022 Mar;27:148-169. doi: 10.1016/j.preghy.2021.09.008. Epub 2021 Oct 9. PMID: 35066406.
5. Haram K, Svendsen E, Abildgaard U. The HELLP syndrome: clinical issues and management. A Review. BMC Pregnancy Childbirth. 2009 Feb 26;9:8. doi: 10.1186/1471-2393-9-8. PMID: 19245695; PMCID: PMC2654858.
6. Ramadan MK, Badr DA, Hubeish M, Ibni S, Hijazi H, Mogharbil A. HELLP Syndrome, Thrombotic Thrombocytopenic Purpura or Both: Appraising the Complex Association and Proposing a Stepwise Practical Plan for Differential Diagnosis. J Hematol. 2018 Jan;7(1):32-37. doi: 10.14740/jh347w. Epub 2017 Jan 10. PMID: 32300409; PMCID: PMC7155857.