THROMBOTIC MICROANGIOPATHY IN A PREGNANCY WITH TYPE 1 DIABETES MELLITUS: A CASE REPORT

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INTRODUCTION

Thrombotic microangiopathies (TMAs) are a spectrum of disorders involving microangiopathic haemolytic anaemia (MAHA), thrombocytopenia & organ injury. In pregnancy, differentiating between TMAs is clinically challenging but important due to potentially significant impacts on fetal & maternal outcomes.

CASE

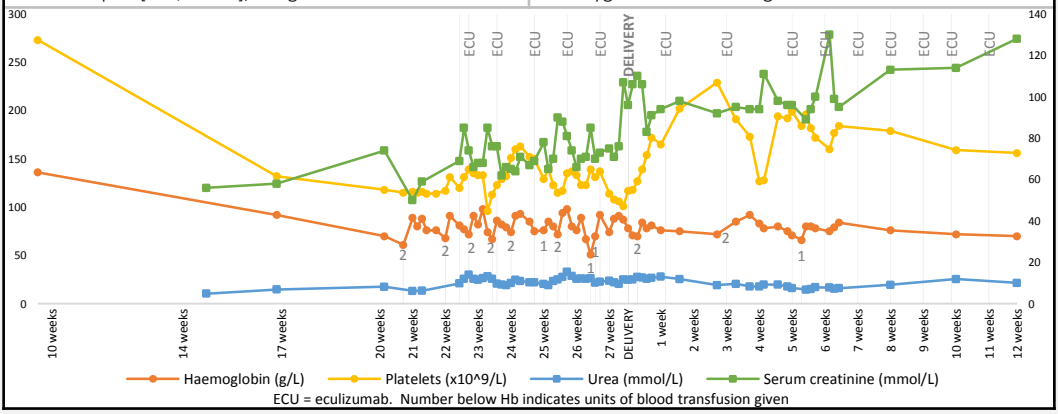
- 26yo primipara with fatigue & mild pedal oedema
  - History of poorly-controlled type 1 diabetes mellitus with known macroalbuminuria
- New onset TMA of unclear cause
  - MAHA: haemoglobin [Hb] 70g/L, schistocytes, haptoglobin <0.06g/L, LDH 747U/L
  - Thrombocytopenia: platelets 98x10^9/L
  - Microscopic haematuria with glomerular morphology; urine protein:creatinine ratio [uPCR] 0.5g/mmol

MANAGEMENT & ANTENATAL COURSE

- Transferred to our tertiary centre
  - Fetal wellbeing confirmed on ultrasound
  - Thrombotic thrombocytopenia purpura [TTP] excluded: normal ADAMTS13 level
  - Blood transfusions given to increase Hb >80g/L
  - Prednisolone trialled for possible autoimmune cause
- Renal function worsened over two weeks
  - Renal biopsy: moderately advanced diabetic nephropathy; TMA without glomerular endotheliosis
  - Eculizumab started for presumed atypical haemolytic uraemic syndrome [aHUS]
- Clinically deteriorated over next 5 weeks
  - Hypertension, hyperreflexia, headache & visual disturbance; worsening oedema
  - Worsening renal function & proteinuria (uPCR 0.84g/mmol)
- Caesarean section at 27+4 weeks for suspected pre-eclampsia [PET/HELLP]; 847g liveborn female infant

POSTPARTUM PROGRESS

- Immediate recovery uncomplicated
  - Significant symptomatic improvement; blood pressure well controlled on oral anti-hypertensives
  - Platelets rapidly normalised, uPCR improved (0.51g/mmol), Hb stable
  - Discharged on day 8 postpartum
- Genetic testing for common aHUS genes returned a heterozygous mutation of unknown significance in exon 2 of the CFI gene (c.292A>G, p.Thr98Ala)
- At 4 months postpartum
  - Ongoing oral anti-hypertensives (maximal ACE inhibition) & eculizumab weekly
  - Ongoing evidence of haemolysis, still requiring occasional blood transfusion
  - Renal function slowly worsening; nephrotic range proteinuria ongoing
- Baby discharged at 1 month corrected age, on home oxygen for chronic lung disease



ECU = eculizumab. Number below Hb indicates units of blood transfusion given

DISCUSSION

[references available on request from corresponding author]

- A logical approach to distinguishing between disorders causing TMAs in pregnancy is necessary to appropriately target management.
- aHUS & PET/HELLP share many similarities which make diagnosis challenging.
  - Clinical features: PET/HELLP classically associated with hypertension & proteinuria[1] & aHUS with severe renal dysfunction[2], but both can involve liver dysfunction, neurological disturbances & haematological abnormalities.
  - Diagnostic tests: no definitive tests available.
  - Pathophysiology: dysregulation of the alternative complement pathway & subsequent endothelial dysfunction[3,4].
- Eculizumab, a monoclonal humanised antibody, inhibits complement protein C5 & downstream terminal complement activation.
  - In aHUS: significant benefits for endothelial injury & haematological parameters[5].
  - In PET/HELLP: trialled as a salvage therapy to prolong pregnancy in extreme prematurity[6].
- The ratio of soluble fms-like tyrosine kinase 1 (sFlt-1) to placental growth factor (PlGF) is elevated in pregnancies at increased risk of PET/HELLP[7]. Retrospective analysis of sFlt-1:PlGF ratios in this case suggest eculizumab may have been helpful in reducing endothelial dysfunction & prolonging pregnancy at this extremely preterm gestation.