International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2023; 7(6): 92-94
Received: 13-08-2023
Accepted: 21-09-2023

Dr. Hannah Darling
Department of Medicine, Worthing Hospital, University Hospitals Sussex NHS Foundation Trust, Lyndhurst Road, BN11 2DH, United Kingdom

Dr. Emily Penney
Department of Medicine, Worthing Hospital, University Hospitals Sussex NHS Foundation Trust, Lyndhurst Road, BN11 2DH, United Kingdom

Dr. Tina Kapoor
Department of Medicine, Worthing Hospital, University Hospitals Sussex NHS Foundation Trust, Lyndhurst Road, BN11 2DH, United Kingdom

Dr. Surajit Das
Department of Medicine, Worthing Hospital, University Hospitals Sussex NHS Foundation Trust, Lyndhurst Road, BN11 2DH, United Kingdom

Corresponding Author:
Dr. Hannah Darling
Department of Medicine, Worthing Hospital, University Hospitals Sussex NHS Foundation Trust, Lyndhurst Road, BN11 2DH, United Kingdom

Fulminating pre-eclampsia at approximately 15 weeks gestation: A case report

Dr. Hannah Darling, Dr. Emily Penney, Dr. Tina Kapoor and Dr. Surajit Das

DOI: https://doi.org/10.33545/gynae.2023.v7.i6b.1403

Abstract
Pre-eclampsia is currently defined as new-onset of hypertension occurring after 20 weeks gestation, with significant proteinuria or maternal end organ dysfunction. The exact pathophysiology remains uncertain however it has been hypothesised that anti-angiogenic factors arising from the developing placenta contribute to its development. This case report describes the presentation of a 37 year old patient clinically presenting with pre-eclampsia at 15 weeks gestation. A literature review revealed 5 previously reported similar cases, indicating the need for better understanding of the pathophysiology and awareness of the condition at early gestations. We explore the possible differential diagnosis of haemolytic uraemic syndrome and thrombotic thrombocytopenic purpura and discuss the reasoning for the definitive diagnosis of fulminating early onset pre-eclampsia.

Keywords: Pre-eclampsia, Pre-term, HELLP syndrome, hypertension pregnancy induced, haemolytic uraemic syndrome

Introduction
At present The National Institute of Clinical Excellence (NICE) defines pre-eclampsia as new onset hypertension (over 140 mmHg systolic or over 90 mmHg diastolic), presenting beyond 20 weeks gestation with significant proteinuria and / or other maternal organ dysfunction [1]. Complications of pre-eclampsia can be severe and include eclampsia, HELLP syndrome, stroke, pulmonary oedema and fetal compromise such as intrauterine growth restriction and placental abruption [2]. It is thought that pre-eclampsia complicates 5-7% of pregnancies worldwide. Despite this the aetiology is currently not well understood but it is thought to involve abnormal placentation and remodelling of placental vessels [2].
Mortality over the years has significantly decreased through the use of increased antenatal surveillance, prenatal aspirin therapy in high risk patients, antihypertensive medications and timely delivery of the foetus [3]. However 16% of maternal deaths in higher income countries are still attributed to hypertensive disorders in pregnancy [2] highlighting the importance of their early recognition and ongoing education and research.
Here we report a case of a patient with classical features of pre-eclampsia at 15 weeks gestation which challenges the current diagnostic criteria of the disorder and leads to more questions about the aetiology as the placental development is also in early stages. We go on to discuss possible alternative diagnoses and present a literature review of similar cases.

The Case
A 37 year old multiparous Caucasian female presented to our district general hospital with headache, blurred vision, swelling of hands and feet and reported episodes of epistaxis. Urine pregnancy test was found to be positive. Bedside ultrasound examination revealed a live intrauterine pregnancy dated at 15 weeks gestation which was in keeping with the patient's reported last menstrual period.
Past medical history included obesity (BMI 42) but no other medical conditions. She was gravida 5 para 3. Two deliveries were at term caesarean sections. The most recent pregnancy had been complicated by severe hypertension manifesting from 15 weeks gestation and subsequent pre-eclampsia after 20 weeks. Due to clinical deterioration and uncontrolled hypertension, a caesarean section was performed at 25 weeks. Her clinical condition rapidly

Examination revealed a clinical picture of cardiac failure, she had normal reflexes and no clonus. Her BP was 240/155 mm/Hg and urinalysis showed significant proteinuria (>300 mg/dl). Laboratory investigations revealed anaemia (Hb 109), thrombocytopenia (Plt 63), AKI (Creatinine 160, eGFR 35). She had mild hyperbilirubinaemia [29], normal liver enzymes and synthetic function, LDH was raised (953). PCR (protein: creatinine ratio) was 1117.6. Blood film showed polychromasia of red cells with anisocytosis and spherocytosis which is consistent with microangiopathic haemolytic anaemia (MAHA) syndrome.

A bedside echocardiogram showed severe left ventricular hypertrophy with normal ejection fraction. Liver ultrasound scan was normal.

Treatment for severe pre-eclampsia was commenced including IV labetalol, IV magnesium sulphate and fluid restriction. Despite aggressive treatment her condition deteriorated and medical termination of pregnancy was agreed following extensive counselling. She remained under close observation in the intensive care unit but no organ support was required. Following delivery, her condition stabilised and at discharge her BP was stable on labetalol (116/75 mm/Hg) with blood parameters steadily improving. She received bereavement counselling and was strongly advised against any future pregnancy. Contraception choices were discussed.

At 6 month follow-up, blood results showed significant improvement in renal function with a creatinine of 94 and an eGFR of 67.

Discussion

Current understanding of the pathophysiology of preterm pre-eclampsia suggests the relatively ischaemic placenta appears to be the source of anti-angiogenic factors which disrupt maternal endothelium and the fenestration of glomerular capillaries. Women with hypertension in early pregnancy appear to be more sensitive to these circulating anti-angiogenic factors, tyrosine kinase-1 and soluble endoglin, consequently developing pre-eclampsia at lower concentrations of these factors [4]. This may be significant in this case as the patient had previously developed severe essential hypertension in pregnancy. Other recognised risk factors of pre-eclampsia in this case include high BMI, maternal age and a long term period between pregnancies

Given the abnormal blood film, other laboratory findings and the onset before 20 weeks differential diagnoses of atypical haemolytic uraemic syndrome (aHUS) and thrombotic thrombocytopenic purpura (TTP) were considered. Following discussions with renal physicians and leading experts in maternal medicine, a diagnosis of early onset fulminating pre-eclampsia was established. This was consolidated post-delivery with clinical and biochemical improvement. The table below compares how we can differentiate between these three conditions.

Table 1: a table comparing the differential diagnoses of pre-eclampsia, aHUS and TTP. MAHA: Microangiopathic haemolytic anaemia - characterised by schistocytes, anaemia and polychromasia on blood smears resulting from mechanical injury of red blood cells [5, 6, 7]

	Pre-eclampsia/HELLP	aHUS	TTP
Clinical presentation	▪ ↑BP ▪ Headache, visual disturbance, epigastric pain, peripheral oedema	▪ ↑BP less common ▪ Shortness of breath, fatigue, nausea	Neurological signs- headache, irritability, seizure, coma, bruising
Laboratory tests	▪ Anaemia, ▪ Thrombocytopenia ▪ Elevated transaminases ▪ Raised LDH ▪ MAHA ▪ Elevated PCR ▪ Renal function likely to be low or normal	▪ Anaemia ▪ Thrombocytopenia ▪ Raised LDH ▪ MAHA ▪ Renal function significantly impaired	▪ Thrombocytopenia ▪ MAHA ▪ Renal function likely to be low or normal ▪ Low ADAMTS13 ▪ ADAMTS13 autoantibody
Onset (If pregnancy associated)	>20 weeks	Most commonly immediately post natal	Most commonly third trimester
Management and disease progression	Resolves within 6 weeks of delivery	Without complement inhibitor therapy most progress to chronic kidney disease	Most require treatment with FFP and/or plasma exchange for clinical improvement
Cause	Anti-angiogenic factors disrupting maternal endothelium	Defective complement regulation	Antibody mediated depletion of the protease ADAMTS13- levels <10% is diagnostic
Renal biopsy	Glomeruloendotheliosis	Thrombosis within vessels and glomeruli	Thrombosis within vessels and glomeruli

Due to rapid onset of organ dysfunction requiring immediate treatment, tests for ADAMST13, Von Willebrand factor and autoantibodies were not carried out. However, it has been suggested that a platelet count >30 × 109/l and creatinine >150 µmol/l is satisfactory to exclude TTP [8]. Also a notable cohort study found that 86% of pregnant women with a diagnosis of aHUS went on to develop CKD with >50% requiring dialysis or a renal transplant [5]. Therefore, our diagnosis of pre-eclampsia was further strengthened by the notable improvement of renal function following delivery.

A literature search revealed 5 previously documented cases where pre-eclampsia was diagnosed prior to 20 weeks. The cases had hypertension and proteinuria at gestations ranging from 13 to 19 weeks and each one had multiple risk factors for pre-eclampsia. Of the cases, 2 had biochemical evidence of HELLP syndrome, 3 resulted in medical termination and 1 in delivery at 23+3/40. In all cases blood pressure and renal function improved following delivery [9-13].

In one of these cases, diagnosis was supported by a renal biopsy where microscopy demonstrated changes consistent with pre-eclamptic nephropathy [11]. A renal biopsy would help to differentiate between the previously considered diagnoses and a primary renal pathology. A renal cause had been considered in our case however renin: aldosterone ratios and urinary catecholamines were found to be normal and ultrasound showed no evidence of renal artery stenosis. Unfortunately a renal biopsy was not carried out as the patient was subsequently lost to follow up.

Conclusion

The literature so far has referred to cases such as these, occurring prior to 20 weeks, as atypical pre-eclampsia. The case

we present here is only the 6th documented presentation of this nature. A delay in recognition and treatment could lead to significant risk of maternal morbidity and mortality. Therefore we hope this case report will raise awareness of early onset pre-eclampsia and the importance of a multidisciplinary approach in the management of similar cases.

Acknowledgements
We would like to thank the patient who provided their consent for the writing of the article. There was no funding sought or given to this work. The authors report no conflict of interest.

References

1. National Institute for Health and Care excellence. CKS is only available in the UK [Internet]. NICE; c2022. Available from: https://cks.nice.org.uk/topics/hypertension-in-pregnancy/management/pre-eclampsia/ [Accessed 29th November 2023].
2. American College of Obstetricians and Gynecologists. Gestational Hypertension and Preeclampsia. Obstetrics & Gynecology. 2020 Jun;135(6):e237-60.
3. Rana S, Lemoine E, Granger J, Karumanchi SA. Preeclampsia: Pathophysiology, challenges, and perspectives. Circulation Research. 2019 Mar 29;124(7):1094-112. Available from: https://www.ahajournals.org/doi/10.1161/CIRCRESAHA.118.313276
4. Williams D. Long-Term Complications of Preeclampsia. Seminars in Nephrology. 2011 Jan;31(1):111-22. [Accessed 29th November 2023].
5. Gaggl M, Aigner C, Csuka D, Szilágyi Á, Prohászka Z, Kain R, *et al*. Maternal and Fetal Outcomes of Pregnancies in Women with Atypical Hemolytic Uremic Syndrome. Journal of the American Society of Nephrology. 2017 Dec 27;29(3):1020-9.
6. Goodship THJ, Cook HT, Fakhouri F, Fervenza FC, Frémeaux-Bacchi V, Kavanagh D, *et al*. Atypical hemolytic uremic syndrome and C3 glomerulopathy: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney International. 2017 Mar;91(3):539-51.
7. Nelson-Piercy C. Handbook of obstetric medicine. Boca Raton: Crc Press, Taylor & Francis Group; c2015.
8. Coppo P, Schwarzinger M, Buffet M, Wynckel A, Clabault K, Presne C, *et al*. Predictive Features of Severe Acquired ADAMTS13 Deficiency in Idiopathic Thrombotic Microangiopathies: The French TMA Reference Center Experience. Morty RE, editor. PLoS ONE. 2010 Apr 23;5(4):e10208.
9. Maya ID. Hypertension and Proteinuria in a 17-Year-Old at 19 Weeks' Gestation. American Journal of Kidney Diseases. 2008 Jan 1;51(1):155-9.
10. Imasawa T, Nishiwaki T, Nishimura M, Shikama N, Matsumura R, Nagai M, *et al*. A Case of Pure Preeclampsia with Nephrotic Syndrome Before 15 Weeks of Gestation in a Patient Whose Renal Biopsy Showed Glomerular Capillary Endotheliosis. 2006 Sep 1;48(3):495-501.
11. Thomas W, Griffiths M, Nelson-Piercy C, Sinnamon K. Pre-eclampsia before 20-week gestation: diagnosis, investigation and management. Clinical Kidney Journal. 2012 Oct 15;5(6):597-9.
12. Zhu Y, Sun Y, Yang H. Chronic hypertension superimposed on preeclampsia at 13 gestational weeks: a case report with review. PubMed. 2012 Jun 1;125(11):2067-9.
13. Hazra SK, Waugh J, Bosio P. Pure pre-eclampsia before 20 weeks of gestation: a unique entity. BJOG: An International Journal of Obstetrics and Gynaecology. 2003 Nov 1;110(11):1034-5.

How to Cite This Article
Darling H, Penney E. Fulminating pre-eclampsia at approximately 15 weeks gestation: A Case Report. International Journal of Clinical Obstetrics and Gynaecology 2023; 7(6): 92-94