Severe early-onset preeclampsia associated with autoimmune hypothyroidism

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Background

Thyroid dysfunction is linked to vascular complications, mediated in part by endothelial cell damage.[1] Overt hypothyroidism in pregnancy, while rare, is associated with an increased risk of severe obstetric complications, including preeclampsia-like syndrome, intrauterine growth restriction and placental abruption.[2,3] In turn, there is evidence to suggest that pre-eclampsia may worsen coexisting hypothyroidism,[4] thereby further increasing the risk of adverse pregnancy outcome. Proposed mechanisms include dysregulation of placental type III deiodinase and reduced absorption of oral thyroxine replacement therapy through preeclampsia-mediated gut oedema.[4]

Case

A 32-year-old primigravida with known autoimmune hypothyroidism presented with headache and peripheral oedema at 23+1/40. An elevated BP of 164/94 mmHg and significant proteinuria (urine PCR 168g/mol) suggested early onset preeclampsia. Examination demonstrated ankle oedema with no hyperreflexia, clonus, or abdominal tenderness. Blood pressure control was challenging, requiring triple antihypertensive therapy with titration over a two week period to labetalol 300mg QID, methyldopa 500mg TDS and nifedipine 30mg MR OD. Worsening peripheral and facial oedema and abdominal ascites on ultrasound were noted. Reflexes remained normal, and other than lethargy, the patient was asymptomatic. Investigations for alternate causes of severe hypertension were unremarkable (table 3) and a high sFlt-1/PlGF ratio of 498 (ref < 38) was consistent with severe preeclampsia. It is proposed high sFlt-1/PlGF ratio can also be predictive of adverse fetal outcome.[5]

Table 1. Antenatal history

G1P0
Phx PCOS, hypothyroidism (anti TPO pos) – dx 3 years prior, booking TSH normal on thyroxine 150mcg OD
Booking BMI 26
Rh negative, nil antibodies
Declined aneuploidy screening
Serology negative
Gestational diabetes – early OGTT 17/40, diet controlled
Dating US at 9/40
T2 US 22/40 - Morph NAD, placenta clear, EFW 21st%

Table 2. Basic Investigations

	23/40	26/40
Hb	113 g/L	114 g/L
Platelets	**109 x10^9/L**	**105 x 10^9/L**
Creatinine	38 umol/L	55 umol/L
LFT	ALT 17 U/L	ALT 21 U/L
Urate	**0.38 mmol/L**	**0.45 mmol/L**
Urine PCR	**168 g/mol**	**2623 g/mol**
TSH	**6.63 mIU/L**	**116mIU/L** (ref. 0.09-4.1)
Free T4	9.7 pmol/L	**6.7 pmol /L**(ref 8.3-17.2)
T3	-	**2.5 pmol/L** (ref 4.3 - 8.1)

Table 3. Differential diagnoses investigations

Renal tract US	NAD incl. doppler
Autoimmune screen	Negative
Urine/serum metanephrines	Within normal limits
24-hr urinary cortisol	Within normal limits
sFlt-1/PlGF ratio	**498** (ref < 38)

Table 4. Growth Ultrasounds

23+2	25+2
EFW 555g 31st%	**EFW 648g 6th%**
AC 29th%, HC 21st%	**AC 5th%, HC < 5th%**
UAPI 1.6 (>95th%)	**UAPI 2.14 (off ref. chart)**
Normal MCA PI and CPR	**CPR 0.63 < 5%**
Normal AFI	Ductus venosus normal
	Normal AFI

The thyroxine dose was initially increased by 20% due to high TSH with normal T4. Despite this, thyroid function rapidly deteriorated, with TSH progressing up to 116 mIU/L, and T4/T3 reaching nadirs of 6.7 / 2.5 pmol/L. High dose thyroxine replacement 600mcg daily and liothyronine (T3) 10mcg BD improved TSH to 9 mIU/L and T4 and T3 into normal range. IV thyroxine was not available. Serial ultrasounds showed plateauing fetal growth with early onset symmetrical growth restriction at 25+2/40. Dopplers progressively worsened to show intermittent absent end diastolic flow, triggering transfer to an interstate tertiary centre at 26+3/40. Repeat US showed new persistent reversal of end-diastolic flow, triggering delivery via classical caesarean section at 27/40. The female infant weighed 680g (< 3rd%) and required prolonged admission due to complications of prematurity and IUGR. By four weeks adjusted age she weighed 2.7kg and was doing well. Maternal antihypertensives and thyroxine were weaned over the first month postpartum.

Discussion

Of the few case reports of preeclampsia associated with overt hypothyroidism, most describe early intrauterine fetal demise as thyroid function worsens. In this case, multidisciplinary collaboration between with the Obstetrics and Gynaecology and Endocrinology teams with input from interstate Maternal-Fetal-Medicine allowed stabilisation beyond a viable age. Complex mechanisms link thyroid dysfunction and hypertensive disease and optimising both conditions simultaneously is essential in management.

1. Wilson KL. Subclinical thyroid disease and the incidence of hypertension in pregnancy.Obstet Gynecol 2012;119:315–20.
2. Inversetti A. Severe hypothyroidism causing preeclampsia like syndrome. Case report in Endocrinology. 2012:586056.
3. Alfadda A. Preeclampsia-like syndrome that is associated with severe hypothyroidism in a 20-week pregnant woman. Am J Obstet Gynecol 2004; 191: 1723-1724.
4. Adu-Gyamfi E. The interplay between thyroid hormones and the placenta: a comprehensive review, Biology of Reproduction 2019.
5. Bian X. Short-Term Prediction of Adverse Outcomes Using the sFlt-1/PlGF Ratio in Asian Women with suspected Preeclampsia, Hypertension 2019; 74: 164-172.