MATERNAL GRAVES DISEASE WITH FETAL THYROTOXICOSIS AND GOITRE

The National Maternity Hospital
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Background

- Graves' disease (GD) is uncommon, affecting approximately 0.2% of pregnancies.
- Fetal and neonatal thyrotoxicosis occurs in between 1-5% of patients with active or prior GD, typically beyond 20 weeks gestation, and can cause serious morbidity and mortality.
- Trans-placental passage of maternal TSH-receptor antibodies (TRAb) stimulates the fetal thyroid to cause hyperthyroidism, typically in those with TRAb levels >3X upper limit of normal.
- Signs identifiable on ultrasound include fetal tachycardia, goitre, intrauterine growth restriction, accelerated bone maturation, oligo/polyhydramnios, cardiac failure, fetal hydrops, and fetal demise.
- Maternal TRAb is recommended in the first trimester, with repeat at 18-22 weeks gestation if elevated. Ultrasound surveillance is recommended in the second half of pregnancy to monitor for signs of fetal thyrotoxicosis in those with elevated TRAb levels.
- Clinical response to treatment is monitored by measuring fetal heart rate and goitre size, with targets aimed at normalising fetal heart rate (110-160bpm). The lowest effective dose of medication to normalise fetal heart is used.

Case

- A 34-year-old female was referred at 21+2 weeks gestation from another hospital due to concerning cardiac findings noted on routine prenatal ultrasound.
- Her medical history was significant for TRAb positive GD with moderate thyroid ophthalmopathy and total thyroidectomy ten months previously due to uncontrolled thyrotoxicosis, with resultant hypothyroidism, on L-thyroxine 150mcg daily.

- Upon presentation to our centre, fetal tachycardia of 170-180bpm was noted. (Fig 1)
- Ultrasound (US) scan showed fetal right ventricular hypertrophy and pericardial effusion (Fig 2), as well a neck mass measuring 1.9 x 2.7 x 2.8cm, strongly suspicious for fetal goitre. (Fig 3)
- Maternal laboratory studies: TSH 2.38mIU/L (0.27-4.2), free T4 16.0pmol/L (12-22), TPO antibody negative <3.0IU/ml, TRAb markedly elevated >30IU/L (0-1.8).
- Following multidisciplinary discussion, a diagnosis of fetal thyrotoxicosis secondary to placental passage of stimulating maternal TRAb was made, with resultant fetal goitre and cardiac dysfunction.
- The patient was commenced on high dose carbimazole (20mg BD) at 21+6 weeks gestation.
- Weekly follow-up with US scanning showed interval improvement, with resolution of pericardial effusion and fetal heart rate normalisation.
- Maternal TFTs were closely monitored and she remained euthyroid on an increased dose of L-thyroxine (200 micrograms daily).
- Concern was expressed regarding the size of the fetal goitre and risk for airway obstruction at delivery.
- Following multidisciplinary discussion, Caesarean section was performed at 34 weeks gestation and a healthy male infant was born, with spontaneous breathing and normal heart rate at delivery, and Apgar scores of 9 and 9 at 1 and 5 minutes.

Outcome and Follow-up

- Maternal carbimazole was immediately discontinued post-delivery and L-thyroxine dose reduced to 150 micrograms daily. She had an uncomplicated course post Caesarean section.
- The baby was closely monitored in the neonatal intensive care unit (ICU). He became unwell on day 5 of life, developing a supraventricular tachycardia, with thyrotoxicosis confirmed on laboratory studies (Free T4 >100pmol/L).
- Carbimazole, propranolol and lugol's iodine were all used to treat the infant and thyroid hormone levels normalised within days, with gradual clinical improvement.
- He was discharged home well four weeks after birth, remaining on propranolol 0.3mg four times daily and carbimazole 0.5mg twice daily, with close paediatric outpatient follow-up.

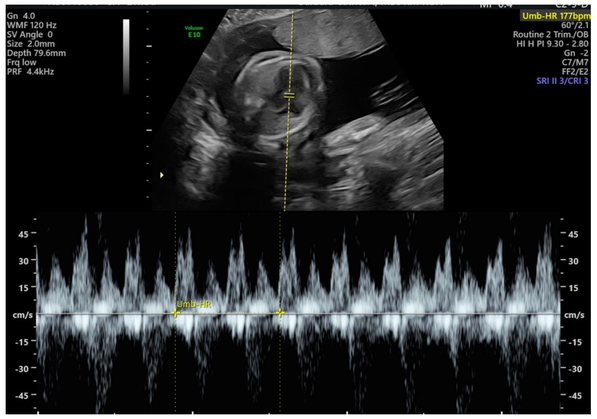

Fig 1. Doppler study showing fetal tachycardia 177bpm

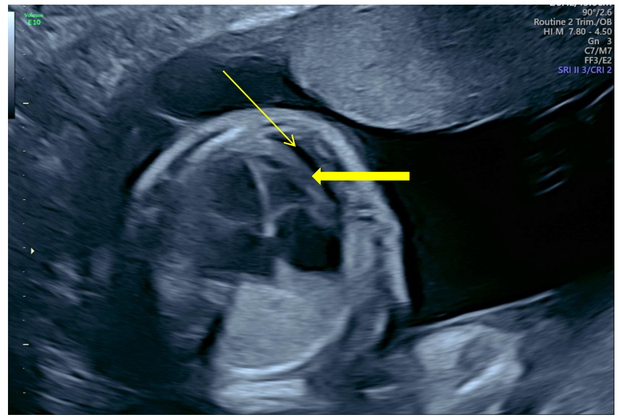

Fig 2. Fetal cardiac ultrasound showing pericardial effusion (thin arrow) and thickened right ventricular wall (thick arrow)

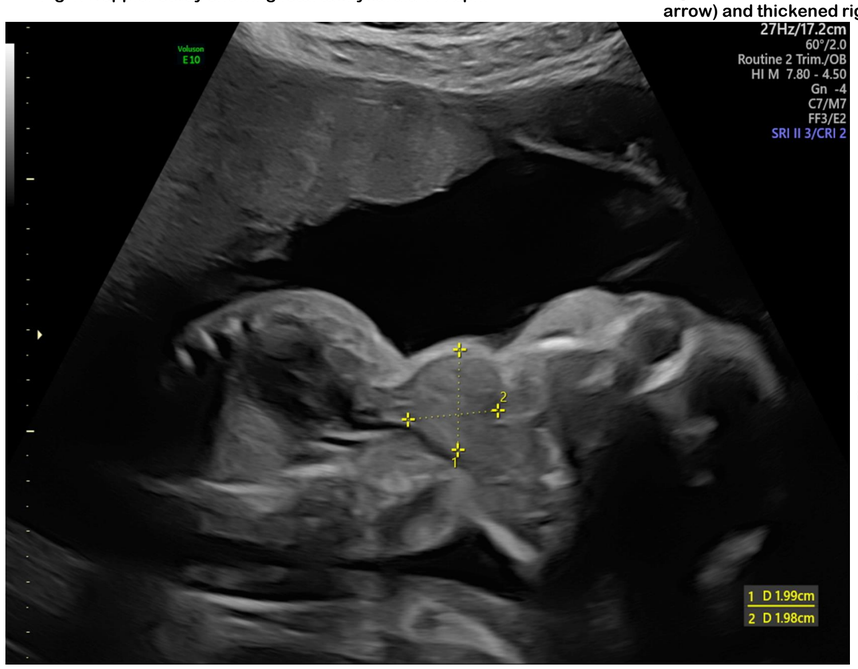

Fig 3. Ultrasound showing fetal neck mass with size indicated by yellow markings

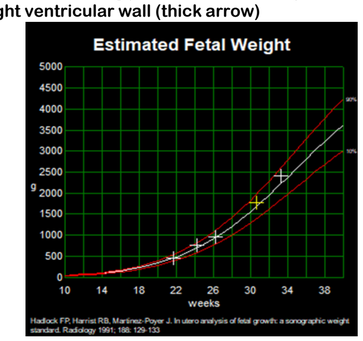

Fig 4. Estimated fetal weight chart showing good interval growth during period of treatment

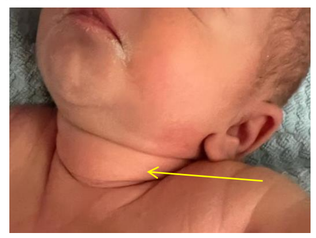

Fig 5. Image of neonatal goitre (arrow), taken post delivery

Conclusion

- Fetal thyrotoxicosis is an uncommon condition, though it is an important diagnosis to consider in patients with a personal history of thyrotoxicosis who present with fetal tachycardia and/or cardiac complications in utero
- Pre-conceptual counselling is important for all prospective mothers with history of hyperthyroidism
- While thyroidectomy can be employed as definitive management for GD, this case reminds us that circulating TRAb levels may remain high for prolonged periods post-operatively and this can have important and serious complications when patients are planning pregnancy
- The management of this condition is complex and requires specialist input across multiple disciplines including maternal medicine, endocrinology, neonatology, radiology and cardiology.