Successful pregnancy outcome in a woman with Turner's syndrome

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Abstract

Women with Turner's syndrome have a high incidence of cardiovascular complications, endocrine and hypertensive disorders. Those with the 45X chromosome complement require oocyte donation and in vitro fertilisation to conceive. Pregnancies in such women are challenging to manage due to the high risk of pregnancy-related hypertensive disorders, impaired glucose tolerance, fetal growth restriction and preterm birth. Women also need to be aware of the significant risk of aortic dilatation, dissection or rupture in pregnancy, which may be fatal. Despite these risks, favourable obstetric outcomes are achievable with careful pre-pregnancy counselling and cardiovascular assessment, intensive multidisciplinary antenatal monitoring and individualised delivery planning. We report the case of a 33-year-old woman with Turner's syndrome, pre-existing hypertension, insulin-dependent diabetes and primary hypoparathyroidism who had a successful pregnancy with good maternal and fetal outcomes despite the complexity of her medical conditions.

Keywords

High-risk pregnancy, diabetes, hypertension, infertility, Turner's syndrome

Case report

A 33-year-old woman diagnosed with Turner's syndrome in childhood became pregnant after five cycles of in vitro fertilisation (IVF) with donor oocytes. She suffered from recurrent ear infections as a child, necessitating an adenoidectomy and myringotomy aged four. Karyotyping performed at the age of 10 due to short stature (126 cm) revealed monosomy 45X. She received growth hormone until the age of 16 to induce adult height. Oestradiol was commenced at age 13 to stimulate puberty, then switched to combined sequential hormone replacement therapy to protect the endometrium and induce progesterone withdrawal bleeds. Cardiac imaging revealed a small sub-aortic membrane with no significant gradient across the left ventricular outflow tract (peak of 12 mmHg only), good left ventricular function and no coarctation or dilatation of the aorta. She attended for annual echocardiogram and cardiology review and remained asymptomatic. She was admitted to hospital with persistent vomiting aged 22, found to be in diabetic ketoacidosis and diagnosed with type 1 diabetes. At the age of 27, she developed hypertension which was treated with lisinopril. She attended for pre-pregnancy counselling aged 28. Her height was 153 cm, weight 62 kg and BMI 26. Her antihypertensive medication was changed to methyl dopa, as angiotensin-converting enzyme inhibitors are contraindicated in pregnancy. She commenced folic acid 5 mg daily. With the support of the diabetes team over the next four years, she reduced her HbA1c from 8.4% to obtain optimal glycaemic control with a continuous subcutaneous insulin pump. She also underwent laser treatment for diabetic retinopathy.

Her fifth IVF cycle was successful and supported by oestradiol, progesterone, prednisolone, aspirin and low-molecular-weight heparin (LMWH). She received intralipid infusions on days 4–9 of her IVF treatment protocol in a research context, as investigations for recurrent implantation failure showed high levels of natural killer cells. As she had recurrent implantation failure, prophylactic dose LMWH was also continued along with high-dose folic acid due to her diabetes and low-dose aspirin as pre-eclampsia prophylaxis. Excellent glycaemic control was maintained with the insulin pump. First trimester and anomaly scans were normal. She was reviewed regularly in both the combined cardiac and combined diabetic antenatal clinics. Retinal screening and echocardiography were performed each trimester with no evidence of dilatation of the aortic root. She developed primary hypoparathyroidism which was treated with calcium and vitamin D supplements. Fetal growth was assessed by ultrasound at 28 and 32 weeks with the estimated fetal weight following the 90th centile for gestational age. At 30 weeks, her methyl dopa requirement had increased from 250 mg to 1 g twice daily, and she had moderate peripheral oedema. Intramuscular

betamethasone was administered for fetal lung maturation under sliding scale insulin cover. At 34 weeks, she experienced frequent hypoglycaemic episodes and worsening hypertension, and with the baby presenting breech, the decision was made to deliver by elective Caesarean section. A healthy baby girl was delivered weighing 2580 g. Postnatally, mother and baby were well, breast feeding established and combined hormone replacement therapy recommenced. Her postnatal echocardiogram remained normal. She will continue to have lifelong endocrinology and cardiology follow-up.

Discussion

Turner's syndrome is named after Dr Henry Turner, an American endocrinologist who described the syndrome in 1938. It affects 1 in 2000 live born females. Many more affected pregnancies miscarry spontaneously at early gestations.¹ Turner's syndrome can be detected prenatally, by karyotyping usually performed when a cystic hygroma (septated fluid collection due to lymphoedema) is seen on first trimester ultrasound. The most common karyotype, 45X occurs secondary to nondisjunction at meiosis. There may be few features present at birth; so unless there are signs of coarctation of the aorta, most present in childhood. Clinical features include short stature, broad or shield chest, low posterior hair line, webbed neck and a wide carrying angle (cubitus valgus). Children with Turner's syndrome may also have recurrent ear infections. Those with 45X Turner's syndrome have streak ovaries with no follicles (due to accelerated follicle atresia in fetal life and infancy), thus hypergonadotrophic hypogonadism. They may present with primary amenorrhoea and absence of secondary sex characteristics.² Treatment with growth hormone and then oestrogen replacement is required to induce puberty and obtain adult height, and then combined hormone replacement therapy is continued long term. However, up to 50% have mosaic karyotypes such as 45X/46XX (numerous others exist), and therefore may not display the classic features. If there are any follicles present in the ovaries, they may have spontaneous puberty, then secondary amenorrhoea or premature menopause. In these women, natural conception may occur in 1–2%

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although there is a high incidence of miscarriage and chromosomal abnormalities.³ Careful contraceptive counselling is required to avoid unintended pregnancy, given the risk of serious cardiovascular complications.

Adult women with Turner's syndrome have a normal IQ but often have multiple medical conditions.¹ Coarctation of the aorta only affects 10%, with other cardiac problems such as a bicuspid aortic valve (15%) and aortic dilatation (8–42%) being more common. These women in particular are at risk of aortic dissection or rupture. Up to 50% develop hypertension, and many have autoimmune conditions such as diabetes, hypothyroidism or vitiligo. One-third may have a horseshoe kidney or abnormal collecting system. Long-term risks include osteoporosis and premature menopause. Women with 45X Turner's syndrome require donor oocytes and IVF to conceive. They should have a careful cardiovascular assessment and be screened for the above medical conditions prior to fertility treatment as these are high-risk pregnancies. Hypertensive disorders are common with at least double the risk of pre-eclampsia.^{4,5} Women may have pre-existing hypertension and diabetes, are likely to be primigravid and in combination with IVF have multiple risk factors for pre-eclampsia. Low-dose aspirin should be offered to reduce this risk.⁶ The most concerning risk for the mother is aortic dilatation, dissection or even rupture, which can be fatal. The risk is exacerbated by hypertension, increased in pregnancy (particularly in the third trimester and postpartum), and a maternal mortality rate of 2% has been reported.^{5,7} Although the risk of dissection is highest in those with a bicuspid aortic valve or coarctation of the aorta, it may occur in those with a structurally normal heart, at a younger age (mean 31 years) and at smaller aortic diameters than the general population; thus, regular cardiovascular assessment is required in pregnancy and throughout life.^{5,8–11} Aortic root diameters vary with age, sex and body surface area, thus appropriate nomograms should be referred to.^{12,13}

Mode of delivery is debatable, but the chances of operative intervention are high due to concerns regarding short stature, small pelvis, prematurity and growth restriction.^{3,4,11,14} However, one recent case report describes a woman with no associated medical conditions, who did not develop any obstetric complications and had an instrumental delivery of an appropriately grown baby at term.¹⁵

Conclusion

This case, along with several recently published papers^{4,15} demonstrates that favourable maternal and fetal outcomes are achievable in pregnant women with Turner's syndrome despite the significant risks posed by their associated medical conditions. Detailed pre-pregnancy counselling and cardiovascular assessment are vital, in addition to individualised, intensive multidisciplinary antenatal monitoring and delivery planning.

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Declaration of conflicting interests

None declared.

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Ethical approval

Written consent has been obtained from the patient.

Guarantor

EC.

Contributorship

EC, AB, IO and NN were all responsible for the care of the woman, and all contributed towards the writing and editing of the case report.

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