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Prenatal Diagnosis and Fetal Sonographic Features of Swyer Syndrome

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Abstract

Swyer syndrome, also known as complete gonadal dysgenesis, is characterized by an individual who has an XY karyotype but is phenotypically female. It is typically diagnosed in adolescence after investigations for primary amenorrhea. The estimated prevalence is 1 in 20,000 to 80,000 births. Mutations in the DNA-binding region of the SRY gene account for approximately 15 to 20% of cases, with the remaining cases caused by other gene mutations. There are no reports of the established diagnosis of Swyer syndrome prenatally, or of the sonographic features that may be associated with it. This report outlines the details of a 33-year-old primigravida in whom a fetal cystic hygroma was noted on ultrasound at 12 weeks gestation. Chorionic villous sampling revealed a diagnosis of fetal Swyer syndrome. The fetus progressed to develop severe fetal hydrops and a parental decision for termination of pregnancy was made at 15 weeks of gestation.

Keywords
- prenatal testing
- Swyer syndrome
- fetal hydrops

Introduction

Swyer syndrome, also known as complete gonadal dysgenesis, is a rare disorder of sex development. It is characterized by an individual who is phenotypically female but has an XY karyotype. This syndrome is predominantly diagnosed because of delayed puberty in adolescent females and is often revealed after investigation of primary amenorrhea. Its prevalence is estimated as being between 1 in 20,000 and 80,000 births. Mutations in the DNA-binding region of the SRY gene account for approximately 15 to 20% of cases, with the remaining 80 to 85% of cases caused by other gene mutations (Map3K1, NROB1, and DEAH37). To our knowledge, there are no reports of the established diagnosis of Swyer syndrome prenatally, or of the sonographic features that may be associated with it.

Case Presentation

A 33-year-old primigravida was seen for antenatal booking at $12^{2/7}$ weeks gestation. She had no relevant past medical or surgical history. A first-trimester ultrasound scan was performed that demonstrated a singleton intrauterine pregnancy with a crown-rump length of 67.7 mm, consistent with her menstrual dates. A cystic hygroma was noted with nuchal translucency thickness that measured 8.8 mm (as shown in ►**Fig. 1**). She was referred to our tertiary maternal–fetal medicine unit for further assessment and investigation and was seen there at $12^{6/7}$ weeks gestation. She was counseled about invasive genetic testing and chorionic villous sampling was performed. A TORCH (toxoplasmosis, rubella, cytomegalovirus, herpes simplex, and human immunodeficiency virus) screen was performed.

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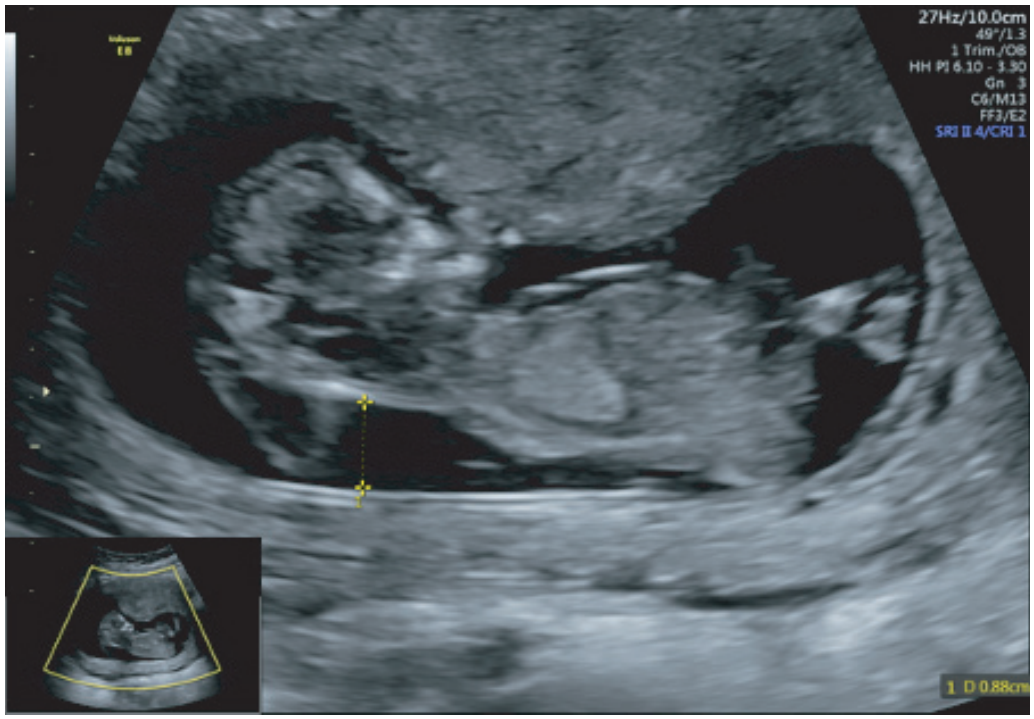

Fig. 1 Ultrasound performed at $12^{1/7}$ weeks gestation demonstrating a singleton intrauterine pregnancy with a cystic hygroma.

The result from the prenatal array comparative genomic hybridization study and chromosome studies was received 1 week later and demonstrated array-CGH karyotype arr [GRCh37]Yp11.32p11.2(2410188_6592914)x0 and fetal karyotype 46,Xdel(Y)(p11.32p11.2), a SRY gene mutation consistent with a diagnosis of Swyer syndrome (as shown in ►**Fig. 2**). The result of the TORCH screen was negative.

The patient was reviewed with her partner at $14^{1/7}$ weeks gestation and she was counseled regarding the diagnosis and its implications. A further ultrasound scan at this gestation

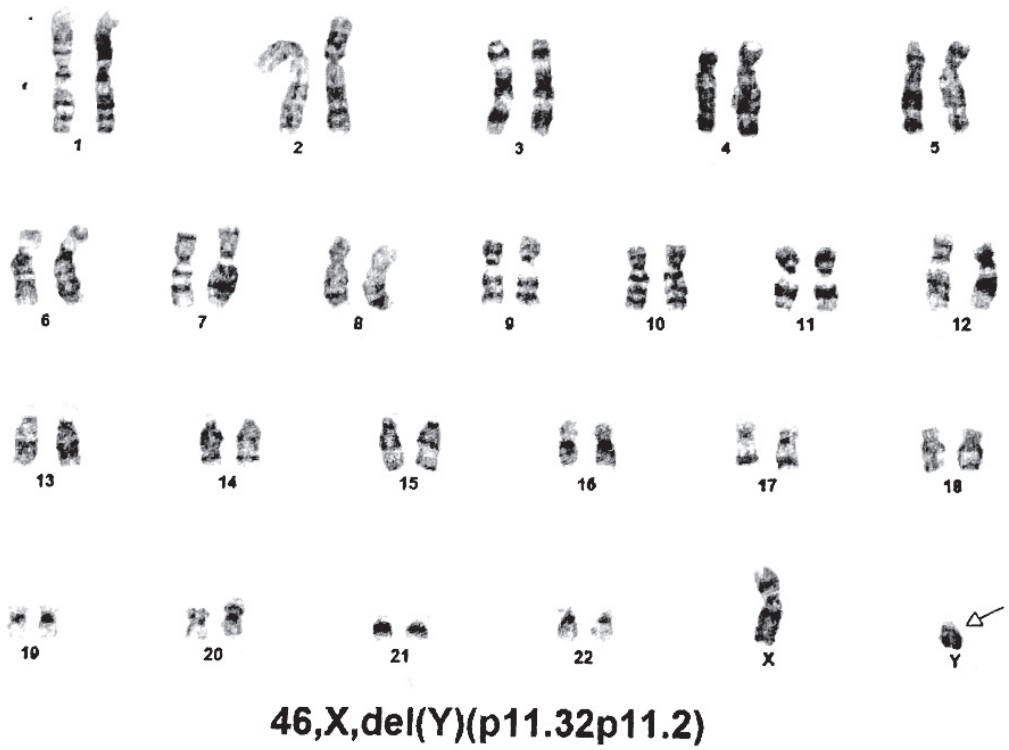

Fig. 2 Karyotype of the fetus from chorionic villous sampling cell culture.

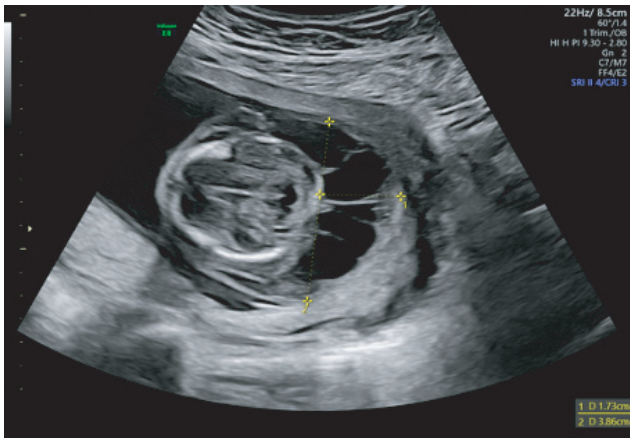

Fig. 3 Cystic hygroma at 14 + 1 weeks gestation.

demonstrated a live pregnancy with fetal hydrops and cystic hygroma (as shown in ►**Fig. 3**). The couple were counseled in relation to all of their options for this pregnancy. On further review at $15^{5/7}$ weeks gestation, there was a deterioration in the findings which were indicative of severe fetal hydrops. This included bilateral pleural effusions, pericardial effusion, abdominal ascites, and skin edema (as shown in ►**Fig. 4**). The woman and her partner requested termination of pregnancy because of the poor prognosis. After counseling regarding different methods for this procedure, it was duly performed using mifepristone and misoprostol at 16 weeks gestation. The option of pathological examination of the fetus was declined. The couple was reviewed for follow-up in the maternal–fetal medicine clinic 8 weeks post termination of pregnancy. Genetic counselling was advised prior to any further pregnancies. Parental karyotyping was performed at this visit. This revealed a normal chromosome complement and banding pattern for both parents, and in particular, there was no evidence of a rearrangement involving a sex chromosome. This would, therefore, indicate that recurrence is highly unlikely and this anomaly likely arose from a de novo mutation.

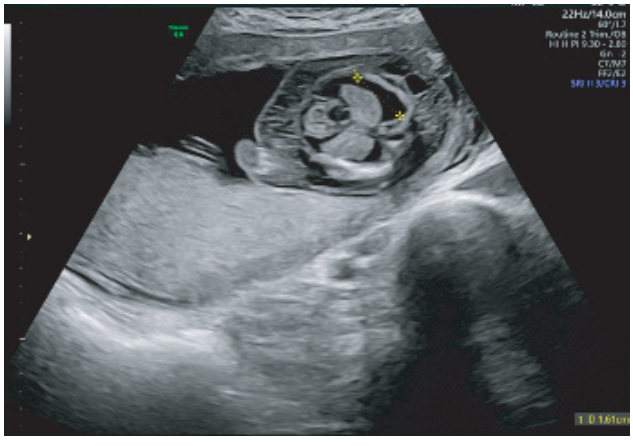

Fig. 4 Worsening fetal hydrops at 15 + 5/40.

Discussion

A diagnosis of cystic hygroma in the first trimester is associated with a 66% risk of chromosomal abnormality, which is most commonly Trisomy 21 followed by Trisomy 18.[1] It is also well established that cystic hygroma is associated with Turner syndrome,[2] which is another form of gonadal dysgenesis. In this case, fetal karyotyping revealed an unexpected diagnosis of Swyer syndrome by the detection of a mutation in the SRY gene. The SRY gene is a sex determining region of the Y chromosome and is critical to testicular development in early embryonic life. In Swyer syndrome, the fetus has a 46XY karyotype with a mutation in the SRY gene, and hence testicular formation does not occur, antimullerian hormone is not produced, and this results in a female phenotype.

The diagnosis of Swyer syndrome is generally made in adolescence[3] and occasionally in childhood as a coincidental finding on cytogenetic analysis. While this case outlines the established diagnosis of Swyer syndrome in the first trimester, it is notable that such a diagnosis was established postnatally in a case that involved gender discrepancy on noninvasive prenatal testing (NIPT). In this case report, NIPT was performed and reported as a male fetus; however, on ultrasound a female fetus was visualized.[4] Due to the rarity of this condition, and the lack of knowledge of its natural prenatal course, there were significant challenges in relation to parental counseling regarding potential outcomes for the fetus. Expert counseling from a pediatric endocrinologist was arranged. In the interval of time from 12 to 15+ weeks of gestation, it was apparent that the fetus became severely hydropic, and the couple opted for termination of pregnancy. The onset of severe hydrops was of assistance to the couple in making this decision. In general, the prenatal diagnosis of Swyer's syndrome raises ethical tissues in relation to the termination of pregnancy for a condition where there may be future reproductive issues but no structural or systemic abnormalities otherwise.

This case raises the possibility that cystic hygroma may be a fetal sonographic feature of other sex development disorders apart from Turner syndrome. It raises questions about the natural prenatal course of Swyer syndrome, and the fact that there may be a natural loss rate in utero. Finally, the sonographic features of prenatal Swyer syndrome are outlined in this case report, highlighting that it may be another cause of nonimmune fetal hydrops.

Implications for Clinical Practice

- This case raises the possibility that cystic hygroma may be a sonographic feature of other sex development disorders apart from Turner syndrome
- Prenatal diagnosis of Swyer syndrome raises ethical issues in relation to termination of pregnancy for a condition where there may be future reproductive issues but no structural or systematic abnormalities otherwise.
- The sonographic features of prenatal Swyer syndrome are outlined in this case report, highlighting that it may be another cause of nonimmune fetal hydrops.

Consent
Informed written consent was obtained from the patient for this case report.

Note
This case report was written in accordance with the amended Declaration of Helsinki.

Authors' Contributions
DTK wrote the case report and attended to the patient. MD and ALB contributed to the writing of the manuscript and attended to the patient. JM contributed and supervised the writing of the manuscript and also attended to the patient.

Consent to Publish
Written informed consent was obtained from the patient for publication of this case report and any accompanying figures/images.

Ethical Approval
Ethical approval was not required from our institution.

Conflict of Interest
The authors have no conflicts of interest to declare.

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