Case Report

Prenatal Phenotyping of Fetal Congenital Adrenal Hyperplasia: Applying the Prader Scale to a Fetus

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Abstract

Here, we present a 30-week-old female fetus with congenital adrenal hyperplasia. Target fetal ultrasound rated the degree of virilization according to the Prader scale. This report illustrates the subtle fetal genitalia assessment of a fetus with variations of sex development, such as vaginal atresia and abnormal curse of the urethra in the case of urogenital sinus. To the best of our knowledge, this is the first report describing the prenatal range of virilization of external and internal genitalia.

Keywords: Congenital adrenal hyperplasia, fetal, Prader scale, prenatal, ultrasound

Introduction

Congenital adrenal hyperplasia is an autosomal recessive condition caused by CYP21A2 gene mutations responsible for 21-hydroxylase deficiency. It is characterized by reduced production of cortisol and aldosterone. The accumulation of cortisol precursors is responsible for the virilization of the genitalia as a prenatal manifestation.[1] Here, we present a 30-week-old female fetus with congenital adrenal hyperplasia. Target fetal ultrasound rated the degree of virilization according to the Prader scale.

Antenatal Findings

A healthy French nulliparous woman was initially referred to our fetal medicine unit because of an unusual aspect of the external genitalia detected at the second-trimester ultrasound screen. We performed serial ultrasound examinations Iglika Simeonova-Brachot (ISB), using general electric medical systems, Zipf, Austria ultrasound machine, and a RM7C 2–7-MHz curved array transducer. The level III obstetric ultrasound at 24 weeks confirmed the variations in sex development. The study of the external genitalia showed a genital tubercule at 16 mm and empty and fused urogenital folds. Fetal anogenital distance was 10 mm, which corresponded to the 75th percentile for a girl and the 5th percentile for a boy.[2] The adrenals were homogeneous, but their height was >95th percentile.[3] The fetal uterus was well visualized in the fetal pelvis between the bladder and the rectum. Amniocentesis was performed. Array CGH was normal, with female karyotype. The amniotic fluid sample found an elevation of 17-hydroxyprogesterone level. The genetic analyses revealed severe bi-allelic mutations in the CYP21A2 gene.

Detailed level III ultrasound focused on the pelvic structures as well as the perineal region and the entire urinary tract at 30 weeks, showed complete fusion of the labia and severe clitoromegaly with length at 20.6 mm [Figure 1a and b]. The fetal uterus had a normal appearance 21 mm long by 7 mm wide [Figure 2a and b]. We found a short and hypoplastic vagina [Figure 2c] in contrast to the normal fetal vagina, which represents a hypoechoic structure, parallel to the rectum and prolonged to the perineum [Figure 2d]. A single urethral-like orifice was observed during fetal urination; it opened at the base of the clitoris and corresponded to a urogenital

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sinus [Figure 2e]. The fetal anatomy matched the stage 3–4 of the Prader Scale.

The patient and her partner received information from a pediatric endocrinologist, a medical geneticist Pascaline Letard (LP), and an experienced pediatric surgeon Marie Auger-Hunault (AM). The parents were informed about all surgical options, including restoring functional anatomy by surgery repair of the urogenital sinus and the possibilities of delaying surgery. The parents also received psychological support.

Postanatal Findings

The newborn was assigned female at birth. She receives postnatal treatment with hydrocortisone, fludrocortisone, and sodium chloride supplementation.

Postnatal physical examination assessment of the external genitalia [Figure 3a and b] found highly pigmented, thick-skinned, and transversely striated labia. There was almost complete labial fusion. There was a single urogenital opening at the base of the clitoris and an enlarged and curved genital tubercule measured 2 cm. The postnatal phenotype corresponded to stage 3 of the Prader Scale. Postnatal ultrasonography demonstrated two enlarged adrenal glands with a specific "cerebriform pattern" of congenital adrenal hyperplasia, uterine fluid accumulation, localized the right ovary in the abdominal cavity, and confirmed the presence of a vagina. Noncontrast pelvic magnetic resonance imaging (MRI) examination [Figure 3c and d] was performed using 3T magnet and a dedicated phased-array surface coil at 8 months under sedation. The urethra length was measured as the distance between the bladder neck and urogenital confluence at 13 mm. Higher termination of the vagina was slightly above the level of the distal end of the pubis [vagina type 2, Figure 3c]. The spatial resolution of the urethral meatus made it impossible to distinguish between Prader 3 or 4 classifications.

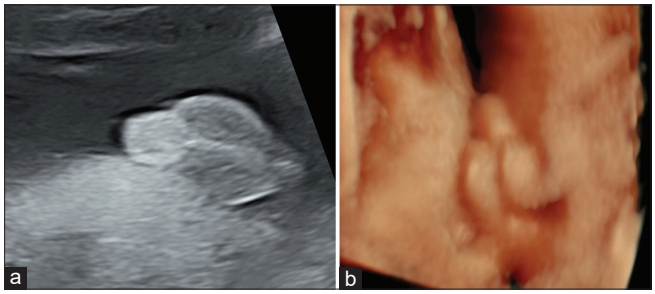

Figure 1: Detailed level III ultrasound at 30 weeks showed complete fusion of the labia and severe clitoromegaly with length at 20.6 mm (a and b)

Discussion

Here, we present a target fetal ultrasound staging the degree of virilization according to the Prader Scale. To the best of our knowledge, this is the first report describing the prenatal range of virilization of external and internal genitalia. Frequently, an MRI is decided after suspicion of severe fetal pathology on level III ultrasound with incomplete and inconclusive findings. Nevertheless, the normal vagina and uterus are usually collapsed and difficult to identify on prenatal MRI.[4] The improved image quality of the modern ultrasound had a significant impact on the prenatal diagnostic process. Using high-frequency ultrasound and a transperineal approach, a sonographer can clearly display fetal soft-tissue structures such as the vagina and uterus.[5] The main imaging sign previously described in complex female genitourinary system abnormalities is the well-identifiable voluminous fluid-filled vagina. To the best knowledge, there is no complete information available on the prenatal presentation

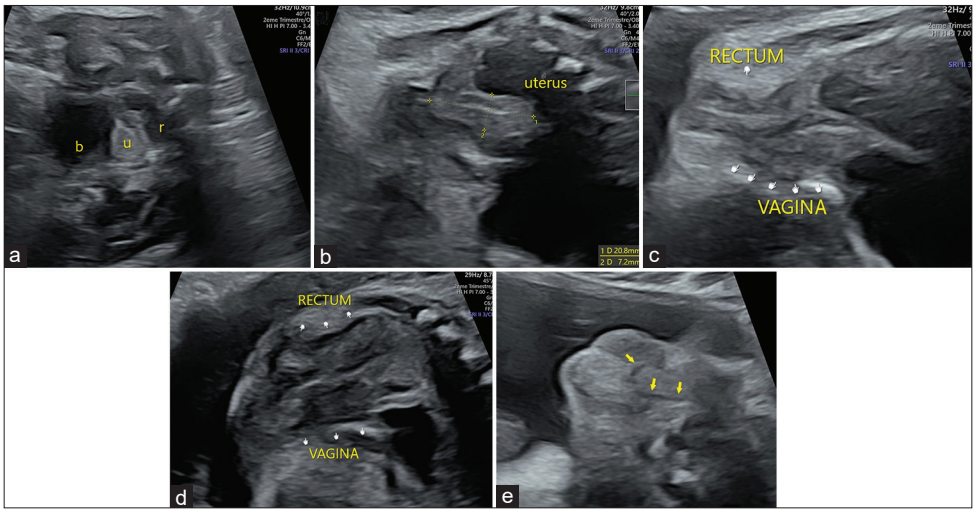

Figure 2: Detailed level III ultrasound at 30 weeks. (a) The fetal uterus (u) is well visualized in the fetal pelvis between the bladder (b) and the rectum (*r*), (b) The fetal uterus had a normal appearance with 21 mm long by 7 mm wide, (c) A short and hypoplastic vagina in contrast to a normal fetal vagina (d) Which represents a hypoechoic structure, parallel to the rectum, and prolonged to the perineum, (e) A single urethral-like arrows observed during fetal urination, it opened at the base of the clitoris and corresponded to a urogenital sinus. The fetal anatomy matched the stage 3–4 of the Prader scale

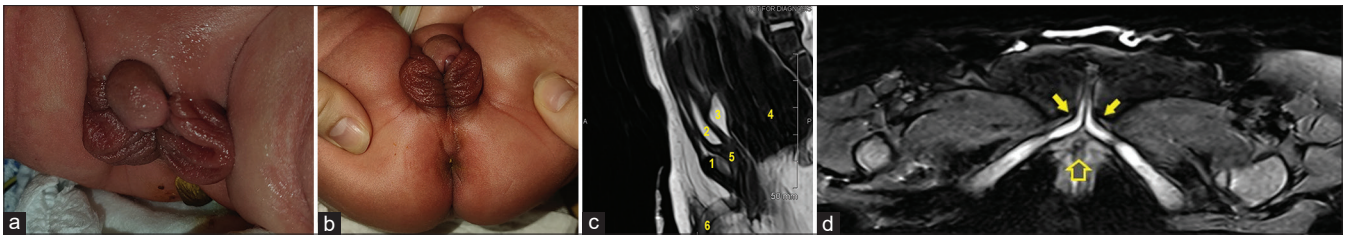

Figure 3: (a and b) Postnatal physical examination assessment of the external genitalia found highly pigmented, thick-skinned, and transversely striated labia. There was almost complete labial fusion. There was a single urogenital opening at the base of the clitoris and an enlarged and curved genital tubercule measured 2 cm. The postnatal phenotype corresponded to stage 3 of the Prader scale, (c) Midsagittal magnetic resonance imaging (MRI) T2-weighted image (T2WI) realized at 8 months with sedation: Pubic symphysis (1) Urinary bladder, (2) Uterine cavity with hyperintense fluid content, (3) Rectum, (4) Vagina, (5) Partial volume effect of both hypertrophied erectile tissue analogous to corpus spongiosum and corpus cavernosum, (6) The urethra length was measured as the distance between the bladder neck and urogenital confluence at 13 mm. (d) Axial MRI T2WI fat suppression passing by the ischium. Long arrows are pointing at hypertrophied erectile tissue analogous to the corpus cavernosum. Open arrow is pointing at the urethra

of the different degrees of virilization according to the scale developed by Prader. Prenatal sonographers and pediatricians should speak the same language. The additional phenotype information, delivered by sonographers, can help both families and pediatricians to better evaluate the severity of the pathology and, therefore, to provide reliable information about the management during pregnancy and the neonatal period. Thus, a multidisciplinary fetal team can support parents in making informed decisions.

Conclusion

Our case report represents a prenatal case of congenital adrenal hyperplasia. This report aims to illustrate the subtle fetal genitalia assessment of a fetus with variations of sex development.

Ethics statement

As this was a retrospective case report, no approval was required from the local ethics committee. Consent was obtained from the family regarding the publication of the case, including investigations and images.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given the consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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