Case Report

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Penoscrotal Hypospadias Presenting As Ambiguous Genitalia Mimicking Congenital Adrenal Hyperplasia: A Case Report with Review of Literature

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ABSTRACT

Ambiguous genitalia is a rare congenital anomaly where sex of the newborn cannot be readily distinguished because of atypical appearance of the external genitalia. Hypospadias can also present as ambiguous genitalia. We report a case of a preterm male baby born with ambiguous genitalia with undescended testis and low set ear. Initially congenital adrenal hyperplasia was suspected but 17-alpha-hydroxyprogesterone level was normal, later diagnosis of penoscrotal hypospadias was made. Ultrasonography revealed bilateral testicular sac. Ambiguous genitalia though is commonly caused due to congenital adrenal hyperplasia, it can also be a manifestation of penoscrotal hypospadias. Hormonal, biochemical and radiological approach along with genetic analysis will help reach definitive diagnosis.

Keywords: Ambiguous genitalia; Disorders of sexual differentiation; Congenital Adrenal Hyperplasia; Penoscrotal hypospadias; 17-hydroxy-progesterone;

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INTRODUCTION

Ambiguous Genitalia (AG) are a congenital anomaly where sex of the newborn cannot be readily distinguished because of atypical appearance of the external genitalia. [1] It encompasses a variety of disorders labeled as Disorders of Sexual Differentiation (DSD) which means discordance between the external genitalia and the gonads. Approximately 1 per 4500 children are born with AG, 98% of these are due to Congenital Adrenal Hyperplasia (CAH).[2]It is a medical emergency with social significance.

Hypospadias is one of the most common congenital anomaly affecting about 1/150 male babies, it is normally depicted by the proximal displacement of the urethral opening, penile curvature, and a ventrally deficient hooded foreskin.[3] It is either distal (coronal and distal shaft) or proximal (mid-shaft, proximal shaft, penoscrotal, perineal). It can sometimes also present as AG. Severe hypospadias can also overlap with DSD.[4] Endocrinological evaluation is advised to exclude other causes of DSD.[3]

CASE REPORT

We report a case of a single, preterm (32 week of gestation via Ballard's scoring) male baby born to G2P1A0L1 via vaginal delivery at 36 WOG by date with birth weight of 1.3kg and Apgar score of 6/10 at 1 minute and 8/10 at 5 minute. Baby was kept in an incubator and septic workup and chest X-ray was done. Physical examination revealed ambiguous genitalia (Figure1) and bilateral undescended testis .Intravenous Cefotaxime at 50ml/kg/dose twice daily and intravenous Amikacin at 15 ml/kg once every 36hours was initiated empirically for suspected neonatal sepsis. Capillary glucose and electrolytes were regularly monitored suspecting CAH (most common condition causing AG and often manifesting as electrolyte and blood glucose disturbances). Peripheral blood smear demonstrated decrease platelets whereas remaining investigations were within normal limit. On 3rd Day of Life , thrombocytopenia (94000 /cumm) was detected indicated sepsis . On 5th day , hypoglycemia , hyperkalemia (6.2mmol /L) and hyponatremia (133mmol/L) were reported making CAH most likely in background of AG. There was no further episodes of hypoglycemia. Fluid and electrolytes were closely monitored.

CAH was ruled out as 17-alpha-hydroxyprogesterone (1.52ng/dl) was normal. Karyotyping was suggested but was declined by parents. Phototherapy was instituted for hyperbilirubinemia at 3rd day of life (capillary bilirubin 18.2mg/dl) and on 11th day (18.5mg/dl). Breastfeeding was only established at 10th day . Ultrasonography (USG) showed bilateral testicular sac while USG cranium was normal and echocardiogram revealed atrial septal defect (2.2mm) with left to right shunt and mild tricuspid regurgitation with mild pulmonary arterial hypertension.

Diagnosis of penoscrotal hypospadias was made on the basis of clinical (proximal displacement of the urethral opening), biochemical (normal glucose and electrolyte), hormonal (normal 17-alpha-hydroxyprogesterone) and radiological (bilateral testicular sac in USG) evidences though it initially mimicked CAH. The subsequent blood and electrolyte parameters were normal. Baby discharged on 17th day of life. Patient was kept in regular follow up (Figure 1). USG scrotum was repeated at 6 month of age which revealed ; normal right testes with right mild hydrocele, right inguinal hernia and left tested high up in inguinal canal with normal size (Figure 2) .The patient has been scheduled for repair surgery for hypospadias at the age of one year .

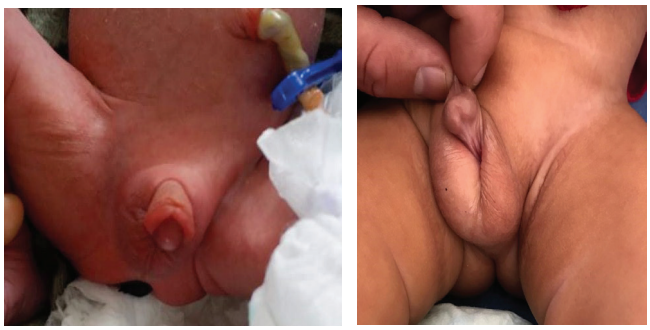

Figure 1. Ambiguous Genitalia at 1 Hour of Life (weight 1300 grams) and at 6 months of age (weight 5700 grams)

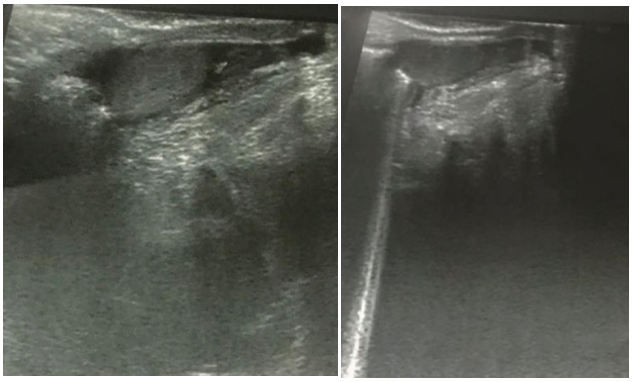

Figure 2. Left testes high up in inguinal canal with normal size and right testes located in right scrotal sac.

DISCUSSION

Disorders of Sexual Differentiation is a congenital condition where development of chromosomal , gonadal or anatomical sex is atypical , and comprises of sets of metabolic and anatomic defects resulting in atypical appearance of genitalia. [5]

The gonads as well as genital structures all originate from the same bipotential embryologic tissues, and only through well-coordinated and localized expression of genes does normal sex differentiation and development progress. The pathology can be appear at various phases of sex determination and development, from early in the differentiation of the bipotential gonad to the final stages of genital formation.[6]

Mild variation in newborn genitalia is common, but an atypical findings points towards the DSDs. Initial diagnostic workup for DSDs includes electrolytes, glucose, 17-hydroxy-progesterone, testosterone, gonadotropins, karyotype and pelvic ultrasound. In cases of non-palpable gonads, the first objective of checking the androgen levels, most importantly 17-hydroxy progesterone, and electrolytes is to evaluate for CAH. Genetic testing is often performed for diagnosis of karyotypic abnormalities and syndromes with genital anomalies. [6]

CAH is often the most common cause of genital ambiguity in neonates, others include partial androgen insensitivity syndrome (Partial AIS). AIS is caused by mutations in the androgen receptor gene on the

X chromosome, and dictates response to androgen such as testosterone or dihydrotestosterone (DHT).[6] Unfortunately, a great number of cases do not have an identifiable cause, particularly among 46XY DSDs.[8]

Palpable bilateral gonads are generally associated with a 46XY karyotype. AG cases with non-palpable gonads should bring up concern for a 46XX infant with virilization (such as CAH), or alternatively could be a 46XY infant with either cryptorchidism or absent gonads.[6]

Androgens controls masculinization of the genital tubercle into penis between 8-12th week of gestation , with tubularization of the urethra from the perineum to the tip of the glans . Disruption of this process results in hypospadias.[4] In about 70%, the urethral meatus is located distally on the penile shaft ; this is considered a mild form that is not associated with other urogenital deformities . The remaining 30 % are proximal and often more complex.[7] Endocrinological evaluation is advised to exclude DSD in these cases , especially in case of concomitant unilateral or bilateral unilateral undescended testes . UDT is a common abnormality , affecting about 1/20 males at birth .[4] Severe hypospadias overlaps with DSD , so babies without a fused scrotum containing two testes and who present with 'hypospadias need full DSD investigations at birth.[4]

Care is needed in diagnosis, as some infants with DSD and AG may be diagnosed as "simple hypospadias". Since hypospadias is an anatomical anomaly of anterior urethral development, the rest of the external (and also internal) genitalia are normal. Patients with DSD, by contrast, have a more extensive genital anomaly, reflecting the failure of all androgen-dependent development. A useful rule-of-thumb is to assume that any baby with "hypospadias", as well as an undescended testis and/or bifid scrotum, should be investigated for DSD. [4]

The most common diagnosis among AG were CAH (14%), AIS (10%), mixed gonadal dysgenesis (8%), clitoral/labial anomalies (7%), hypogonadotropic hypogonadism (6%), and 46XY small-for-gestational-age (SGA) males with hypospadias (6%). About 11.2% exhibited a distinctive genital configuration described as penoscrotal hypospadias with transposition .[8]

Hypospadias repair aims to achieve cosmetic and functional normality . Currently surgery is recommended between 6 and 18 months of age [3] Immediate gender assignment as male is onlysafe when the scrotum is fused and both testes are descended fully (i.e. androgen-dependent genital development is normal).[4] Hypospadias can be

corrected at any age with comparable complication risk, functional, and cosmetic outcome; however, the optimal age of repair remains conclusive. Although long-term outcome regarding cosmetic appearance and sexual function is fairly good, after correction, men may inhibit in seeking sexual contact. [3]

Initial management of AG is very stressful for families and pediatrician/ neonatologist thus approach must be sensitive and timely. First conversation with new parents should be clear, precise and gender-neutral. Despite this, the diagnostic dilemma that is frequently observed with DSDs leads to emotional and psychological distress to parents. Staying gender-neutral until the decision is finalized helps prevent misunderstandings and confusion.[5, 6] AG can be traumatic to the individual with growing age as stigma, secrecy, and shame are commonly prevail with this condition. Hence intervention by experienced mental health providers for individual and family is intrinsic.[6]

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