Case Report

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Management of Intersex: A Challenge in Low Resource Settings

Koledade Ak[1],[*] Abdullahi ZG[1], Adeoye TO[1], Umar AM[1], Sada S[1], Aliyu RM[1], Ajani S[1], Maduka SG[1], Mahmud F[1], Taingson M[2], Ahmad B[3], Shittu SO[1]

[1] Department of Obstetrics and Gynaecology, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria. [2]Department of Obstetrics and Gynaecology, Barau Dikko Teaching Hospital, Zaria, Nigeria. [3]Urology Unit, Department of Surgery, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria.

***Correspondence**: Dr. Afolabi Korede Koledade, Department of Obstetrics and Gynaecology, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria.*

***E-mail**: akdade@yahoo.com*

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ABSTRACT

Background: Intersex refers to people with congenital variations in chromosomes, gonads, sex hormones or genitals that can neither be categorized as male or female. Features may include genital ambiguity, combinations of chromosomal genotype, and sexual phenotypes different from XY (Male) and XX (female). The availability or accessibility of a wide range of investigative components for managing intersex remains a major challenge for health systems in low-resource settings. There are also missed cases that present later in life when their gender assignment contradicts the secondary sexual developments. Depending on the gender of rearing, they present to the gynaecologist or urologist. However proper clinical evaluation and early diagnosis of intersex can reduce the psychological trauma that the patient and their families go through. We present two patients who presented to the gynaecologic clinic of ABUTH within a period of 2 years. **Conclusion:** Early diagnosis and management of intersex remains a major challenge for health systems in low-resource settings like ours. However proper clinical evaluation can make early detection possible and also help in its diagnosis.

Keywords: Intersex; Management, Low Resource; Settings

INTRODUCTION

Intersex refers to people with congenital variations in chromosomes, gonads, sex hormones or genitals that can neither be categorized as male or female. Features may include genital ambiguity, combinations of chromosomal genotypes, and sexual phenotypes different from XY (Male) and XX (female).[1-4]

In 2006, the term Disorders of Sexual Differentiation or Disorders of Sexual Development (DSD), which refers to congenital conditions, where the development of chromosomal, gonadal or anatomical sex is atypical was introduced. However, this has been controversial because studies showed that there is a negative impact

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and some form of stigmatization on patients. Hence, the World Health Organization and a lot of medical personnel still use the term, Intersex.[5-7] Intersex is with an incidence of 1 in 1000 to 4500 live births worldwide.[8,9] The classification of DSD or Intersex according to the International Consensus Conference is Virilized XX, Under-virilized XY and Mixed sex chromosome pattern. [5]

In the early phase of sexual development, XX and XY fetuses are indifferent till 7 weeks when the gonads become bipotent and XY foetus starts to develop testes and the ovaries develop in XX foetus. Gonadal differentiation and function determine the genital phenotype. The XY foetus produces Mullerian inhibitory substance and androgens to develop the wolffian duct for the male internal genitalia while the XX foetus develops the mullerian duct for the female internal genitalia. The male external genitalia originate as a result of the effect of 5alpha reductase on functional receptors.

The development of the sex gonads in the form of testes in males and ovaries in females, as well as the development of the sex cords and external genitalia under the influence of presence or absence of specific hormones can go wrong at any point and result in mal development which we identify as intersex.[10]

The evaluation and management of newborns with intersex is multidisciplinary working closely with the parents as quickly as possible to establish the gender. The team at best should include a gynaecologist, pediatric urologist, endocrinologist, geneticist, neonatologist, and child psychiatrist/psychologist.[11,12] In some patients with intersex, sex and or gender assignments are relatively straight forward but it may not always be clear. Hence, a thorough evaluation of the endocrine function, karyotype, and potential for reproduction is helpful. Getting these varieties of specialists is a challenge in most developing countries and even in developed countries, a lot of centres are short of the full compliments of the management team. There are also missed cases that present later in life when their gender assignment contradicts the secondary sexual developments. Depending on the gender of rearing they present to either the gynaecologist or the urologist.[13]

The outcome of management of patients with intersex is dependent on not only the parents but family and friends' ability and commitment to supporting the patients' personalities as well as their ability to accept their condition, quality of medical and surgical care. The outcome spectrum ranges from poor to good. However, in complex cases, all outcome factors cannot be ideal, especially fertility potential and sexual responsiveness. The support of family and loved ones goes a long way in achieving a satisfying and productive quality of life.[14]

Cultural influence which may encourage preference for a particular gender, lack of awareness, inadequate examination of the external genitalia at birth, and lack of diagnostic facilities results in late presentation.[15,16]

CASE HISTORY

We present these cases of two patients who presented to the gynaecologic clinic of Ahmadu Bello University Teaching hospital (ABUTH) within a period of 2016 to 2017.

Case 1

A 30 year old FA1 raised as a female who presented with ambiguous genitalia since birth. She had normal growth and development comparable to her peers. Thelachre was at 11 years, adrenache at 13 years, and menarche at 14 years with a normal 28 day cycle and 5 day flow. She was the last child of 5 children in a monogamous non-consanguineous setting with no family history of a similar condition in any female sibling. Her parents had presented to several hospitals where they were advised to delay treatment. They were later advised on surgery when she was 7 years of age but it was not done due to financial constraints.

She was examined and found to be phenotypically female, with normal female carriage and hair distribution. She had well developed breasts (tanner stage 5) with partial masculinization of the external genitalia. The labia minora were fused posteriorly about 4cm in length and hypoplastic. The labia majora were also hypoplastic. The clitoris was 5cm long and hypertrophied, the urethral orifice and the introitus were

patents with an intact hymen.

Investigations done revealed normal electrolytes, urea, and creatinine while the hormonal assay was suggestive of hyper-gonadotrophic hypogonadism values. The abdominopelvic scan showed normal female internal genitalia and the intravenous urogram was normal. The buccal smear was negative for female sex chromatin also known as barr bodies. However, 17-OH Progesterone, 21-0H Progesterone analysis, and Karyotype could not be done because of financial constraints.

She was counselled on the findings and eventually had posterior labial separation and excision of the body of the hypertrophied clitoris **(**Figures 1a and 1b**)**. She was discharged 8 days post operatively with good post-operative recovery.

Case 2

An 11 year old FA2 raised as a female presented with ambiguous genitalia noticed by her parents since birth. They were reassured in the hospital where she was born that the clitoris was just enlarged but that he was a girl. Erection was noticed by the patient and mother at different times and last episode was about 4 weeks prior to the presentation. The child was constantly bullied by peers in an all-girls boarding secondary school because of her abnormal genitalia. She was yet to attain thelachre, adrenache, and menarche with no change in voice. She was the first of six siblings all phenotypically females in a monogamous non-consanguineous family setting.

Examination revealed a happy looking child with no axillary nor pubic hair with a height of 1.62m and weight of 46kg. Breast development was tanner stage 1. What appeared like the labia majora were enlarged with some ruggae and the urethra open ventrally extending from the perineum between the labia up to about 1.5cm short of the tip of the glans which was consistent with perineal hypospadias. There were palpable undescended gonads on both sides of labia majora close to the inguinal region and freely mobile. There was a phallus which was 4cm in length in the flaccid state with severe chordae. There was also peno-scrotal transposition. Investigations done included an abdominopelvic ultrasound which showed absent female internal organs, with bilateral inguinal testicles measuring 2.57cm by 0.87cm on the right and 2.25cm by 0.75 cm on the left with normal Doppler blood flow pattern. Intravenous urogram showed normal upper renal tract bilaterally. Buccal smear cytology was devoid of barr bodies suggestive of a likely XY Karyotype. Karyotype showed 46XY 44autosomes and 2 sex chromosomes (XY). The hormone profile showed elevated testosterone 2.0ng/ml, normal range for females being 0.2-0.95 ng/ml while other hormones were within normal limits. The testosterone level was within the normal range for males of this age 0-2.6ng/ml suggestive of functional testes. However, the thyroid stimulating hormone was 5.9miu/ml (0.5-5.0miu/ml). The patient and his parents were counselled on findings and were co-managed with urologist. A male genitalia re-construction with chordae release, hypospadias repair and bilateral orchidopexy was done **(**Figures 2a and 2b).

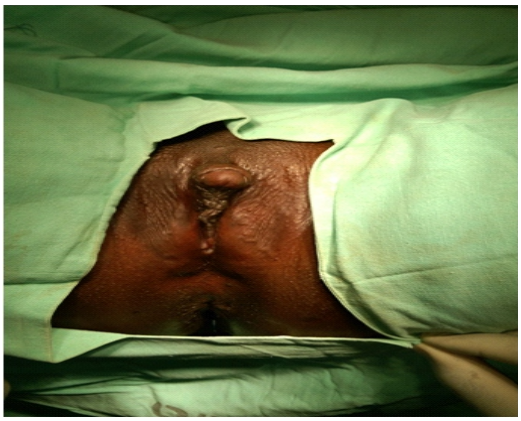

Figure 1a.

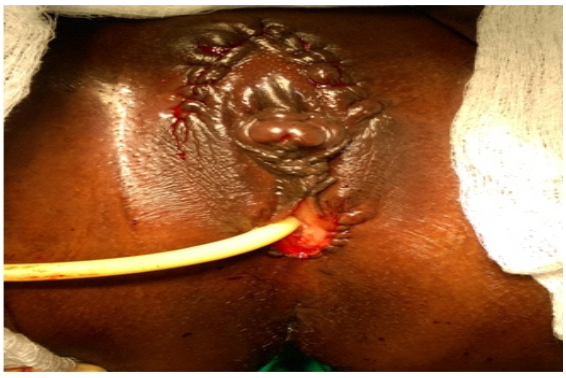

Figure 1b.

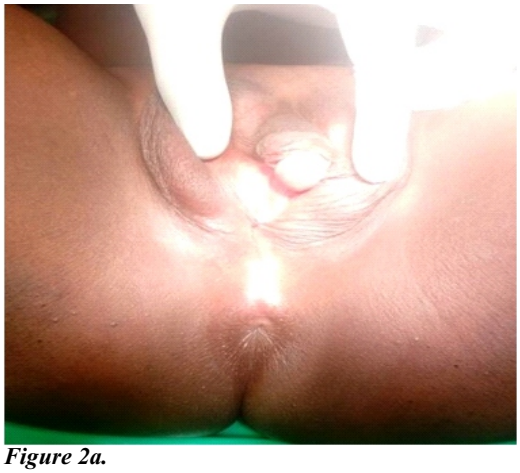

Figure 2a.

Figure 2b.

DISCUSSION

The delivery of a baby with DSD is usually disturbing not only to the couple but to the family at large. There is a lot of emotional and even psychological stress as gender assignment is an important process. In Nigeria and indeed a wider part of Africa the first challenge comes on the seventh day of life when the baby is usually named. Most African names and even religious names are gender specific and so the child is usually named in line with the perception of the external genital or the most desired gender. Also, socio-cultural practices like circumcision in the male and ear piercing in the female are typically carried out in the early neonatal period. The subjective assignment of gender may eventually become a greater source of embarrassment when the child grows to manifest secondary sexual characteristics that are not in line with the gender of rearing.

Intrauterine diagnosis with the aid of high resolution or 3D ultrasound machines would go a long way in helping to effect appropriate management in the neonatal period. Also, early diagnosis at birth is also helpful in order to pursue prompt investigation and institution of appropriate treatment. However, if the diagnosis is missed or delayed the management becomes awkward, particularly for the patient who usually may have to assume a different gender role from the one assigned at birth.

It is worthy of note that the mother of the patients were said to have had antenatal care, but the intrapartum diagnosis was missed. This is not surprising because despite the relative availability and emphasis on the importance of anomaly ultrasound scan in pregnant women during antenatal care which can be done from 11 weeks gestation, most of the ultrasound machines in low-resource settings may not have high resolution or are less than 3D, hence picking up intrauterine anomalies may not be high yielding.[17,18,19] They also had hospital delivery but appropriate counseling and referral to centres where they would have benefitted from specialized care and management were not offered to them. They were only reassured each time they presented to express their concerns until it became a social embarrassment as seen in case 2 who had to be withdrawn from an all-girls boarding school.

Another major challenge or contribution to their delayed management was inadequate finance as well as unavailability of all appropriate investigations required in their management. As seen, not all investigations were done. For example, in case one, only a buccal smear which is not confirmatory was done as she could not afford a Chromosomal karyotype test.

CONCLUSION

Availability and access to appropriate laboratory and radiological investigation remain a challenge when managing patients with intersex in low-resource settings. Proper evaluation within the limits of our health system and family support is useful in the prompt diagnosis and management of patients with intersex.

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