Case Series

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Mixed gonadal dysgenesis in Yaoundé: A preliminary experience about three cases

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SUMMARY

Mixed gonadal dysgenesis is characterised by unilateral chromosomal abnormality, which is probably the result of anaphase lag during mitosis. The 45, XO/46, XY karyotype is the most common form of mosaicism involving the Y chromosome. It is a rare clinical entity with a worldwide incidence of 1.5/10,000 live births. Its epidemiology in Sub-Saharan Africa is not known. This study reports experience in the management of 3 cases at the Yaounde Gynecologic-Obstetric and Paediatric Hospital. From November 2009 to November 2014, 3 cases were successfully managed at our institution. **Results:** All patients presented with asymmetrical gonadal differentiation. On one side of the body, a poorly-developed testicular gonad and on the other side a gonadal streak. A persistent Müllerian remnant was equally found in the 3 cases. Management of mixed gonadal dysgenesis should be done in tertiary health care centres. A multidisciplinary team approach is recommended.

Key words: Management, mixed gonadal dysgenesis, Yaoundé

INTRODUCTION

Mixed gonadal dysgenesis or 45, XO/46, XY karyotype is a form of mosaicism involving a numerical abnormality of the Y chromosome. It is an uncommon abnormality, with an incidence of 1.5/10,000 livebirths.[1] In Sub-Saharan Africa, this pathology is probably underdiagnosed and few authors have reported their experience concerning this condition.

The aim of this study was to describe preliminary experience of our service relating to the diagnosis and therapeutic aspects of the 45, X/46, XY mosaicism.

CASE PRESENTATIONS

Over a period of 5 years (2009–2014), three patients with 45, XO/46, XY mosaicism were registered in our service. The criteria for inclusion in the study was the presence of the mosaicism found through karyotype and the age (0–18 years). The chromosome analysis was carried out in the cytogenetics laboratories teaching hospitals in Lyon and Geneva. This was funded by the Swiss NGO 'children action.' Anti-Müllerian hormone levels were assessed in all the patients. Clinical and cytogenetic data were gathered from the medical records. These data consisted of:

- Age at first evaluation
- Presenting complain
- Sex of rearing
- Phenotype of ambiguous genitalia
- The management: Laparoscopy, gonadectomy, genitoplasty, substitutive hormonal therapy.

The characteristics of external and internal genitalia were described based on the masculinisation

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sore suggested by Ahmed *et al.*[1] and applied by Cools *et al.*[2]

RESULTS

We registered 3 cases over a period of 6 years (2009–2015). None of our cases had any description of associated structural abnormalities of the Y chromosome in the 46, XY cell line. Their ages at first evaluation were 3, 6 and 16 years. The presenting complain was an abnormally of the external genitalia in 1 cases and hypospadias in the other 2 cases. The 3-year-old patient had benne raised as a girl and the two others as boys.

All patients presented with asymmetrical gonads, the ectopic meatus was perineal in one patient and proximal in two cases [Figure 1]. Regarding external genitalia, one was considered ambiguous and the remaining two were males. The 16-year-old patient had been circumcised and the preputial foreskin was intact in the others. In the 3-year-old patient, investigation of internal genitalia revealed a normal uterus and the Mullerian tissues were found in the rest. The 16-year-old patient presented with short stature, but there was no mental retardation in our small series.

Coelioscopic evaluation in the 3-year-old patient showed a normal vagina with a high opening above the bladder and a cervix. This implied that genitoplasty would be quite difficult. After the team and discussion with parents, we decided to maintain the sex of rearing, so a gonadectomy was performed. In the 6-year-old patient, the decision was to perform a gonadectomy and later urethroplasty according to the Koyanagi's technique.

For the 16-year-old patient, Mullerian tissue remnants seen during laparoscopy were resected [Figures 2-7] and the Bracka's first stage urethroplasty was performed with no complications [Figures 8-15]. He is awaiting a second operation in a year's time.

DISCUSSION

In our series, the mean age at first evaluation was higher than that reported dy Rosa *et al.*[3] who had a mean of 2 years. Delayed diagnosis is seldom in our African context and especially concerning a rare abnormality. Pre-natal diagnosis of the 45, XO/46, XY mosaicism can be made from specimens collected by amniocentesis. Although this is still uncommon in Africa, it should not be ignored. The clinical, morphological and biological characteristics of our subjects were similar to those found in literature.[4] Clinically patients with mixed gonadal dysgenesis present as in our cases, with asymmetrical gonadal differentiation. On one side of the body, a poorly-developed testicular gonad and on the other side a gonadal streak. The short stature was noted in a phenotypic male, supporting earlier



Figure 1: Preoperative aspect of external genitalia



Figure 2: Skin opening for coelioscopy



Figure 3: Introduction of a size 10 trocar



Figure 4: Laparoscopic view of Müllerian remnants



Figure 5: Pfannestiel incision



Figure 6: Resection of the Müllerian remnant

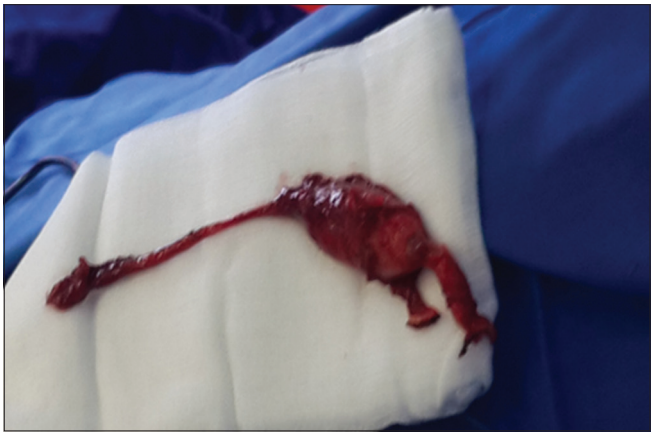


Figure 7: Müllerian remnant resected



Figure 8: Bracka's urethroplasty: first stage

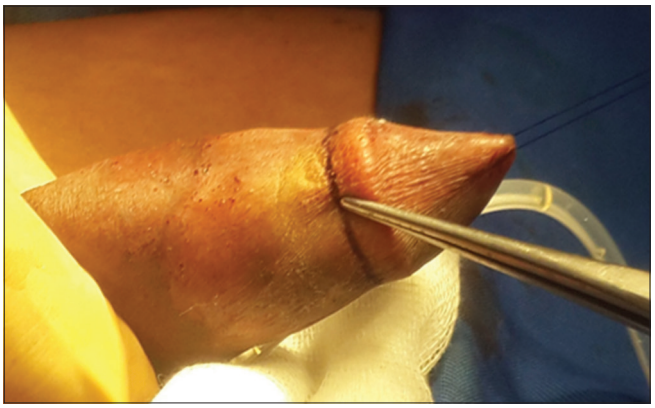


Figure 9: Bracka's urethroplasty: Drawing incision lines

reports[5] which suggest that it is related to deficiencies of both their hypothalamic-gonadal and their primary gonadal function.

Regarding the management, surgical procedures should be scheduled accordingly. If the sex of rearing is female prophylactic gonadectomy is recommended given the high risk of gonadoblastoma and dysgerminoma. Given the high prevalence of tumours among these subjects long-term monitoring by ultrasound is necessary. In patients with male sex of rearing, orchidopexy should be performed in case of cryptorchidism, post-pubertal biopsy and gonadectomy depending on the histological results.

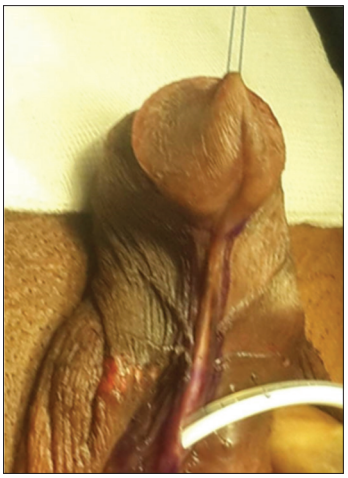


Figure 10: Bracka's urethroplasty: insertion of a Foley's catheter

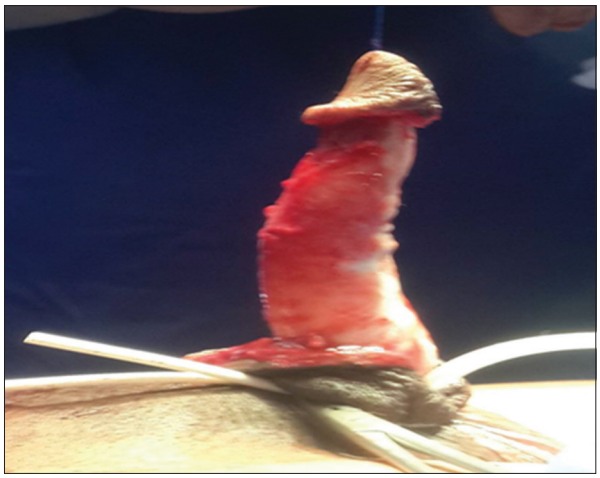


Figure 11: First artificial erection test



Figure 12: Second artificial erection test after correction of chordee

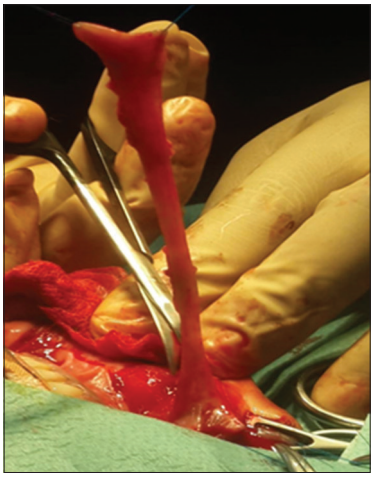


Figure 13: Harvesting the buccal mucosa graft



Figure 14: Preparing the graft



Figure 15: Immediate postoperative aspect

Hormonal therapy is also one of the major aspects of the multi-disciplinary management of this rare condition which should be done in a tertiary centre. Evaluation of long-term follow-up should also address the psychological impact in these patients.

CONCLUSION

A multi-disciplinary team approach including several specialties such as Paediatrics, Clinical genetics, Endocrinology, Paediatric surgery and Psychology is

important not only for early recognition of these patients but also for their proper management. Early diagnosis is important to decrease the psychological impact in these patients.

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Conflicts of interest

There are no conflicts of interest.

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