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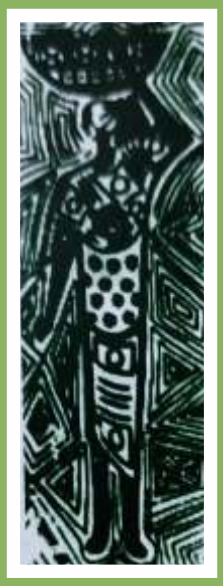

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Clinical and Laboratory Profile, Parental Perception and Management of Micropenis in Childhood: Experience at a Referral Centre in Abidjan, Cote d'Ivoire

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Abstract

Background: Micropenis is a congenital condition that is part of the group of disorders of sex differentiation (DSD). It is a condition that has not received much attention among children in our environment.

Objective: To describe the epidemiological, clinical profile, and therapeutic profile of children with micropenis and the management outcome.

Methods: This was a descriptive, retrospective study of children with micropenis at the Paediatric unit of the Military Hospital, Abidjan, over six years (May 2016 to June 2022).

Results: A total of 70 children with micropenis were studied. The mean age was 9.3±3.9 years (1 month to 15 years). About one-third (30%) of the children were obese. The mean penile length was 2.55 ±0.65 cm (1 cm to 4 cm). In more than three-quarters of the cases, the mothers discovered a small-sized penis and anxiety in 91.4% of the parents. In the majority of cases (62.9%), the aetiology was unknown, while primary and central hypogonadism were observed in 24.3% and 11.4%, respectively. Affected children received testosterone treatment with favourable outcomes in all cases. The mean increase in penile length was 2.68 cm ± 0.97 (minimum of +1 cm and maximum of 6 cm).

Conclusion: It is essential to raise awareness about micropenis among the population and health personnel to reduce undue anxiety in parents and children.

Keywords: Disorder of Sex Differentiation, Hypogonadism, Micropenis, Penis, Testosterone.

Introduction

Micropenis is a congenital condition belonging to the group known as the Disorders of Sex Differentiation (DSD). Its definition is based on the length of the stretched penis and was first introduced by Schonfeld and Beebe.[1] It is defined as a penis whose stretched length is less than minus 2.5 standard deviations (SD) below the mean for the age group, without the presence of other penile abnormalities. Thus, for full-term newborns, a stretched penis that is less than 1.9 cm in length is termed micropenis.[2] The incidence of micropenis was 1.5 per 10,000 male children born between 1997 and 2000 in the United States of America.[3,4]

Micropenis can be an isolated anomaly, or it can be syndromic.[3] The development of the penis occurs under the influence of androgens during the embryonic period, and a true micropenis is linked to a hormonal anomaly occurring after the 12th week of gestation.[3,5] An incorrect diagnosis can cause considerable parental anxiety that is sometimes difficult to overcome.[2] The aetiologies are varied and can be classified into three categories: hypogonadotropic hypogonadism, hypergonadotropic hypogonadism, and idiopathic causes.[6]

Therapeutically, there are two approaches to the management of micropenis: hormonal treatment and surgical repair.[2] There is a lack of studies on childhood micropenis in Africa, while no study has been done in Côte d'Ivoire. This study aimed to describe the characteristics of children with micropenis and the treatment received in order to create awareness about the condition. Parental perceptions of the condition are also described.

Methods

Study design and setting

This was a cross-sectional study involving children aged 0 to 15 years who were managed for micropenis at the paediatric unit of the Military Hospital, Abidjan over six years (May 2016 to June 2022). The perceptions of the parents concerning the condition were obtained through direct personal interview or telephone interview. The parents of one child refused to participate and was excluded.

Sampling and Data Collection

All children with micropenis who met the inclusion criteria during the study period were consecutively recruited. For each child recruited, relevant clinical and demographic data such as age, birth order, place of residence, age, level of education, and parents' profession were obtained. Information relating to the age at discovery, the circumstances of discovery and the person who discovered the micropenis were also obtained. Examination findings, including anthropometry, pubertal staging and external genitalia, were documented. Laboratory measurements of serum testosterone, luteinising hormone (LH) and follicle-stimulating hormone (FSH) levels were carried out in all the children—information regarding the treatment modality for each patient, whether hormonal or surgical, was also documented. The treatment outcome and the experiences of parents and children in relevant age groups were also reported.

Measurement procedure and operational definitions

The age was estimated from the recorded date of birth. The body weight was determined using a baby weighing scale or a portable weighing scale according to the age and the ability to stand. Infants were weighed naked, while older children were weighed in light clothing (underwear) and barefooted. The weight was recorded to the nearest 100 g. The length or height (as appropriate) was measured using a horizontal or vertical measuring rod. The operator was assisted in patients who were yet to stand. The measurement was recorded to the nearest 0.1 cm. Body Mass Index (BMI) was calculated as weight (in kilograms) divided by height (in metres). [8] Children were said to be obese if the BMI was greater than +2 standard derivation (SD) according to the age/sex-appropriate WHO growth charts. [8] Malnutrition was defined as BMI/age Z-score less than -2. Moderate malnutrition was described as a Z-score between -2 and -3 and severe if the Z-score was less than -3. 9 The pubertal stage was assessed using the five stages (I, II, III, IV and V) of Tanner classification. This involved the assessment of pubic hair and breast development in girls, while testicular volume and pubic hair were

assessed in boys.[10,11] Testicular volume was evaluated using an orchidometer.

The penile length was measured with the child lying supine from the base of the penis (on the pubis) to the tip of the glans, with gentle traction using a rigid right-angle calibrated ruler. [12-14] Micropenis was defined as penile length less than -2.5 SD for age in the reference tables. [3] An increase in penile length of at least one centimetre was termed therapeutic success. Serum hormonal values (LH, FSH and testosterone) were also assessed from the references according to sex and age.[15,16]

Statistical analysis

Data entry and analysis were carried out using Microsoft Office Excel® XP 2013 and Epi info® 7 software. The categorical variables were described in frequencies and percentages, while the quantitative variables were described as means with standard deviation, median, and ranges as appropriate.

Ethical considerations

The study was approved by the Ethics Committee of the Military Hospital, Abidjan, and authorisation was obtained from the director and the hospital's local scientific committee. The examination of the child's genitalia was carried out in the presence of at least one parent. Anonymity and confidentiality were ensured while extracting information from the hospital records.

Results

Epidemiological characteristics

Among the 11,624 sick children who attended the hospital during the study period, 512 children presented with an endocrine pathology, including 72 cases of micropenis, with a prevalence of 14.06% among endocrinopathies and an annual incidence of 12 cases/year. (Figure 1).

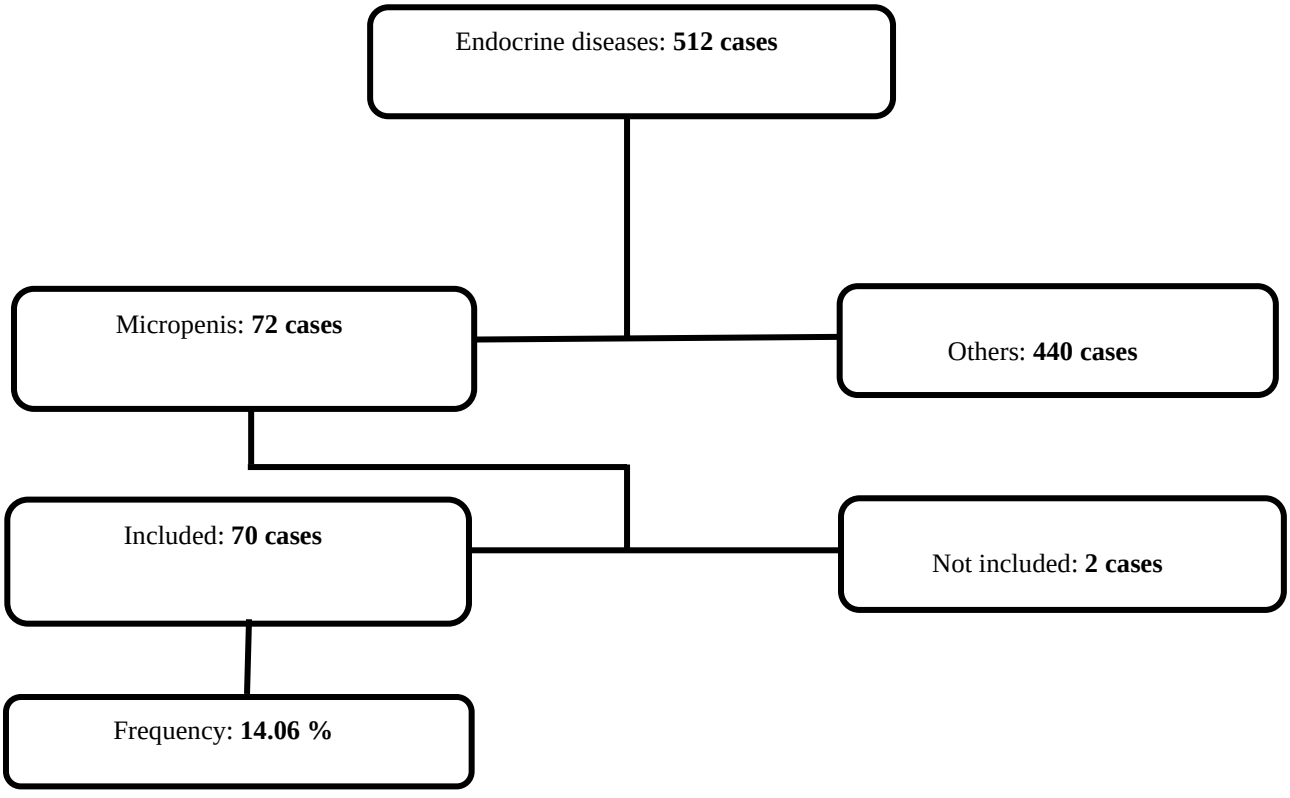

Figure 1: Flow diagram of the frequency of micropenis in children

The mean age of the children was 9.3±3.9 years, ranging from 1 month to 15 years. The predominant age group was 10-15 years (45.7%). Children of the first or second birth orders (44.3% and 30.0%) were more affected. The children most often came from the Cocody area of Abidjan (40%). The mean age of mothers was 39.4±6.2 years and 46.3± 8.7 years for the fathers. In almost all the cases (92.8% for mothers and 98.6% for fathers), the parents had at least a secondary education level and were gainfully employed (84.3% of mothers and 98.6% of fathers).

Clinical characteristics and laboratory parameters

Almost a third of the children (30%) were obese, while 10% had short stature. Close to three-quarters of the children were prepubertal (72.9%). The average penile length was 2.55±0.65 cm with a minimum of 1 cm and a maximum of 4 cm, and almost all (98.6%) patients had palpable testes bilaterally. One patient (1.4%) with Down syndrome had a unilateral undescended testis. Serum levels of LH, FSH and testosterone were measured in all the children studied. The mean levels of these hormones were 1.67 IU/L for FSH, 0.96 IU/L for LH and 0.36 IU/L for testosterone. In more than a third of cases (34.9%), the testosterone level was low and was associated with LH deficiency in 10% of cases.

Aetiologies

Hypogonadism occurred in about a third of cases (35.7%), with 11.4% and 24.3%, respectively, for central and primary causes. The aetiology was not found in 62.9% of cases.

Treatment and outcome

Most patients (94.3%) received at least two doses of testosterone injections. The outcome was favourable in 100% of cases with normal penile length. The mean final length was 5.25 ±1.13 cm with a minimum of 3 cm and a maximum of 9 cm. The mean increase in length gain was 2.68±0.97 cm with a minimum of 1 cm and a maximum of 6 cm. Three-quarters of the children (75.7%) had an increase in penile length of 2 to 4 cm. An increase in height or length of the child and a transient appearance of pubic hair were reported, but treatment was generally well tolerated.

Feelings of parents of children with micropenis

In almost two-thirds of cases (64.3%), micropenis was discovered at birth, with 77.8% noticed at home and by mothers in 77.1% of cases, as shown in Table I. Parental anxiety was documented in 91.4% of cases, and more than half (54.3%) did not know that treatment existed. The penis was massaged with shea butter in 18.6% of cases. Beliefs of parents concerning the cause of the condition included being a divine will (48.6%), unknown (40%) and an occultic manifestation (11.4%). In the majority of cases, the causes of delay in consultation reported were ignorance (57.1%) and fear of stigmatisation (42.9%). Table II also shows that satisfaction was expressed after treatment in almost all cases (90.9%).

Discussion

The incidence of micropenis in the study was 12 cases per year with a frequency of 6 cases per 1000. In Morocco, Berrani *et al* reported 113 instances of micropenis over eight years, representing an incidence of 14.1 cases/year.[13] A Nigerian study by Adekanye *et al*.,17, which determined the prevalence of abnormalities of external genitalia and groin among 663 primary school boys, reported that micropenis was detected in 27 (4.07%) pupils.

Following the establishment of a paediatric endocrinology unit in Côte d'Ivoire in 2016, there has been an increase in the diagnosis of micropenis. This could lead to an increase in the number of new cases of micropenis

diagnosed in the coming years. The mean age of 9.3 years in the present study is similar to a South Korean study, which reported a mean age of 9.8 years.[18]

Table I: Circumstances of discovery of micropenis

Circumstance of discovery	Number (n = 70)	Percentages
When was this anomaly discovered?		
At birth	45	64.3
Others	25	35.7
Where was this anomaly observed?		
At home	53	77.8
At school (during systematic visits by doctor/nurse)	7	10.1
To the hospital	9	13.1
Who discovered this anomaly		
Mother	54	77.1
Father	7	10.0
Doctor	3	4.3
Others (Aunt, grandmother, child, nurse)	6	8.6
Are there cases in the family?		
Yes	4	5.8
No	13	18.8
Do not know	52	75.4
Treatment was done before		
Yes (shea butter)	13	18.6
No	51	72.9
Do not know	6	8.6

Sadra *et al*. in Iran and Sagna *et al*. in Morocco reported an older age of 11.65±1.59 years and 16.3 years, respectively, in subjects whose ages ranged from 10 to 22 years.[19,20] Berrani *et al*. in Morocco found a lower mean age of 6.8 years.[13] In Nigéria, Iroro *et al*. documented micropenis among children with age between nine months and 168 months. [21] This difference in the mean age could be due to the different ages at the time of presentation or increased awareness that leads to presentation at an earlier age.

Micropenis was seen commonly in children who occupied first or second place among siblings. First pregnancies are sometimes not well tolerated by mothers. This can result in the ingestion of certain medications, such as anti-ulcer drugs or paracetamol, which may have implications for sexual development. Indeed, *in-utero* exposure to paracetamol has been documented as a risk factor for genital malformations, particularly cryptorchidism, in boys exposed during certain periods of pregnancy.[22,23] Also, certain medications, namely antiemetics (metoclopramide, domperidone, prochlorperazine) and H2-blockers (cimetidine, ranitidine), are among the important causes of hypogonadism responsible for micropenis.[24] Although the scope of the study did not allow exploration of drugs administered to mothers during pregnancy, future studies may provide more information on this since some of these drugs can easily be procured over the counter. More than a third of the children with micropenis came from the community of Cocody, which is close to the study site as well as Adjamé and Abobo. It would be considered the community of the affluent class of Ivorian

society.[25] Micropenis consultations could seem like luxury visits to many other parents in relatively indigent communities. Almost all the parents had at least a secondary education level and were gainfully employed. This could have resulted in increased awareness and seeking medical consultations.

Table II: Perceived feelings and satisfaction

Perception and satisfaction	Number (n = 70)	Percentages
Origin of the condition		
Divine Will	34	48.6
Occult hand	8	11.4
Unknown	28	40.0
How does the child feel about the situation?		
Anxious	26	37.1
Calm	40	57.1
Others	4	5.8
How do parents deal with the situation?		
Anxious	64	91.4
Calm	6	8.6
How do those around you experience the situation?		
Anxious	49	73.2
Calm	4	5.9
Others	14	20.9
Did you know there is a treatment		
Yes	32	45.7
No	38	54.3
Reason for delay in presentation		
Ignoring	40	57.1
Shame	30	42.9
Are you satisfied with the management?		
Unsatisfied	6	9.2
Satisfied	30	45.4
Very satisfied	39	45.5

Nearly a third (30%) of children with micropenis were obese. In some obese children who may have “buried penis” in the peri-pubic fat, it is important for accurate measurements to be taken, so as not to erroneously label them as cases of micropenis. The mean penile length in the current study was similar to reports from Morocco and Iran, with 2.2 cm and 2.95 cm, respectively.[13,19] The range of minimum value of a stretched penile length in the present study was slightly lower than the value obtained in the Nigerian study by Iroro *et al*. 21. In contrast, the maximum value of 4cm was similar to 4.6cm recorded by the same study and all values were less than the 5th percentile for their patient's ages.[21]

The aetiologies could not be determined in more than half of the cases in our study. However, the Moroccan study only reported 39% of cases being idiopathic and found central abnormalities of testosterone secretion in 14.2% of cases, abnormalities of testosterone receptors (partial androgen insensitivity) or 5α reductase deficiency in 30.1%, and genetic causes in 16.81%.[13] Genetic causes could not be confirmed in the present study because of the unavailability and unaffordability of facilities for genetic

mutation analysis. Such tests are only carried out by subcontracting to laboratories outside the country. The cost of karyotype is approximately 434,000 XOF (668 Euros), and that of SRY gene determination is 589,120 XOF (907 Euros). Only one patient (with Trisomy 21) could afford the cost of karyotyping. The challenge of genetic studies could account for the high frequency of cases of micropenis classified as idiopathic in the present study. Genetic (Noonan syndrome, Laurence Moon syndrome, Willi Prader, Bardet Biedl) or chromosomal abnormalities (Klinefelter syndrome, Down syndrome, triploidites) can be associated with micropenis in 10% of cases in the literature.[13] Idiopathic micropenis is usually considered a diagnosis of exclusion and can be linked to environmental endocrine disruptors or genetic abnormalities.[26,27]

The diagnosis of micropenis is based on measurements following a very rigorous technique to avoid any errors.[3] Training of health professionals in the recognition of micropenis and providing information on referral pathways to the experts and centres equipped for optimal management are essential. Another important aspect is the development of National or Regional charts for measurements so that the true prevalence can be established since penile sizes are known to have ethnic variations.

There are medical and surgical treatment options for micropenis. The objective of treatment is to avoid dysmorphophobia and to ensure an everyday sex life and normal urination. [28] The medical treatment of micropenis is based on hormonal therapy, particularly testosterone. It can be used intramuscularly or transdermal as creams or gels.[29] In our study, intramuscular preparations were used to reduce manipulation by parents. The mean increase in penile length of 2.68±0.97 cm in the present study was similar to a French study by Velásquez-Urzola *et al*, [30], who reported a mean increase in penile length of 2.1±0.8 cm in children with an isolated micropenis. [30] The authors[30] also noted that the increase was better when treatment was started during the neonatal period, where the most severe forms of micropenis were found.[30] Similarly, Bin-Abbas *et al*, [31] documented a mean increase in penile length of 2.4 cm, while a lower rate of increase (1.4±0.7 cm) was reported by Ishii *et al*, [32] after intramuscular testosterone treatment. The differences in response rates may be attributed to different patients' characteristics in the various studies. Still concerning hormonal treatment, Charmandari *et al*, [33] reported an increase in penile length of 0.5-2.0 cm after three to four months of percutaneous daily administration of dihydrotestosterone gel (traditionally used in patients with 5-alpha reductase deficiency) in patients with micropenis caused by other diagnoses. The authors[33] also reported that some children who failed to respond to testosterone treatment showed a favourable response to the dihydrotestosterone gel.

The second modality of treatment, which is the surgical reconstruction of the micropenis or elongation by plastic surgery, is a therapeutic option attempted after the failure of well-conducted medical treatment. Surgery is rarely performed in children because of complex procedures with several complications, such as unsightly scars. These surgeries also require a skilled medical team and highly specialised centres, [28] and these are presently not readily available in resource-constrained settings such as ours.

In a sizeable percentage of cases, micropenis was discovered by the mothers and at birth. This discovery constituted a source of anxiety to parents and relatives. However, prompt medical care could not be accessed because of taboos and stigmatisation related to issues of sexuality. Additionally, the expertise required for the management of micropenis in our setting is not widely available. Many health professionals in our

country may feel that no treatment can be instituted for the condition. Furthermore, the condition, micropenis, is not life-threatening, therefore, may be neglected, but because of the psychosocial distress which patients and families may experience, this should not be so. Only 4.3% of cases of micropenis were discovered by doctors. Therefore, awareness among health professionals is important to facilitate early diagnosis and management of micropenis.

Conclusion

Micropenis remains under-explored in our context. Health professionals are encouraged to perform a thorough physical examination in children in order to diagnose and institute management for micropenis early. This will help to alleviate anxiety in affected children and parents, being that treatment is largely effective. The necessary tests to confirm aetiology should be made available and affordable so that optimal management can be instituted.

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