

Micropenis Associated or Not with Cryptorchidism in the Endocrinology Department of Yopougon University Hospital in Ivory Coast: Epidemiological, Clinical, Paraclinical and Therapeutic Aspects

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Abstract

Background: Congenital malformations such as micropenis and cryptorchidism do not have immediate dramatic consequences. However, the diagnosis is often unknown at birth, and therefore late. In Ivory Coast, there are few studies on cryptorchidism and micropenis. We conducted this study to identify the epidemiological, clinical, etiological and therapeutic characteristics of the micropenis associated or not with cryptorchidism at Yopougon University Hospital. **Methods:** We conducted a retrospective descriptive study in the Department of Endocrinology-Diabetology of the Yopougon University Hospital carried out over 13 years from January 2005 to December 2018. All patients were included regardless of the presence of a micropenis associated or not with cryptorchidism in the clinical or paraclinical examination. **Results:** A total of 14 micropenis were reported associated in 6 cases with cryptorchidism. It was unilateral cryptorchidism in 4 patients or 66.66% of cases. The average age of affected patients was 21.32 years with extremes ranging from 10 months to 48 years. The reason for consultation was micropenis in 12 out of 14 cases or 85.75%. The associated signs apart from cryptorchidism were obesity in 42.86% of cases, gynecomastia in 35.71% of cases. The aetiology was dominated by idiopathic causes. Treatment with testosterone enanthate was more effective in pre-pubertal children than in adults. **Conclusion:** The diagnosis of micropenis associated or not with cryptorchidism is late because of the frustrations, taboos and psycho-social states that it causes. However, drug treatment is effective when treatment is started early.

Keywords

Micropenis, Cryptorchidism, Hospital Environment, Ivory Coast

1. Introduction

Congenital malformations are morphological and functional anomalies present at birth. They find their origin in the genetic constitution of the embryo or in an extrinsic defect in its development in utero. These malformations are induced by genetic, metabolic, infectious, drug, ionizing radiation and toxic causes [1]. According to the WHO, each year, 303,000 newborns died before the age of 28 days due to congenital anomalies. However, not all of these malformations have immediate dramatic consequences. This is the case for micropenis and cryptorchidism. The diagnosis is often unknown at birth and suspected in childhood. It is during adolescence or adulthood that the patient consults, driven by the somatic and/or psycho-social repercussions. Cryptorchidism is defined as a testicle spontaneously and permanently located outside the scrotum at any point in its normal migration path. Thus, the cryptorchid testicle can be found in an intra-abdominal position, inside the inguinal canal, at its external orifice or at the root of the bursa [2]. Congenital cryptorchidism is the most common congenital anomaly among newborn boys, and it has a prevalence at birth of 1.1% to 8.4% in boys with a birth weight over 2500 g [3]. Cryptorchidism is associated with a 2- to 4-fold increased risk of testicular germ cell tumors and an increased risk of infertility, due to an impaired spermatogenesis [4]. Orchiopexy between 6 and 12 months is the recommended treatment for cryptorchidism [5] [6]. Micropenis is defined as a stretched penis length less than 2.5 standard deviations (SD) below the mean [7]. In sub-Saharan Africa, despite progress in surgery, many patients are not operated on at an age when the functional prognosis is still favorable [8]. In our countries, the delay in consultation and the financial problem are the mainly difficulties on the surgery. In Ivory Coast, there are few studies on cryptorchidism and micropenis. We conducted a retrospective study on 14 cases of micropenis associated or not with cryptorchidism, in order to study the epidemiological-clinical, diagnostic and therapeutic characteristics in Ivory Coast.

2. Methodology

In this study, we report the experience of the endocrinology-diabetology department of Yopougon University Hospital over a period of 13 years between January 2005 and December 2018. This is a descriptive cross-sectional study with a retrospective collection of 14 cases of micropenis associated or not with cryptorchidism. The study was stopped due to the fact that it was a preliminary study which could not be continued because the Yopougon University Hospital was closed in 2019 for renovation. Although the service has not been reopened to date, we wanted to publish this data to show that micropenis is not such a rare

pathology despite the small sample size and identify the difficulties of its management in our context. This study will serve as a data base for a prospective study with a larger number of cases.

We included all patients who were seen in endocrinology consultation for micropenis associated or not with cryptorchidism confirmed on clinical or para-clinical examination.

We excluded incorrectly completed files and patients with abnormalities of the penis other than micropenis and/or without cryptorchidia.

Data collection was based on a survey form which provided information on:

- socio-demographic data aspects (age of discovery, profession, level of education);
- clinical data namely: the existence of micropenis by measuring the stretched length of the penis from the pubic bone to the tip of the glans, the position of the testicle by palpation of the inguinal areas, the position of the urethral meatus on the penis (hypospadias, epispadias), olfactory disorders (anosmia, hyposmia) and other associated signs and malformations like Turner or Klinefelter type or others;
- paraclinical data with hormonal assessment such as dosage of testosterone, FSH-LH, AMH, karyotype and morphological assessment (testicular ultrasound, pituitary MRI);
- therapeutic modalities (medical and surgical treatment) and evolution (extension or not of the length of the penis).

The diagnosis of micropenis is considered if the length of the penis is less than or equal to 2.5 standard deviations from the mean for age. The measured penis size must be compared to the values of reference tables, such as the Schonfeld, Feldman curve.

The prepubertal state is defined as a testicular volume of less than 4 ml.

The data were processed and analyzed with Epi info software, Excel and Word in its 2007 version.

In summary, we had 19 micropenis files, 5 of which were excluded due to incomplete files. We excluded: patients with abnormalities of the penis other than the micropenis and/or without cryptorchidia, 1 case of oscillating testicles and 2 cases of hypospadias and 2 cases for absence measuring the size of the penis.

3. Results

3.1. Epidemiological Data

14 files of patients consulting for micropenis were reported.

Eight (8) patients out of 14 had consulted in the last 5 years of the study period, *i.e.* 57.14% of cases (**Table 1**).

The average age of the patients was 21.32 years with age limits between 10 months and 48 years and a standard deviation of. The age groups over 15 years and 10-14 years were the most representative in 50% and 35.71% of cases respectively (**Table 2**).

Table 1. Distribution of patients according to consultation period.

Consultation period	Number (n)	Percentage (%)
2005 - 2009	1	7.14
2010 - 2013	5	35.72
2014 - 2018	8	57.14
Total	14	100

Table 2. Distribution of patients according to age.

Age group (year)	Number (n)	Percentage (%)
0 - 9	2	14.29
10 - 14	5	35.71
≥15	7	50.00
Total	14	100

3.2. Clinical Data

The reason for consultation in endocrinology or pediatric surgery was micropenis in 12 patients *i.e.* 85.71% of cases. 14 micropenis were reported associated in 6 cases with cryptorchidism, *i.e.* 42.86% of cases. It was unilateral cryptorchidism in 4 patients or 66.67% of cases with 2 cases of right and left cryptorchidism respectively; and 2 cases of bilateral cryptorchidism (33.33%). In our series, the average penis size was estimated at:

- 1 cm < 2.5 SD in patients aged 0 to 2 years;
- 3 cm < 2.5 SD in patients aged 2 to 9 years;
- 3.86 cm < 2.5 SD in patients aged 9 to 14 years;
- 6.28 cm < 2.5 SD in patients aged 14 and over.

Six patients out of the 14 were overweight, *i.e.* 42.86% of cases.

The other associated signs were gynecomastia in 5 cases (35.71%), stature delay in 2 cases (14.28%), pubertal delay in 2 cases (14.28%) and one case of hydrocephalus (7.14%).

3.3. Paraclinical Data

The hormonal assessment consisted of baseline testosterone and gonadotropins (LH, FSH) measurements. It was performed in 10 patients, or 71.43% of cases. No dynamic test had been carried out. No patient was able to perform the inhibin B and AMH assay. Testosterone was low in non-pubertal patients (8) and abnormally low in 4 out of 6 patients, or 66.67% of cases. Of the 6 pubescent patients, 4 patients were able to perform the gonadotropin assay with 3 cases of hypogonadotropic hypogonadism. One patient (7.14%) had performed a spermogram which revealed azoospermia. The karyotype performed in 2 patients came back normal (46XY).

Morphologically, the abdominopelvic ultrasound made it possible to classify the prepubertal patients, *i.e.* a total of 8 patients with 7 patients aged under 14 years and one (1) patient aged over 15 years (testicular volume less than 4 ml). It

allowed us to confirm inguinal cryptorchidism in 6 patients or 42.85% of cases. None of the patients with hypogonadotropic hypogonadism were able to perform pituitary MRI. Two patients had an X-ray of the left wrist and hand to determine the bone age with a bone age lower than the chronological age of the patients.

The aetiology was dominated by idiopathic causes (64.28%). Those patients who have hypogonadism hypogonadotropic (28.57%) have not done the MRI (**Table 3**).

3.4. Therapeutic and Evolutionary Data

Hormonal treatment was based on testosterone enanthate and hCG in case of associated cryptorchidism, 6 patients or 42.86% benefited. One patient underwent an orchiectomy and another underwent a two-stage orchidopexy. The outcome was favorable for 1 patient (P3), or 16.67% of patients who received treatment with testosterone enanthate. Among the 6 patients who benefited from treatments with testosterone enanthate (3 treatments on average) intramuscularly we had between: 10 years to 14 years: only 1 patient (P3) who benefited from the treatment with a favorable result, this is *i.e.* an increase in the size of the penis. 15 years and over: 5 patients (P7, P8, P11, P12, P13) had benefited from the treatment, 3 of whom had a stable course and the other 2 had been lost to follow-up (**Table 4**).

Table 3. Summary of morphological characteristics of patients.

Patient (P)	Inguino-scrotal and abdominal ultrasound	X-ray of the wrist and left hand	Karyotype	Etiological diagnosis
P1	Inguinal testicle	-	-	Idiopathic hypogonadism
P2	Absence of testicle	-	-	Testicular agenesis
P3	-	-	-	Idiopathic hypogonadism
P4	-	-	-	Idiopathic hypogonadism
P5	Inguinal testicle	-	-	Idiopathic hypogonadism
P6	-	-	-	Hypogonadotropic hypogonadism
P7	-	Bone age < chronological age	-	Idiopathic hypogonadism
P8	Inguinal testicle	Bone age < chronological age	-	Hypogonadotropic hypogonadism
P9	Inguinal testicle	-	-	Idiopathic hypogonadism
P10	-	-	-	Idiopathic hypogonadism
P11	Deep inguinal testicle	-	-	Idiopathic hypogonadism
P12	-	-	-	Idiopathic hypogonadism
P13	-	-	46XY	Hypogonadotropic hypogonadism
P14	Inguinal testicle	-	46 XY	Hypogonadotropic hypogonadism

Table 4. Summary of epidemiological-clinical and biological characteristics of patients.

Patient (P)	Age	Reason for consultation	Penis size in (cm)	Associated pathologies	Testosterone (ng/ml)	LH (mUI/ml)	FSH (mUI/ml)
P1	10 months	Micropenis	1	Bilateral cryptorchidism	0.19	-	-
P2	8 years 6 months	Micropenis	3	Obesity, gynecomastia	0.025	0.27	0.98
P3	10 years	Micropenis	3.5	Obesity	0.3	2.5	3.16
P4	10 years 6 months	Micropenis	3.8	gynecomastia Obesity	0.11	0.1	0.83
P5	12 years	Micropenis	4	Overweight right cryptorchidism	0.052	0.14	0.17
P6	12 years	gynecomastia	3.5	gynecomastia Obesity hydrocephalus	0.025	0.1	0.6
P7	13 years 8 months	Micropenis	4.5	Stature delay, Pubertal delay	0.025	5.7	0.37
P8	18 years	Micropenis	4.5	Bilateral cryptorchidism Stature delay	0.1	0.1	0.4
P9	25 years	Micropenis	6	Left cryptorchidism	6.3	-	-
P10	27 years	Micropenis	6	-	-	-	-
P11	29 years	Pubertal delay	7.5	Gynecomastia, right cryptorchidism, Pubertal delay	0.025	-	-
P12	40 years	Micropenis	9	-	11.18	7.15	2.18
P13	44 years	Micropenis	5	Overweight	0.06	0.1	0.59
P14	48 years	Micropenis	6	Gynecomastia, right cryptorchidism, Obesity	0.25	0.04	0.29

4. Discussion

The prevalence of micropenis is increasing according to studies in Europe (Montpellier University Hospital) and Africa as well as in the rest of the world [9]. The causes of male congenital malformations are multifactorial. However, to explain the increase in this prevalence, some authors supported the hypothesis of prenatal contamination by pesticides [10]. Although the prevalence of micropenis increases over time in our study, it still remains lower than the data reported in the literature. Certainly, linked to the lack of awareness of the existence of a treatment service for this pathology but also in our region, any theme on sex remains a taboo subject with difficulty in talking about it.

The average age in our series was 21.32 years, with limits of 10 months and 48 years. Ben Abdelouahab [11] and H. Latrech [12], report 7.5 years and 16.3 years respectively. This observed difference is due to the study population. Indeed, in our series, we recorded more adults than children while Ben Abdelouahab's se-

ries is made up of children and that of Latrech is made up of adolescents. Elsewhere, the delay in consultation due to the taboo and frustration which accompanies this genital anomaly in men could also explain this age difference but also the existence of hope for the normalization of penis size at puberty, or as an adult. The measured penis size must be compared to the values of reference tables, such as the Schonfeld, Feldman curve.

The diagnosis of micro penis is considered if the length of the penis is less than or equal to 2.5 standard deviations from the mean for age.

In our series, the average penis size was: From newborn to infant (0 to 2 years) = 1 cm < 2.5 SD - Pre-pubertal children (3 to 9 years) = 3 cm < 2.5 SD - Pubescent children (10 to 14 years old) = 3.86 cm < 2.5 DS - Children from 15 years old and adults = 6.28 cm < 2.5 DS. All these values are less than 2.5 DS which confirms the micropenis. We had 6 patients with cryptorchidism associated with the micropenis, *i.e.* 42.86% of cases. Soumeya Fedala *et al.* reported 40% cryptorchidism associated with micropenis [12].

This association is rarely found in the literature. However there would be a link. Indeed, especially bilateral cryptorchidism neglected or poorly managed in childhood could lead to a micropenis in adolescence and adulthood. Cryptorchidism could be the result of insufficient secretion of pituitary gonadotropins (LH, FSH) in the second half of fetal life with reduced testosterone production. Apart from cryptorchidism, other signs can be associated with micropenis depending on the etiologies. Thus, the micropenis associated with obesity brings to mind certain rare genetic syndromes, difficult to highlight in our daily practices. These are Bardet-Biedl, Prader-Willi, MORN or Noonan syndromes [11]. Micropenis associated with gynecomastia suggests peripheral or central hypogonadism. Because any situation that would lead to a decrease in testosterone would be likely to simultaneously lead to gynecomastia [13] (Table 5).

For treatment, the treatment with testosterone enanthate carried out in a pre-pubertal child was effective with lengthening of the penis, compared to three patients over 15 years old in whom the evolution was marked by failure. Observation reported in the literature. According to the series by Y. Sagna *et al.* 12 patients aged 10 to 14 years had benefited from testosterone enanthate treatments with favorable treatment for all [7].

Table 5. Etiologies of micropenis according to different series.

Etiology	Our series (CI)	H. Latrech <i>et al.</i> (Maroc) [12]	Fedala <i>et al.</i> (Algérie) [14]
Idiopathic	64.28%	41%	50%
GH deficiency	-	23%	7%
HH	28.57%	14%	40%
Genetic cause	-	13	-
Testicular dysgenesis	7.14%	9%	3%

HH: hypogonadotropic hypogonadism GH: growth hormone.

5. Limitations of the Study

The main limitation of this study remains its retrospective aspect with a lack of data. Financial limitation was the basis for the non-performance of a certain number of paraclinical examinations with an irregular follow-up rate and loss to follow-up.

6. Conclusion

The micro penis associated or not with cryptorchidism is diagnosed late because of the psycho-social states on the one hand and the financial difficulties in carrying out etiological explorations on the other hand. Drug treatment undertaken early seems effective. This study shows the interest in raising awareness and informing healthcare workers: midwives, nurses and doctors, parents and governments in order to put in place the means for early diagnosis and treatment.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Survey Sheet

FILE NO:

I. SOCIO-DEMOGRAPHIC CHARACTERISTICS

- 1) Age |___| years
- 2) Profession |_| (1 = informal sector; 2 = middle manager; 3 = senior manager; 4 = unemployed; 5 = student or student; 6 = retirees)
- 3) Level of education |_| (1 = Primary; 2 = Secondary; 3 = Superior; 4 = Uneducated)
- 4) Place of Residence |_| (1 = urban; 2 = rural)
- 5) Socio-economic level |_| (1 = Favorable; 2 = Unfavorable; 3 = Medium)

II. CLINICAL CHARACTERISTICS

- 6) Year of first consultation |____|
- 7) Reason for consultation
|_____|
- 8) Discovery period |_| (1 = at birth; 2 = in childhood; 3 = in adulthood; 4 = during a routine examination; 5 = in a context of desire for paternity)
- 9) Background |_| (1 = pituitary tumor; 2 = family malformations; 3 = other pathologies); Specify |_____|
- 10) Diagnosis |_| (1 = cryptorchidism; 2 = micropenis; 3 = cryptorchidism and micropenis)
- 11) Side of the undescended testicle |_| (1 = left; 2 = right; 3 = bilateral)
- 12) Palpable testis |_| (1 = Yes; 2 = No)
- 13) Condition of the contralateral testicle |_| (1 = Normal; 2 = Abnormal)
- 14) External genitals
 - Verge |_| (1 = normal; 2 = abnormal) size in cm |____|
Micropenis |_| (1 = Yes; 2 = No)
 - Scrotum |_| (1 = Normal; 2 = Abnormal)
 - Scrotum staining |_| (1 = normal; 2 = abnormal)
- 15) Inguinal hernia |_| (1 = Yes; 2 = No)
- Associated anomalies |_| (1 = micro scrotum; 2 = obesity; 3 = stature delay; 4 = hypospadias; 5 = gynecomastia; 6 = others...)
- 16) Puberty delay |_| (1 = Yes; 2 = No)
- 17) Olfactory disorders (anosmia, hyposmia) |_| (1 = yes; 2 = no)

III. PARACLINICAL CHARACTERISTICS

- 18) Ultrasound: 1 = Inguino-scrotal testicle; 2 = abdominal testis; 3 = Absence of the testicle)
- 19) Hormonal dosage |_| (1 = yes; 2 = no); Value (normal = N, abnormal = A)
- 20) Testosterone (ng/mL) = |___| () LH (mUI/L) = |___| () FSH (mUI/L) = |___| ()
- 21) Spermogram |_| (1 = yes; 2 = no); (normal = N, abnormal = A) ()
- 22) Cerebral MRI |_| (1 = yes; 2 = no); (normal = N, abnormal = A) ()
- 23) CT scan |_| (1 = yes; 2 = no); (normal = N, abnormal = A) ()
- 24) Karyotype |_| (1 = yes; 2 = no); (normal = N, abnormal = A) ()

IV. Etiologies

25) Anomaly of the gonadotropic axis

- Hypogonadotropic hypogonadism (1 = yes; 2 = no)
- Testicular failure (hypergonadotropic hypogonadism) (1 = yes; 2 = no)
- or testicular dysgenesis (1 = yes; 2 = no);

26) Partial insensitivity to androgens (1 = yes; 2 = no)27) Pituitary adenoma (1 = Yes; 2 = No)28) Testosterone Synthesis Abnormal (1 = Yes; 2 = No)29) Genetic Causes (1 = Yes; 2 = No)30) Idiopathic causes (1 = Yes; 2 = No)

V. TREATMENT

31) Hormonal treatment (1 = yes; 2 = no) If yes: (1 = testosterone enanthate; 2 = HCG)Evolution: (1 = favorable; 2 = failure); if yes: 32) Surgical treatment (1 = yes; 2 = no); if yes:

(1 = orchidopexy; 2 = elongation phalloplasty; 3 = stretch prosthesis)

Evolution: 1 = single; 2 = Complicated, to be specified | _____|