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Diagnosis of Male Hypogonadism: Experience of a Subsaharan African Endocrinology Department: Transversal Study from January 1st, 2020 to July 31st, 2022

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Abstract

Introduction: Hypogonadism should be suspected in a man who has symptoms and signs of testosterone deficiency. Clinical manifestations depend on the severity and duration of testosterone deficiency, whether the testicular deficit is concerning only androgen synthesis, spermatogenesis, or both. The objective of our study was to evaluate the clinical and aetiological characteristics of male hypogonadism in Dakar's suburb. **Patients and methods:** We conducted a transversal study from January 1st, 2020 to July 31st, 2022. We included all male patients aged at least 14 years old with hypogonadism confirmed by a low level of early-morning free testosterone based on two different dosages. For all patients included, sociodemographic and diagnostic parameters were collected by using a pre-established registration form. **Results:** In total, 20 patients were selected. The average age was 36.3 years old [14 - 62 years old]. Half of the patients were overweight. Five patients had an abdominal circumference greater than 94 cm (37 inches). The other comorbidities found in our patients were type 2 diabetes (n = 1), hypertension (n = 1) and primary hypercholesterolemia in 2 patients. The functional signs reported by the patients were: couple's infertility in 17 patients, decreased libido in 14 patients, erectile dysfunction in 13 patients, premature ejaculation in 2 patients and anejaculation in 4 patients. The physical examination revealed a bilateral testicular atrophy in 17 patients and a unilateral testicular atrophy in 2 patients; no patient had varicocele or urethral meatus abnormalities. Ten patients presented a micropenis. A eunuchoid morphotype was present in 6 patients and a short stature was noted in 2 patients. It was peripheral hypogo-

nadism (HH) in 18 patients and hypogonadotropic hypogonadism (Hh) in 2 patients. The hypogonadotropic hypogonadism was isolated in both cases. The testicular echography confirmed testicular atrophy and showed cryptorchidism in 5 patients. The pituitary MRI performed in 2 patients with Hh showed an aspect of empty sella turcica in one patient and was normal in the second patient. **Conclusion:** In our practice, the diagnosis of male hypogonadism is most often made in adulthood. The most usual clinical presentation is failure of pubertal sexual development associated or not with a eunuchoid morphotype. The anomalies of spermatogenesis are found in most patients. Infertility is the primary motive for consultation.

Keywords

Diagnostic, Hypogonadism, Male, Senegal

1. Introduction

Male hypogonadism is a global or partial alteration of testicular functions characterized by an androgen deficiency associated or not with qualitative or quantitative spermatogenesis abnormalities [1]. It can be primary, that is of testicular origin (hypergonadotropic, peripheral or primary hypogonadism) or secondary in which case the anomaly is central affecting the hypothalamic-pituitary axis (hypogonadotropic, central or secondary hypogonadism) [2].

Signs and symptoms of hypogonadism depend on the age of onset, the severity of androgen deficiency and the underlying cause of androgen deficiency [3]. When the deficiency appears during fetal life, the clinical picture can be dramatic featuring sexual differentiation abnormalities, urethral meatus abnormalities and cryptorchidism… fortunately this situation is very rare. When the deficit sets in during the peripubertal period, the association of incomplete or failure of pubertal sexual development or delayed puberty and eunuchoid morphotype is pathognomonic of male hypogonadism [4]. In adulthood, the signs are less specific. Although the delayed puberty associated with the eunuchoid morphotype is generally described in adolescents; some adults, due to the significant delays to initial consultation for infertility, may have this clinical presentation [5].

The epidemiology of male hypogonadism is not very well known even if their prevalence seems to have increased in recent years [6] [7]. There are few data regarding male hypogonadism in sub-Saharan Africa [7] [8].

Our work aimed to evaluate the epidemiological and diagnostic particularities of male hypogonadism in a black African environment.

2. Patients and Methods

We conducted a transversal study from January 1st, 2020 to July 31st, 2022 at the National Hospital Center of Pikine's endocrinology outpatient consultation. The study included all male patients aged at least 14 years old presenting testosterone

deficiency symptoms. The inclusion criteria were hypogonadism confirmed by total testosterone less than 300 ng/dL on 2 separate early morning serum tests. For all participants included in the study, the following data were collected using a pre-established form (cf appendix).

2.1. Epidemiological Data

Age, Body mass index, waist circumference, history and conditions, in particular comorbidities that may lead to hypogonadism (Chronic obstructive pulmonary disease, diabetes, metabolic syndrome, cancer, cardiovascular disease, chemotherapy, radiotherapy, testicular trauma, testicular torsion, orchitis, head trauma, surgery or tumor of the sellar region)

Diagnostic Data

- Clinical data: symptoms and signs of testosterone deficiency, anthropometric data, general examination
- Paraclinical data: Gonadotropic axis exploration (FSH, LH, testosterone levels); prolactin levels, sperm analysis (spermogram, sperm culture), karyotype analysis for chromosomal abnormalities, radiological examinations (testicular ultrasound, pituitary imaging).

Ethic consideration: all patients hospitalized and monitored in the department are informed that their medical records could be used for scientific publications while respecting anonymity.

3. Results

Twenty patients corresponding to the inclusion criteria were selected.

Epidemiological data

The mean age of the participants was 36.3 years old (range 24 to 62 years). Apart from the 14 years old patient, 85% of patients were between 18 and 45 years old and 10% of patients were over 45 years old. The aetiological factor of hypogonadism found in our patients were overweight (10 patients), abdominal obesity (5 patients) and type 2 diabetes (1 patient). Five patients were overweight, 3 patients had class 1 obesity and 2 patients had class 2 obesity. None of the patients had a history of testicular trauma or torsion or a history of orchitis or head trauma, hemorrhage, or surgery of the sellar region. The other comorbidities found in our patients were hypertension (n = 1) and dyslipidemia (2 patients).

Diagnostic data

The present complaint was delayed puberty in a 14-year-old patient. All other patients were consulted as adults. The couple's infertility was the first present complaint reported by 17 patients. The sexual dysfunction symptoms reported by the patients were: decreased libido (14 patients), erectile dysfunction (13 patients), premature ejaculation (2 patients) and anejaculation (4 patients). According to the IIEF5 (International Index Erectile function-5), erectile dysfunction was severe in 3 patients, moderate in 5 patients and mild in 5 patients.

Physical examination revealed a bilateral testicular atrophy in 17 patients and a unilateral in 2 patients. No patient had varicocele or urethral meatus abnormalities. Ten patients had a micropenis. A eunuchoid morphotype was present in 6 patients, stature delay was noted in 2 patients. Decreased androgen-dependent hair was noted in 11 patients. Table 1 show the signs and symptoms of testosterone deficiency of the patients

The exploration of the gonadotropic axis suggested hypergonadotropic (HH) or peripheral hypogonadism in 18 patients and hypogonadotropic hypogonadism (Hh) in 2 patients. The exploration of the thyrotropic, lactotropic, somatotropic and corticotropic axis was normal in the 2 patients who presented central hypogonadism. The spermogram was abnormal in the 19 patients in whom the examination was performed. The abnormalities noted on the spermogram were azoospermia (n = 9), oligospermia (n = 4), terratozoospermia (n = 3), asthenospermia (n = 3), aspermia (n = 2) and oligoasthenospermia (n = 2).

The testicular ultrasound confirmed testicular atrophy and also showed cryptorchidism in 5 patients. The pituitary MRI performed in the 2 patients with Hh showed an empty sella turcica in one patient and was normal in the second patient. The karyotype could only be performed in 4 patients. It was in favor of Klinefelter syndrome in 2 patients. The 47 XXY karyotype was associated with a micro-deletion of the Y chromosome in one patient and there was a chromosomal mosaicism in the second patient. The karyotype was normal in the other patients.

4. Discussion

The overall epidemiology of male hypogonadism is unknown due to the absence of large-scale studies in Africa, Asia and South America [6]. Most epidemiological

Table 1. Signs and symptoms of testosterone deficiency of study participants.

Symptoms and signs of testosterone deficiency	Number of patients/20
Delayed puberty	1
Infertility	17
Erectil dysfunction	12
Decrease libido	14
Anejaculation	4
Premature ejaculation	2
Small penis (<5 cm)	10
Small Testes (<6 cm^3)	19
Cryptorchidism	5
Gynecomastia	17
Eunuchoidal stature	6
Decreased androgen-dependent hair	11

studies report an increase in the prevalence of male hypogonadism with age. The first epidemiological studies have significant limitations. They only concerned men aged 40 years or over. Men with known causes of hypogonadism were excluded. There was no harmonization of testosterone dosages and the thresholds to define a low serum testosterone concentration were different. In Europe the prevalence of male hypogonadism is greater than 2% after the age of 40 [9]. The only Senegalese case reported in the literature was 45 years old. In our series the average age of onset hypogonadism was 36.3 years old and 90% of patients were less than 45 years old [8].

Before measuring serum, testosterone levels and making a diagnosis of hypogonadism, it is important to assess whether the man has clinical manifestations of testosterone deficiency or not [5]. Clinical manifestations depend on the severity and duration of testosterone deficiency. A clinical finding that is pathognomonic of severe prepubertal testosterone deficiency is eunuchoidism, which is characterized by extremely small penis and testes, poorly developed scrotum, lack of androgen-dependent hair pattern, a high-pitched voice, and a eunuchoidal body. Although usually detected in boys who present with delayed puberty, eunuchoidism may also be found in adult males who are not diagnosed at an earlier age. In men, decreased or loss of androgen-dependent hair is a specific sign of long-standing, severe testosterone deficiency [9]. In adult men and the elderly, the signs are more discreet. According to the European Male Aging Study (EMAS) the triad: low libido; reduced spontaneous erections and erectile dysfunction is highly suggestive of male hypogonadism in middle-aged and elderly men [10]. In our cohort, symptoms of androgen deficiency were found in all our patients. Impuberism with micropenis, androgen-dependent hair loss, small testicles associated or not with a eunuchoid morphotype were found in more than half of the patients. This pathognomonic clinical presentation of a prepubertal deficit portends a delay in consultation. In fact, 95% of our patients consulted as adults.

The first reason for consultation among our patients was infertility reported by 85% of patients. The prevalence of male infertility is generally estimated to be between 10% and 15%, and most of these men suffer from spermatogenesis [11]. The male component of couple infertility has been estimated at 20% - 40% in sub-Saharan Africa [12]. In patients with hypogonadism, the decrease in the testicular size is an indicator of spermatogenesis abnormality, because the seminiferous tubules represent 80% to 90% of the testicular volume [5]. Testicular atrophy was found in 19 patients. Dysspermatogenesis was noted in the 19 patients who underwent semen analysis. In a study carried out in Niamey relating to the evaluation of the hormonal status of patients consulting for infertility with an abnormal spermogram; male hypogonadism was found in 35 out of 69 patients including 21 cases of hypergonadotropic hypogonadism and 14 cases of hypogonadotropic hypogonadism. In our series, hypogonadism was primary in 18 patients, representing 90% of the cohort.

After the topographical diagnosis of hypogonadism, the next step in diagnosis is the search for a specific cause in order to guide management [5].

Determining whether a man with hypogonadism has organic hypogonadism or functional hypogonadism is important to guide management. It is important to specify whether the damage is organic or functional. Functional hypogonadism (FHG) is more common than organic hypogonadism and generally causes mild symptoms and signs of testosterone deficiency [5]. In FHG, HH is the prevalent form and is often due to metabolic disturbances (such as obesity, type 2 diabetes mellitus and metabolic syndrome) or other illnesses which hamper GnRH secretion [13]. Overweight and obesity are associated with decreased sperm quality and a greater risk of infertility. A systematic review of 30 studies involving 115.158 men found that male obesity was associated with decreased male reproductive potential [14]. The severity of the consequences of obesity on hormonal profile, sperm parameters and DNA damage, as well as pregnancy outcomes may vary due to the presence of other comorbidities. Thirteen studies conducted in the United Kingdom, Australia, India, Italy and the United States showed a prevalence of hypogonadism in patients with type 2 diabetes ranging from 4.4% to over 45% [15]. Since obesity is frequently associated with hypogonadism (mostly functional), determination of body mass index (BMI) and measurement of waist circumference are strongly recommended in all individuals [16]. In our patients, the etiological factors associated with the occurrence of functional hypogonadism were overweight in half of the patients and type 2 diabetes in 1 patient.

However, in our cohort, only two patients presented with HH. Also, the severity of the signs of androgen deficiency is more in favor of an organic origin. In the absence of obvious functional or organic causes, faced with hypergonadotropic hypogonadism, a karyotype study must be carried out [5]. Klinefelter syndrome is the first organic cause of male hypogonadism, 50% to 75% of which are undiagnosed [6]. Only 4 patients benefited from a karyotype study and the latter was in favor of Klinefelter syndrome in 2 patients. This is the main limitation of our study. In the hypogonadotropic hypogonadism, it is necessary to explore the other pituitary secretions and perform imaging of the sellar region [5]. In our 2 patients with hypogonadotropic hypogonadism, the gonadal deficit was isolated and the MRI was normal in one patient and showed an empty Sella turcica in the second.

5. Conclusion

At the end of our study, we can withhold that the main circumstance of discovery of male hypogonadism in our practice is infertility. The average age at diagnosis is around 30; the usual clinical presentation is that of pre-pubertal hypogonadism with signs of severe androgen deficiency. Dysspermatogenesis is found in all infertile patients. The aetiological factors of functional hypogonadism are dominated by excess weight. Less than 1/4 of patients with primary hy-

pogonadism benefit from the karyotype study.

Conflicts of Interest

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

References

[1] Salonia, A., Rastrelli, G., Hackett, G., *et al.* (2019) Paediatric and Adult-Onset Male Hypogonadism. *Nature Reviews Disease Primers*, **5**, Article No. 38. https://doi.org/10.1038/s41572-019-0087-y

[2] Santi, D. and Corona, G. (2017) Primary and Secondary Hypogonadism. In: Simoni M. and Huhtaniemi, I.T., Eds., *Endocrinology of the Testis and Male Reproduction*, Springer International Publishing, Cham, 687-747. https://doi.org/10.1007/978-3-319-44441-3_24

[3] Ross, A. and Bhasin, S. (2016) Hypogonadism: Its Prevalence and Diagnosis. *Urologic Clinics of North America,* **43**, 163-176. https://doi.org/10.1016/j.ucl.2016.01.002

[4] Corona, G., Rastrelli, G., Vignozzi, L. and Maggi, M. (2022) Androgens and Male Sexual Function. *Best Practice & Research Clinical Endocrinology & Metabolism*, **36**, Article ID: 101615. https://doi.org/10.1016/j.beem.2022.101615

[5] Matsumoto, A.M. (2022) Diagnosis and Evaluation of Hypogonadism. *Endocrinology and Metabolism Clinics of North America*, **51**, 47-62. https://doi.org/10.1016/j.ecl.2021.11.001

[6] Mani, S.B. and Clavijo, R.I. (2022) Medical Treatment of Hypogonadism in Men. *Urologic Clinics of North America*, **49**, 197-207. https://doi.org/10.1016/j.ucl.2021.12.008

[7] Thirumalai, A. and Anawalt, B.D. (2022) Epidemiology of Male Hypogonadism. *Endocrinology and Metabolism Clinics of North America*, **51**, 1-27. https://doi.org/10.1016/j.ecl.2021.11.016

[8] Sidibe, E.H. (2006) Hypergonadotropic Hypogonadism with Sella Turcica Tumor Syndrome: Gonadotropic Adenoma? *Annales d'Endocrinologie*, **67**, 348-352. https://doi.org/10.1016/S0003-4266(06)72610-5

[9] Matsumoto, A.M. and Anawalt, B.D. (2020) Testicular Disorders. In: Melmed, S., Auchus, R.J., Goldfine, A.B., *et al.*, Eds., *Williams Textbook of Endocrinology* (14th Edition), Elsevier, Inc., Philadelphia, 668-755.

[10] Wu, F.C., Tajar, A., Beynon, J.M., Pye, S.R., Silman, A.J., Finn, J.D., O'Neill, T.W., Bartfai, G., Casanueva, F.F., Forti, G., *et al.* (2010) Identification of Late-Onset Hypogonadism in Middle-Aged and Elderly Men. *The New England Journal of Medicine*, **363**, 123-135. https://doi.org/10.1056/NEJMoa0911101

[11] Anawalt, B.D. (2013) Approach to Male Infertility and Induction of Spermatogenesis. *The Journal of Clinical Endocrinology & Metabolism*, **98**, 3532-3542. https://doi.org/10.1210/jc.2012-2400

[12] Batou, S.A., Abessolo, F.O., Mba, I. and Mintsa, A. (2018) Analysis of Spermogram Parameters in Relation to Fructose, Citrate and Neutral Alpha Glucosidase of Sperm in Men Consulting for Infertility in Libreville. *International Journal of Biological and Chemical Sciences*, **12**, 2486-2502. https://doi.org/10.4314/ijbcs.v12i6.3

[13] Corona, G., Rastrelli, G., Vignozzi, L., Barbonetti, A., Sforza, A., Mannucci, E. and

Maggi, M. (2021) The Role of Testosterone Treatment in Patients with Metabolic Disorders. *Expert Review of Clinical Pharmacology*, **14**, 1091-1103. https://doi.org/10.1080/17512433.2021.1938548

[14] Campbell, J.M., Lane, M., Owens, J.A. and Bakos, H.W. (2015) Paternal Obesity Negatively Affects Male Fertility and Assisted Reproduction Outcomes: A Systematic Review and Meta-Analysis. *Reproductive BioMedicine Online*, **31**, 593-604. https://doi.org/10.1016/j.rbmo.2015.07.012

[15] Dhindsa, S., Miller, M.G., McWhirter, C.L., Mager, D.E., Ghanim, H., Chaudhuri, A. and Dandona, P. (2010) Testosterone Concentrations in Diabetic and Nondiabetic Obese Men. *Diabetes Care*, **33**, 1186-1192. https://doi.org/10.2337/dc09-1649

[16] Van Hulsteijn, L.T., Pasquali, R., Casanueva, F., *et al.* (2020) Prevalence of Endocrine Disorders in Obese Patients: Systematic Review and Meta-Analysis. *European Journal of Endocrinology*, **182**, 11-21. https://doi.org/10.1530/EJE-19-0666

Appendix: Questionnary

1. Epidemiological data

-Number

-Age

-Body mass index (kg/m^2)

o BMI category

☐ Underweight (<18.5) ☐ normal (18.5 - 24.9) ☐ overweight (25 - 29.9)

☐ obesity grade 1 (30 - 34.9) ☐ obésity grade 2 (35 - 39.9) ☐ obésity grade 3 (≥40)

-Abdominal circumference (cm) ☐ normal (<94 cm) ☐ anormal (≥94 cm)

2. Aetiological factor of hypogonadism:

- Diabetes
- Smoking
- Metabolic syndrome
- Chronic obstructiv pulmonary disease
- Radiotherapy
- Chemoterapy
- Cancer
- Testiccular trauma
- Testicular torsion
- Orchitis
- Sellar region surgery
- Sellar tumor
- Other

3. Clinical data

⇨ Infertility ☐ Yes ☐ No

☐ Primary infertility ☐ Secondary infertility

⇨ Sexual dysfunction ☐ Yes ☐ No

☐ erectyl dysfunction ☐ decrease libido ☐ premature ejaculation ☐ anejaculation

⇨ The International Index of Erectile Function (IIEF-5) Questionnary

1. How do you rate your **confidence** that you could get and keep an erection?
   Very low
   Low
   Moderate
   High
   Very high

2. When you had erections with sexual stimulation, **how often** were your erections hard enough for penetration?
   Almost never/never
   Much less than half the time
   Sometimes (about half the time)
   Most time (much more than half the time)
   Almost (always)

Continued

3. During sexual intercourse, **how often** were you able to maintain your erection after you had penetrated (entered) your partner?
   Almost never/never
   Much less than half the time
   Sometimes (about half the time)
   Most time (much more than half the time)
   Almost (always)

4. During sexual intercourse, **how difficult** was it to maintain your erection to completion of intercourse?
   Extremly difficult
   Very difficult
   Difficult
   Sightly difficult
   No difficult

5. When you attempted sexual intercourse, **how often** was it satisfactory for you?
   Almost never/never
   Much less than half the time
   Sometimes (about half the time)
   Most time (much more than half the time)
   Almost (always)

Interpration

22 - 25: No erectile dysfunction
17 - 21: Mild erectile dysfunction
12 - 16: Mild to moderate erectile dysfunction
8 - 11: Moderate erectile dysfunction
5 - 7: Severe erectile dysfunction

⇨ **Signes**

- Gynécomastia (☐ yes/☐ No)
- Micropénis (☐ yes/☐ No)
- Testicular exam ☐ Normal ☐ Atrophia (☐ Unilatéral ☐ Bilatéral)
  ☐ Cryptorchidie ☐ Anorchidism ☐ Varicocele
- Dysmorphia ☐ No ☐ eunuchoidism ☐ other Androgen dependent hair
  ☐ normal ☐ decreased

4. Laboratory testing

⇨ Total testosterone fasting
-First testing ☐ normal ☐ Low
-Second testing ☐ normal ☐ Low
⇨ Mesurate FSH and LH ☐ elevated FSH and/or LH ☐ Low or inappropriate Normal FSH and LH
⇨ Prolactin ⇨ TSH ⇨ ACTH ⇨ GH, IGF1 ⇨ Cortisolemie
⇨ Sperme analysis ⇨ Karyotype ⇨ Testicular ultrasond ⇨ Pituitary imaging