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Review article

Micropenis

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Abstract

Micropenis is a medical diagnosis based on correct measurement of penile length. If stretched penile length is below the value corresponding to - 2.5 standard deviation of the mean in a patient with normal internal and external male genitalia, a diagnosis of micropenis is considered. Micropenis can be caused by a variety of factors including structural or hormonal defects of the hypothalamic-pituitary-gonadal axis. It can also be a component of a number of congenital syndromes. For the etiological evaluation, endocrinologic tests are important. This article reviews the etiology, diagnosis, treatment and management of micropenis.

Key words: Micropenis, Etiology, Diagnosis, Treatment

Introduction

Micropenis is a medical diagnosis often incorrectly made. A misdiagnosis may cause parental anxiety and may lead to unnecessary examinations and tests. The correct diagnosis is made by measuring stretched penile length. The first description of standard penile length for age was used by Schonfeld and Beebe in their seminal work.[1] In time, the definition of micropenis was accepted as a penile length smaller than 2.5 standard deviations (SD) below the mean.[2] Micropenis may occur as an independent abnormality by itself or as a clinical finding of many syndromes.[3]

Embryology

During embryonic development, following the differentiation of bipotential gonadal ridge to testis, placental human chorionic gonadotropin (hCG)-driven testosterone synthesis begins in Leydig cells at 8-12 weeks, resulting in penile differentiation stimulated by dihydrotestosterone (DHT), a product of transformation. Fetal androgen levels are high between the 8th and 24th weeks of gestation, with peak levels often observed between the 14th and 16th weeks. Consequently, there is a marked increase in penile length during the second and third trimesters, with an increase of approximately 20 mm from weeks 16 to 38.[4,5] It can thus be deduced that a true micropenis is caused by a hormonal abnormality that occurs after the 12th week of gestation.[6] Hormonal activity of the hypothalamic-pituitary axis and that of the testes increases within the first 6 months of postnatal life. The reason for the activation of the axis is, due to pituitary gonadotropin secretion, cessation of the negative feedback effects of both the placental sex steroids and peptides. An increase in both testis volume and penile length is observed physiologically during this active phase.[7] During this period, follicle stimulating hormone (FSH) and luteinizing hormone (LH) levels rise increasing the circulating testosterone, inhibin B, and anti-Mullerian hormone (AMH) levels, sometimes even to higher levels than in adult males.[8,9] Testosterone levels increase in parallel to the activation peak between the 1st and 3rd months and decrease to prepubertal levels from the 4th-6th months onwards.[10]

Table-I: Normal SPL

Age	Mean ± SD	Mean - 2.5SD
Newborn, 30-week gestation	2.5 ±0.4	1.5
Newborn, 34-week gestation	3.0±0.4	2.0
0-5 months	3.9 ±0.8	19
6-12 months	4.3 ± 0.8	2.3
1-2 years	4.7 ± 0.8	2.6
2-3 years	5.1 ± 0.9	2.9
3-4 years	5.5 ± 0.9	3.3
4-5 years	5.7 ± 0.9	3.5
5-6 years	6.0 ± 0.9	3.8
6-7 years	6.1 ± 0.9	3.9
7-8 years	6.2 ± 1.0	3.7
8-9 years	6.3 ± 1.0	3.8
9-10 years	6.3 ± 1.0	3.8
10-11 years	6.4 ± 1.1	3.7
Adult	13.3 ± 1.6	9.3

Etiology

True micropenis is a result of a hormonal abnormality occurring after 12 weeks of gestation. The causes of this condition can be divided into three broad groups: hypogonadotropic hypogonadism (pituitary/hypothalamic failure), hypergonadotropic hypogonadism (primary testicular failure), and idiopathic. These represent the most common etiologies of micropenis.[11,12,13]

Table- II: Highlights the different etiologies.

I. Deficient testosterone secretion

A. Hypogonadotropic hypogonadism

1. Isolated, including Kallmann's syndrome
2. Associated with other pituitary hormone deficiencies
3. Prader-Willi syndrome
4. Laurence-Moon syndrome
5. Bardet-Biedl syndrome
6. Rud's syndrome

B. Primary hypogonadism

1. Anorchia
2. Klinefelter's and poly-X syndromes
3. Gonadal dysgenesis (incomplete form)
4. Luteinizing hormone receptor defects (incomplete forms)
5. Genetic defects in testosterone steroidogenesis (incomplete forms)
6. Noonan's syndrome
7. Trisomy 21
8. Robinows syndrome
9. Bardet-Biedl syndrome
10. Laurence-Moon syndrome

II. Defects in testosterone action

A. Growth hormone/insulin-like growth factor-I deficiency
B. Androgen receptor defects (incomplete forms)
C. 5-a reductase deficiency (incomplete forms)
D. Fetal hydantoin syndrome

III. Developmental anomalies

A. Aphallia
B. Cloacalexstrophy

IV. Idiopathic

V. Associated with other congenital malformations

Diagnostic Evaluation

1. Measurement of penile length:

Correct measurement of penile length is important because the diagnosis of true micropenis depends on it. A correct and accurately measured penile length of -2.5 SD below the mean for age and presence of internal and external genital organs compatible with a 46, XY karyotype are sufficient findings to support a diagnosis of micropenis.[11]

a) Traditional methods utilize a ruler or caliper to measure penile length. Penile length should be measured when the penis is fully stretched, not flaccid; the glans penis should be held with the thumb and forefinger, and the measurement should be taken from the pubic ramus to the distal tip of the glans penis over the dorsal side. The suprapubic fat pad should be pressed inwards as much as possible, and if present, the foreskin must be retracted during the measurement (Figure-I).[11,14]

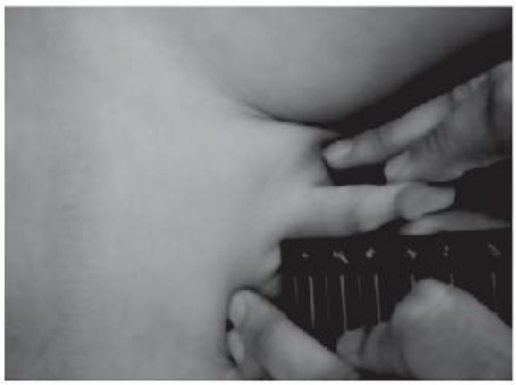

Figure-I: correct technique for SPL measurement.

b) A different approach involves the use of a 10 mL disposable syringe. The needle-side tip of the syringe is cut off, and the piston is inserted into the syringe on the cut side (Figure-II). The open side of the syringe is placed on the penis. The piston is pulled back while pressing the fat pads inwards, which causes the penis to be pulled inside the syringe as a result of suction. Once the penis is stretched inside the syringe, penile length is read from the scale added on the modified syringe.[15]

Figure-II: a modified syringe.

2. Laboratory tests:

First –line tests are serum gonadotrophins (FSH LH), testosterone, DHT,GH, PRL, ACTH, Cortisol, TSH, FT4.

Second-line testicular function test by hCG stimulation test. Inhibin B and AMH, also known as Mullerian-inhibiting hormone are produced by functional Sertoli cells, and determination of their blood levels can be used to detect the presence of functional testicular tissue. Low levels of AMH, accompanied by normal inhibin B levels, and a rare defect in the AMH gene, indicate persistent Mullerian duct syndrome.[9]

Imaging tests are pelvic ultrasound to visualize internal genital organs in suspicious cases and MRI is used to investigate structural midline defects, such as pituitary stalk dysplasia syndrome, central diabetes insipidus characterized by absence of the pituitary bright spot in the posterior neurohypophysis, and pituitary dysplasia.[9,16]

Genetic tests, some authors suggest karyotype assignment using chromosomal analysis or Y-fluorescence in order to determine the sex. Genetic testing may be necessary to eliminate other syndromes.[17]

Differential Diagnosis

1. Inconspicuous penis: Loose penile skin that does not stretch tightly around the body of the penis, penile skin being insufficient or imperfect, excessive fatty tissue, formation of scar tissue following a penile surgery, and presence of a web of skin underneath the penis.[18,19]
2. Buried penis: Children who present with a suspicion of micropenis are often prepubertal and obese, and the small size of their penis is caused by the pressure of the prepubic fat on the penis.[18]
3. Trapped penis: Is referred to as suprapubic fat pads surrounding the penis in the absence of additional skin for the shaft of penis.[19]
4. Webbed penis: Is characterized by a skin tissue connecting the penis to the front side of the scrotum.[17]
5. Penile agenesis, or absence of the penis and curvature of the head of the penis, or chordee, are rare conditions which should also be considered in the differential diagnosis.[17]

Treatment Approaches

Goal:

a) To provide a body image that will not cause embarrassment for the patient

b) To enable the patient to have normal sexual function, and

c) Also enable the patient to standing micturition.

Medical treatment:

a) Testosterone

Initially administered for a short period of time in order to evaluate the response of the penis. Administration can be by intramuscular injection or topical application. In order to observe initial progress, four doses of 25 mg of testosterone cypionate or enanthate in oil are administered intramuscularly once every 3 weeks for 3 months. It may cause temporary acceleration in growth rate and in advancement of bone age.[20]

b) Topical 5-α dihydrotestosterone (DHT) Gel

In prepubertal patients with androgen insensitivity, topical application of DHT gel to the periscrotal region 3 times daily for a total of 5 weeks has been shown to increase serum DHT levels.

c) LH-FSH Applications

Recombinant human FSH-LH treatment during the first few years of life promotes an increase in testicular growth and penile length in patients with hypogonadotropic hypogonadism, although this effect is not very significant.

Surgical treatment:

If the micropenis does not reach an adequate length despite medical interventions, surgical treatment options are considered. The first reconstructive surgery was reported by Hinman.21 in the early 1970s when he performed reconstruction on a patient with micropenis.

Conclusion

Micropenis is a medical diagnosis which is dependent on correct measurement. It may be an independent abnormality or a part of many syndromes. Micropenis can occur as a result of pituitary/hypothalamic insufficiency, primary testicular insufficiency, or can be idiopathic. Endocrinologic assessment helps in determining the etiology of micropenis. Early diagnosis is important for various treatment options.

References

1. Schonfeld WA, Beebe GW. Normal growth and variation in the male genitalia from birth to maturity. J Urol 1942;48:759-777.
2. Aaronson IA. Micropenis: medical and surgical implications. J Urol 1994;152:4-14.
3. Nelson CP, Park JM, Wan J, Bloom DA, Dunn RL, Wei JT. The increasing incidence of congenital penile anomalies in the United States. J Urol 2005;174:1573-1576.
4. Johnson P, Maxwell D. Fetal penile length. Ultrasound Obstet Gynecol 2000;15:308-310.

5. Zalel Y, Pinhas-Hamiel O, Lipitz S, Mashiach S, Achiron R. The development of the fetal penis-an in utero sonographic evaluation. Ultrasound Obstet Gynecol 2001;17:129-131.
6. Evans BA, Williams DM, Hughes IA. Normal postnatal androgen production and action in isolated micropenis and isolated hypospadias. Arch Dis Child 1991;66:1033-1036.
7. Müller J, Skakkebaek NE. Quantification of germ cells and seminiferous tubules by stereological examination of testicles from 50 boys who suffered from sudden death. Int J Androl 1983;6:143-156.
8. Boukari K, Meduri G, Brailly-Tabard S, Guibourdenche J, Ciampi ML, Massin N, Martinerie L, Picard JY, Rey R, Lombès M, Young J. Lack of androgen receptor expression in Sertoli cells accounts for the absence of anti-Mullerian hormone repression during early human testis development. J Clin Endocrinol Metab 2009;94:1818-1825. Epub 2009 Mar 10
9. Grumbach MM. A window of opportunity: the diagnosis of gonadotropin deficiency in the male infant. J Clin Endocrinol Metab 2005;90:3122-3127. Epub 2005 Feb 22
10. Byne W. Developmental endocrine influences on gender identity: implications for management of disorders of sex development. Mt Sinai J Med 2006;73:950-959.
11. Lee, P.A., Mazur, T., Danish, R., Amrhein, J., Blizzard, R.M., Money, J., and Migeon, C.J. (1980) Micropenis. I. Criteria, etiologies and classification. Johns Hopkins Med. J. 146(4), 156–163.
12. Walsh, P.C., Wilson, J.D., Allen, T.D., Madden, J.D., Porter, J.C., Neaves, W.B., Griffin, J.E., and Goodwin, W.E. (1978) Clinical and endocrinological evaluation of patients with congenital microphallus. J. Urol. 120(1), 90–95.
13. Ludwig, G. (1999) Micropenis and apparent micropenis—a diagnostic and therapeutic challenge. Andrologia 31(Suppl 1), 27.
14. Wiygul J, Palmer LS. Micropenis. ScientificWorld Journal 2011;11:1462-1469.
15. Ozbey H, Temiz A, Salman T. A simple method for measuring penile length in newborns and infants. BJU Int 1999;84:10931094.
16. Bressani N, di Natale B, Pellini C, Triulzi F, Scotti G, Chiumello G. Evidence of morphological and functional abnormalities in the hypothalamus of growth-hormone-deficient children: a combined magnetic resonance imaging and endocrine study. Horm Res 1990;34:189-192.
17. Menon PS, Khatwa UA. The child with micropenis. Indian J Pediatr 2000;67:455-460.
18. Borsellino A, Spagnoli A, Vallasciani S, Martini L, Ferro F. Surgical approach to concealed penis: technical refinements and outcome. Urology 2007;69:1195-1198.
19. El-Koutby M, Mohamed Amin el G. Webbed penis: A new classification. J Indian Assoc Pediatr Surg 2010;15:50-52.
20. Guthrie RD, Smith DW, Graham CB. Testosterone treatment for micropenis during early childhood. J Pediatr 1973;83:247-252.
21. Hinman F Jr. Microphallus: characteristics and choice of treatment from a study of 20 cases. J Urol 1972;107:499505.