

Author's response to reviews

Title: Idiopathic Isolated Clitoromegaly: A Report of Two Cases

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Author's response to reviews: see over

Responses to Reviewer 1:

Dear Professor Segars,

Thank you very much indeed for your comments about our manuscript. Additional clinical information was added to the manuscript as you requested.

Respectfully yours,

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Responses to the Reviewer 2:

Dear Professor Monni,

Thank you very much indeed for your comments about our manuscript. Our manuscript was revised by the professional translator for grammatical and language errors. Revisions were indicated with different color words. These revisions were listed below.

Respectfully yours,

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Idiopathic Isolated Clitoromegaly: A Report of Two Cases

Background

Clitoromegaly is a frequent congenital malformation, but acquired clitoral enlargement can be rarely detected.

Methods

Two cases of clitoromegaly which were treated in Ataturk Training Hospital will be presented in this report.

Results

They described gradually growing of their clitoris in the last three years. Neither gynecological nor other systemic abnormalities were detected in both patients. Karyotype analysis and hormonal test results were normal. The abdominal and gynecological ultrasound did not show any cystic lesion or abnormal finding. CT scan of the adrenal glands was normal. Clitoroplasty with preservation of neurovascular pedicles were performed for the treatment of the patients.

Conclusion

The patients presented here were diagnosed as “idiopathic, isolated” clitoromegaly. To the best of our knowledge, there has been no detailed report about idiopathic clitoromegaly in the literature.

Case report

Two cases with clitoromegaly were treated in Ataturk Training Hospital, Izmir, Turkey.

A 22-year-old gravida 0 and 19-year-old gravida 0 presented with adult clitoromegaly, which was emotionally embarrassing. The former case had phallus 20 mm in length, which increased by 30 mm with arousal (Figure 1) and the latter case had phallus 30 mm in length, which increased by 40 mm with arousal (Figure 2). Secondary sexual features were otherwise normal. Sexual hair was normal with no hirsutism and obesity in both cases. They described gradually growing of their clitoris in the last three years. Neither gynecological nor systemic

abnormalities were detected in both patients. They had no drug or family history. They did not describe clitoral irritation secondary to masturbation or other sexual functions. They had just “isolated” clitoromegaly as an abnormal finding on all detailed physical examinations.

Karyotype analysis was done in both cases and reported as 46, XX. Results of routine laboratory tests were normal. Also, preoperatively, levels of electrolytes, oestradiol, SHBG, testosterone, androstenedione, DHEA-S, FSH, LH, 17-OH-P, prolactin, ACTH, cortisol PL, Deoxycorticosterone, Deoxycortisol 11, T3, T4, TSH, β HCG, CEA were estimated and the results were normal. 17-ketosteroid output in 24-hour-urine specimen was normal in both patients. Abdominal and gynecological ultrasound did not show any cystic lesion or abnormal finding. CT scan of the adrenal glands was normal.

No abnormality which could explain clitoromegaly was found in all laboratory and radiological tests. Patients were diagnosed as “idiopathic, isolated” clitoromegaly.

Clitoroplasty with preservation of the neurovascular pedicles were planned and the patients were operated under general anesthesia. A traction suture of 3/0 nylon was placed in the glans of clitoris (Figure 3). An incision was made on the lateral phallus perpendicular to the axis of clitoral shaft, and carried through a 270 degree semicircular arc to the base of the glans as described by Papageorgiou et al [1]. Two longitudinal incisions were made laterally to the dorsal neurovascular bundle. Two crura were identified, clamped and mid-body of the clitoris was resected. The base of the glans was sutured to the divided corpora with 4/0 vicryl, and proximal and distal ends of corpora were closed with 4/0 vicryl. The skin was closed with 4/0 vicryl sutures as well. Pathological examinations of resected specimens were made and reported as “normal corpora tissue”. There was no abnormal microscopical finding in the specimen obtained from clitoral and submucosal tissue.

Patients were followed up for one year post-operatively. There was no early or late post-operative complication. Sensation was normal. Patients were satisfied with the aesthetical and functional and results.

Discussion

Clitoromegaly is a frequently seen congenital malformation, but acquired clitoral enlargement may be rarely detected [2]. A detailed history and physical examination is required for evaluation of clitoral enlargement because clitoromegaly may result from a variety of conditions [3]. The most common cause of clitoromegaly is female pseudohermaphroditism secondary to congenital adrenal hyperplasia (CAH, adrenogenital syndrome), caused by an enzyme defect in the normal pathway of steroid biosynthesis [4]. The result is overproduction of androgenic steroids and masculinization of the external structures, which, because they contain 5 α -reductase, are readily virilized [4]. Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder caused by a defect in any of the five enzymatic steps required to synthesize cortisol from cholesterol. The most common form is 21-hydroxylase (21-OH) deficiency, which accounts for 90-95 % of cases of CAH. A further 5-8 % of cases are associated with a deficiency of 11 β -hydroxylase (11 β -OH) and all other enzymatic deficiencies together account for less than 5 % of cases of CAH [5]. Virilization of the external genitalia may cause profound clitoromegaly but rarely causes formation of a true penile urethra. However, clitoromegaly may be accompanied by fusion of the labioscrotal folds and perineoscrotal hypospadias, and the urogenital sinus may persist so that the vagina does not open to the outside [6]. Tumors are other important factors in the pathogenesis of clitoromegaly. Bilateral hilus cell tumors of the ovary, steroid producing gonadal tumors, adrenal androgen-secreting carcinoma, Leydig cell tumor of the ovary, metastatic carcinosarcoma of the urinary bladder are the reported tumors which caused clitoromegaly in the literature [7-10].

Exposure to androgens is an important cause of clitoromegaly. An interesting case report was presented by Akcam and Topaloglu [11]. They presented an immature case of clitoromegaly secondary to a blood transfusion from an adult. Fetal exposure to danazol may cause clitoromegaly [12].

One of the most frequently reported reason of clitoromegaly was neurofibromatosis (NF) [13]. The majority of clitoromegaly cases related to NF are congenital. Sometimes clitoral cysts could be evaluated as clitoromegaly [3]. They arise from epidermis displaced into the dermis or into the subcutaneous tissue either in prenatal period or after a trauma.

Some syndromes may cause clitoromegaly: Kazlauskaite et al reported a case presenting with generalized fat loss, prominent musculature, hepatomegaly, clitoromegaly, mild hirsutism and diagnosed as congenital generalized lipodystrophy (CGL) [14]. Congenital generalized lipodystrophy (CGL) is an autosomal recessive disorder, characterized by severe metabolic derangement associated with the absence of subcutaneous adipose tissue, and causes clitoromegaly. Fraser syndrome is another rare reason of clitoromegaly [15]. Turner syndrome (TS) is one of the most common chromosomal disorders in females and results from a partial or complete loss of an X chromosome. Abnormalities include short stature and gonadal dysgenesis. Haddad et al presented a case of clitoromegaly and Turner syndrome [16]. Androgen insensitivity syndrome is a heterogeneous disorder with a wide spectrum of phenotypic abnormalities, ranging from a complete female to ambiguous forms that more closely resemble males. The primary abnormality is a defective androgen receptor protein due to a mutation of the androgen receptor gene.

Nevus lipomatous cutaneous superficialis (NLCS) is a relatively rare condition and this clinical condition is characterized histologically by groups of ectopic fat cells dispersed [17]. NLCS may cause clitoromegaly when located on the clitoris.

Another type or pseudohypertrophy of the clitoris is often seen in small girls due to masturbation: Manipulations with the skin of prepuce represents repeating mechanical insult, which expands prepuce and labia minora, thus imitating true clitoral enlargement [2].

Several authors recognized the clitoris as an erotically important sensory organ worth saving. The goals of clitoroplasty are feminization, preservation of function and sensation, and cosmesis. Historically, until 1960s, clitoral hypertrophy was dealt with surgically by amputation clitoridectomy [4]. Surgical methods for correction of clitoral hypertrophy were first described in 1934 by Young who performed an operation for clitoral reduction in a child with congenital adrenal hyperplasia [18]. Several clitoroplasty methods have been reported, but few describe preservation of dorsal and ventral neurovascular bundles in sexually mature women. Clitoroplasty with preservation of the neurovascular pedicle is the best operative technique for the treatment of clitoromegaly.

In conclusion, both patients presented here were evaluated according to the criteria reported in studies on clitoromegaly which appeared in the literature. We could not determine any other illness or syndrome in these patients. Since there was no drug and irritation history, we defined the condition as “idiopathic clitoromegaly”. To our knowledge, there is no detailed report about idiopathic clitoromegaly in the literature. We suggest that clitoromegaly should be classified as shown in Table 1.