

# Non-hormonal Clitoromegaly due to Clitoral Priapism Caused by Appendicitis/Appendectomy

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## What is already known on this topic?

Clitoromegaly is usually caused by hyperandrogenism. There are rare, non-hormonal etiologies of clitoromegaly. Penile priapism has been reported to be related to appendicitis.

## What this study adds?

Prolonged clitoral priapism can present with clitoromegaly in children. Clitoral priapism may also be related to appendicitis/appendectomy. Pseudoephedrine treatment is helpful in clitoral priapism.

## Abstract

Clitoromegaly usually develops due to hyperandrogenism. There are a few cases of clitoromegaly described without clinical and biochemical hyperandrogenism. Clitoromegaly due to clitoral priapism and clitoral priapism after appendectomy have not been reported previously. A 7-year-old girl was referred for enlargement of the clitoris. She reported having a mild, pulsating clitoral pain starting three days after an appendectomy operation. Subsequently, painful swelling and an increase in the size of the clitoris was observed. Her growth and physical examination were otherwise normal. Causes of the clitoromegaly due to androgen excess were excluded after a comprehensive work-up. Color Doppler ultrasound revealed a high peak systolic velocity and resistance in the cavernosal artery, consistent with clitoral priapism. The clitoromegaly and associated symptoms improved significantly with oral pseudoephedrine and intracavernosal aspiration. This unique case illustrates that clitoral priapism is a rare, non-hormonal cause of clitoromegaly and may occur after appendectomy. Pseudoephedrine treatment is helpful in alleviating the symptoms.

**Keywords:** Non-hormonal clitoromegaly, clitoral priapism, clitorism, acute appendicitis, pelvic inflammation, pseudoephedrine

## Introduction

Clitoromegaly is an abnormal enlargement of the clitoris and is usually due to androgen excess (1). However, a few child and adult case reports have described clitoromegaly without hyperandrogenism, including neurofibromatosis, epidermoid cysts, other tumors and syndromes such as Fraser, Donohue, Seckel and Apert Syndrome (1,2,3,4,5,6).

Clitoral priapism is a rare condition that is characterized by a prolonged, painful erection of the clitoris that is not

associated with sexual arousal (7). Engorgement of the clitoris and the surrounding tissues with accompanying pain is the typical presenting symptom.

In children, penile priapism usually occurs in the setting of sickle cell anemia or leukemia (8,9). Other conditions associated with priapism include local malignancies, certain medications, hematologic and thromboembolic disorders, and neurologic conditions such as transverse myelitis (8). Pelvic inflammation caused by appendicitis, can lead to the irritation of the nervi erigentes or pelvic plexus



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causing neurogenic priapism (9). The association of acute appendicitis and priapism is limited to six (four < 18 years of age) male cases reported in the literature (8,9,10,11).

Herein, we report a seven-year-old girl who was referred to a pediatric endocrinology unit due to clitoromegaly after appendectomy. We believe this is the first case of clitoral priapism associated with appendicitis.

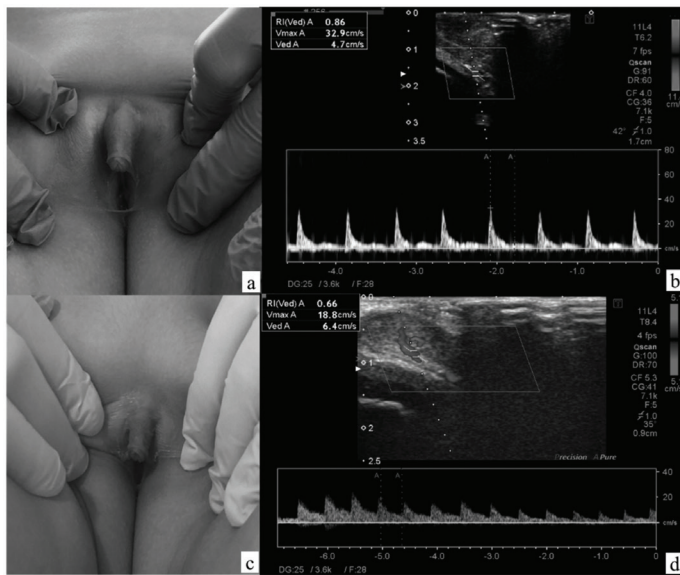
## Case Report

A 7-year-old girl presented with a progressive, painful swelling of the clitoris that had worsened for the two weeks prior to presentation. Symptoms started three months earlier after an episode of acute appendicitis requiring an appendectomy operation. She indicated that there was a mild, pulsating pain, which worsened just before voiding and decreased thereafter. In the last two weeks, she had multiple emergency visits for a stabbing pain in her vulva and a gradual increase in the size of her clitoris. With the exception of the appendicitis/appendectomy, she had no previous illness, no recent history of trauma, medication use or infection. There was no family history of sickle cell anemia or cancer. The physical examination was

unremarkable except for her clitoris, which was stimulated and tender. Clitoris was enlarged and measured at 2.4 cm in length and 1.2 cm in width (normal < 1.0 cm) (Figure 1a). The urethral and vaginal orifices were normal. She had no evidence of posterior fusion. Her pubic hair and breast development were consistent with Tanner stage 1. Her growth was not accelerated [height 118.4 cm, -0.9 standard deviation score (SDS); weight 22.4 kg, -0.4 SDS]. There was no other clinical evidence of hyperandrogenism including acne, oily skin, body odor or temporal balding.

A complete blood count, sedimentation rate and prothrombin and partial thromboplastin times were normal. Hemoglobin (Hb) electrophoresis and urinalysis was normal. There was no evidence of androgen excess on biochemical evaluation (Table 1). Pelvic ultrasound was normal. Karyotype analysis was reported 46,XX.

Color Doppler ultrasound revealed high resistance flow in the cavernosal artery with a decreased venous flow, consistent with clitoral priapism. The cavernosal artery resistive index was 0.86 and peak systolic velocity was 32.9 cm/sec (Figure 1b). The patient was started on oral pseudoephedrine (Sudafed®) 15 mg every eight hours. In the following 72 hours, the clitoral swelling reduced, and the pain associated with urination only happened once when the pseudoephedrine dose was skipped. The dose of pseudoephedrine was increased to 30 mg every eight hours after the first week of treatment. However, the



**Figure 1.** Non-hormonal clitoromegaly due to clitoral priapism  
a) The appearance of the clitoris before treatment. b) The color Doppler ultrasound imaging of cavernosal arterial peak systolic velocity (32.9 cm/sec) and cavernosal arterial resistive index (0.86) before treatment. c) The appearance of the clitoris after treatment. d) The cavernosal arterial peak systolic velocity (18.8 cm/sec) with low resistive index (0.66) after the treatment of clitoral priapism. The imaging studies of clitoral vascularization are lacking in the literature. Although the normal values of the clitoral cavernosal arterial resistive index are not known, the decrease seen after the pseudoephedrine treatment was apparent and parallel with the clinical response

**Table 1. Laboratory findings of the patient at presentation**

	Levels	Reference values
Total testosterone*	0.05 µg/L	(0.00-0.20)
DHEA*	0.4 µg/L	(0-3.4)
DHEAS*	155 µg/L	(440-3320)
Δ4-androstenedione*	0.17 µg/L	(0.06-1.15)
17OHP*	0.29 µg/L	(0.00-0.90)
21-deoxycortisol*	< 0.24 µg/L	(0.06-0.51)
11-deoxycortisol*	0.63 µg/L	(0.00-3.44)
FSH	3.16 U/L	(1.0-4.2)
LH	< 0.2 U/L	(0.02-0.3)
E2	< 5 ng/L	(< 15)
AMH	2.51 ng/mL	(0-8.8)
AFP	0.49 U/mL	(0.49-9.84)
HCG	< 0.5 U/L	(< 5)

\* Assay method was liquid chromatography mass spectrometry. Conversion factors for SI units are: E2, × 3.67 pmol/L; DHEAS, × 2.71 nmol/L; DHEA, × 3.44 nmol/L; Δ4-androstenedione, × 3.49 nmol/L; total testosterone, × 3.47 nmol/L; 17OHP, × 3.02 nmol/L. DHEA: dehydroepiandrosterone, DHEAS: dehydroepiandrosterone-sulfate, 17OHP: 17α-hydroxyprogesterone, FSH: follicle stimulating hormone, LH: luteinizing hormone, E2: estradiol, AMH: anti-mullerian hormone, AFP: alpha fetoprotein, HCG: human chorionic gonadotropin

patient developed tachycardia three weeks after initiation of treatment, leading to discontinuation of pseudoephedrine. Oral ibuprofen (~15 mg/kg/day, every eight hours) treatment was then initiated due to pain associated with clitoral priapism. Due to persistence of the symptoms, intracavernosal needle aspiration and cystoscopy were performed. There was no sign of ischemia or acidosis in the blood gas analysis of cavernosal blood (pH=7.52, PCO<sub>2</sub>=27 mmHg, PO<sub>2</sub>=219 mmHg). Subcutaneous injection of 0.5 mL 0.25% bupivacaine around the clitoris was performed for local anaesthesia with only limited decrease in clitoral pain. Cystoscopy was performed to rule out urologic problems that may be related to the clitoral priapism but this revealed only a mild trabeculation in the bladder. Technetium-dimercaptosuccinic acid scintigraphy and uroflowmetry were normal. Oral ibuprofen treatment was continued. One week after cystoscopy, treatment with oral pseudoephedrine 15 mg every eight hours was resumed because of persistent priapism. There was a significant improvement in the patient's complaints after restarting pseudoephedrine. She reported no pain or swelling but urgency before voiding. The clitoris size regressed to 1.9 cm (Figure 1c). Color Doppler ultrasound was repeated at the end of a month of regular pseudoephedrine treatment and this showed normal peak systolic velocity in the cavernosal artery (18.8 cm/sec) with lower resistance flow (resistive index: 0.66) (Figure 1d). She remained on pseudoephedrine treatment for another three months with reportedly less frequent and milder pain, usually before voiding. At follow-up, six months after diagnosis, the family reported a few, milder episodes of priapism despite discontinuation of pseudoephedrine. There was no further decrease in clitoral size.

## Discussion

Clitoromegaly is generally associated with conditions of androgen excess, such as virilizing forms of congenital adrenal hyperplasia, and virilising adrenal and gonadal tumors. Exhaustive hormonal work-up and the absence of other signs of hyperandrogenism in the presented case excluded androgen excess. Priapism of the clitoris is a rare condition associated with prolonged erection of the clitoris causing engorgement, swelling, and pain to the clitoris and immediate adjacent area. Prolonged penile priapism is known to cause penile enlargement (12). Although not reported previously, we believe that clitoral priapism in our case caused clitoral enlargement similar to that previously only reported in males. All of the patients with clitoral priapism reported so far were adults and the typical initial symptoms were vulvar and clitoral pain with swelling and

tenderness (13,14,15,16,17,18,19). Most reported cases of clitoral priapism were drug-induced, all having alpha-adrenergic blocking potential. The most commonly reported drug associated with clitoral priapism was trazodone (14,16,17).

The presented case, to the best of our knowledge, is the first prepubertal case of clitoral priapism with clitoromegaly as a presenting symptom and is also the first case of clitoral priapism observed after appendicitis/appendectomy, a known etiology for penile priapism. The main physiologic mechanism of priapism consists of impaired outflow from the corpora cavernosa through direct venous obstruction or failure of the alpha-adrenergic relaxation system, resulting in prolonged relaxation of corporal smooth muscle (17,20). There are three types of priapism: ischaemic (low-flow or veno-occlusive) (LFP), stuttering (intermittent or recurrent) and non-ischaemic (high-flow) (20). The high-flow type is characterized by an increase of arterial inflow and does not appear to occur in women (7,16,17). LFP occurs because of venous outflow obstruction, usually seen in the setting of sickle cell anemia or leukemia in children (20). Inflammation is an uncommon etiology of LFP. It has been reported in systemic infections such as mumps, Rocky Mountain spotted fever, tularemia, undulant fever, *Mycoplasma pneumoniae*, *Coxsackie B* and Echovirus 14 (8,10,21,22,23). Appendicitis, Crohn disease, ulcerative colitis and localized urogenital infections, such as chronic prostatitis and urethritis can cause pelvic inflammation that can lead to irritation the nervi erigentes or pelvic plexus causing a neurogenic LFP (9,24,25). There are six reported cases of LFP associated with appendicitis appearing in the literature to date and all of them are males (9). In three of the reported cases, priapism was the main complaint leading to the diagnosis of appendicitis and in the other three cases priapism developed as a postoperative complication (8,9,10,11,26,27), similar to the process seen in our patient.

The intermittent nature of the symptoms and shorter, self-limiting episodes of clitoral priapism in our patient were consistent with stuttering priapism that has a similar etiology with LFP. Sickle cell anemia is the most common cause of stuttering priapism (28). However, priapism secondary to sickle cell anemia has not been reported in females. Furthermore, Hb electrophoresis in our patient was normal. Although the underlying mechanism of stuttering priapism is still unknown, it is thought that neurogenic or endothelial dysregulation of smooth muscle relaxation is involved in the pathophysiology (20,28). In this context, therapeutic agents that help detumescence of erectile tissue by increasing smooth muscle tone of the corpus cavernosum can be used in the treatment.

Pseudoephedrine, more commonly used as an oral decongestant, is often used as a first-line treatment for stuttering priapism (28). Pseudoephedrine acts on two receptors in bronchial smooth muscle to induce relaxation through cAMP and vasoconstriction via  $\alpha$ -adrenergic receptors in the respiratory mucosa. Although smooth muscle contraction is possibly mediated by the effects of pseudoephedrine on  $\alpha$ -adrenergic receptors, its effects on smooth muscle have not yet been studied. In studies conducted in a small number of cases in stuttering priapism due to sickle cell anemia, a variable response to prophylactic treatment with pseudoephedrine has been observed (29,30).

Intracavernosal injections to cavernosaphenous shunts had been performed in other reported cases with appendicitis related LFP (8,9,10,11). Intracavernosal needle aspiration, and local anaesthesia with bupivacaine, resulted in partial benefit in our patient. Unlike appendicitis associated with LFP and other cases of LFP, cavernosal blood gas analysis did not suggest ischemia or acidosis. In the literature, there is no case in which clitoral cavernosal blood gas analysis was performed. Pseudoephedrine treatment, which has been shown to work in cases of stuttering pediatric male priapism (29) and in one case of persistent symptomatic female priapism (17) was also successful in our case. Besides the significant decrease in the patient's complaints and clitoral size, we were able to objectively demonstrate a significant decrease in the cavernosal artery resistive index compared to pre-treatment measurement by Doppler ultrasound imaging.

## Conclusion

Clitoral priapism should be kept in mind as a rare non-hormonal cause of clitoromegaly. Priapism associated with acute appendicitis can also occur in females. Oral pseudoephedrine treatment is helpful in alleviating the symptoms.

## Ethics

**Informed Consent:** The parents gave their written informed consent to publish the data and pictures of the patient.

**Peer-review:** Externally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices - Concept - Design - Data Collection or Processing - Analysis or Interpretation - Literature Search - Writing: Büşra Gürpınar Tosun, Ahsen Karagözlü Akgül, Eda Almus, Sadık Abidoğlu, Serap Turan, Abdullah Bereket, Tülay Güran.

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