Prepubertal diagnosis of Klinefelter syndrome due to penoscrotal malformations: Case report and review of literature

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Abstract

We report a case of 4 months old infant diagnosed as Klinefelter syndrome associated with perineal hypospadias, severe ventral chordee and complete penoscrotal transposition. A review of previous reported cases was carried out. Penoscrotal malformations at birth are very rare in Klinefelter syndrome. Awareness of the current standard indications of Karyotyping can help early detection of these cases.

Introduction

Klinefelter syndrome is a chromosomal malformation linked with extra X chromosome on male karyotype (47XXY). This malformation occurs in 1/1500 to 1/1000 live births.[1] The typical presentation is an adolescent or adult patient with hypogonadotropic hypogonadism, azospermia and gynecomastia due to testosterone insufficiency.[1] Most cases of Klinefelter syndrome present after puberty.[2,3] Klinefelter presentation in childhood, due to genital malformations, is rare.[4] We present a case diagnosed during investigations for penoscrotal transposition and hypospadias and provide a review of similar cases in the literature.

Case report

A 4-month-old boy was referred to our pediatric urology clinic for evaluation and management of concomitant hypospadias, chordee, and penoscrotal transposition. The mother was 35 years old at delivery and had normal prenatal imaging. She had no history of drug exposure, smoking, and alcohol intake during pregnancy. Also, there was no history of chronic disease, such as diabetes mellitus or hypertension. She had an uncomplicated spontaneous vaginal delivery at 39 weeks. The baby's birth weight was 3.3 kg and his postnatal course was unremarkable.

On physical examination, he had perineal hypospadias (Fig. 1), severe ventral chordee, and complete penoscrotal transposition (Fig. 2). The testes were normal in size, consistency and localized in the scrotum (Fig. 3). Karyotype was requested and revealed 47XXY. Abdominal and pelvic ultrasound was unremarkable and no Mullerian structures were noted.

At 11 months old, the boy underwent one stage reconstructive surgery. Intraoperative chordae assessment by artificial erection was performed followed by total mobilization of the urethral plate, and a correction with dorsal plication. A tubularized incised plate repair and scrotoplasty was then carried out. The blood supply of the penile skin was maintained by preserving the dartos fascia at the dorsum of the penis (Fig. 4, Fig. 5).

The postoperative course was straightforward; the patient had good urinary stream and the cosmetic appearance of genitalia during the short-term follow-up was acceptable.

Discussion

Concomitant penoscrotal malformations with Klinefelter syndrome is rare.[5] There are few reported cases and they vary from penile chordee, hypospadias, and penoscrotal transposition. We reviewed the literature for patients diagnosed with Klinefelter syndrome before puberty with penoscrotal malformations; we searched PubMed using key words: Klinefelter syndrome, hypospadias, prepubertal age, chordee, bifid scrotum, and scrotal transposition (Table 1).

Twelve publications were identified; 9 were included and 3 excluded, as the diagnoses were made after puberty due to other signs of Klinefelter syndrome.[6-8] In addition, 3 cases were excluded from a report due to the presence of ovary, ovotestes or atypical Karyotype.[5] Finally, we collected 15 patients, including our current case.

All patients were diagnosed with penoscrotal malformations. Karyotyping was performed as a part of workup for disorder of sexual differentiations in all reported cases. None of the cases had dysmorphic features, cardiopulmonary anomalies, or renal malformations.

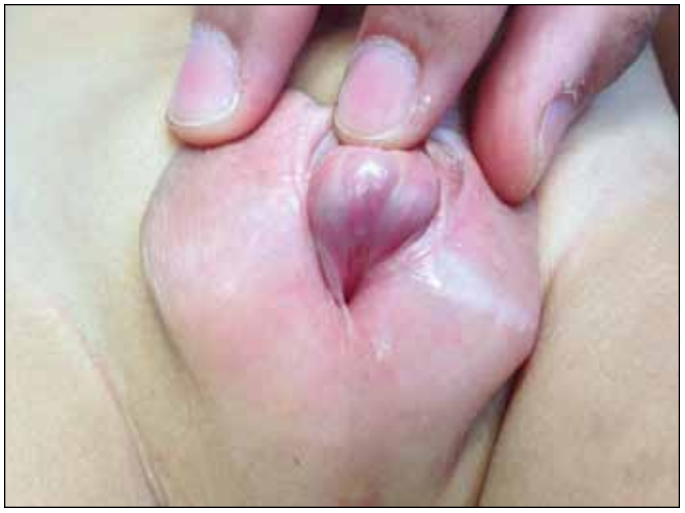

Fig. 1. Shows perineal hypospadias and chordee.

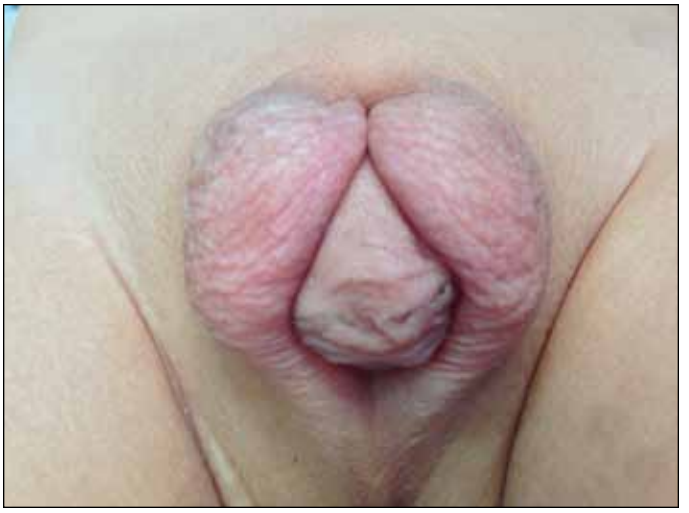

Fig. 2. A display of the complete penoscrotal transposition.

Hypospadias was present in 73.3% of cases, chordee in 66.6%, scrotal transposition in 33.3%, and bifid scrotum in 26.6 %. Notably, all diagnosed cases had hypospadias and/or chordee. The prevalence of cryptorchidism was 40%. This was slightly lower than 55.5% to 69% range in the Klinefelter syndrome cases diagnosed before puberty and without penoscrotal malformations.[4,9]

The genital malformations in Klinefelter syndrome may be related its high heritability and to the maternal administration of estrogen or anti-androgen.[10] However, in our reported cases, maternal and family history was negative. Older reports have suggested older maternal age as a significant contributor to the prevalence of Klinefelter syndrome;[11] however, more recent studies have shown that older maternal age was significantly associated with prenatally diagnosed Klinefelter cases rather than those diagnosed after birth.[12] The mean reported maternal age in the present review, in which all cases were diagnosed postnatally, was 30 years.

Although, low birth weight is an associated risk factor for hypospadias,[13,14] the reported birth weights in this review were normal, except for twins who weighed 1900 g and 2300 g at birth.[15]

The occurrence of perineoscrotal or perineal hypospadias is 20% and the incidence of complete penoscrotal trans-

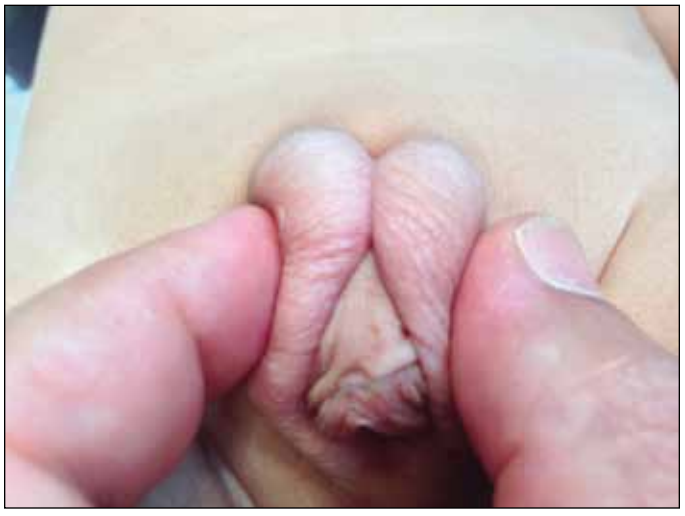

Fig. 3. A demonstration that both testicles were located at the scrotum.

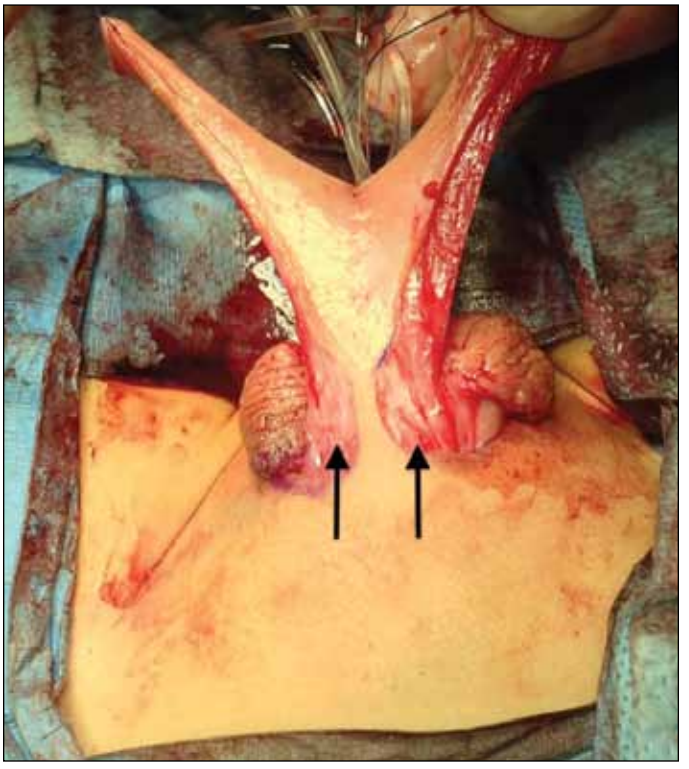

Fig. 4. Arrows point to preserved dartos fascia at the dorsum of the penis.

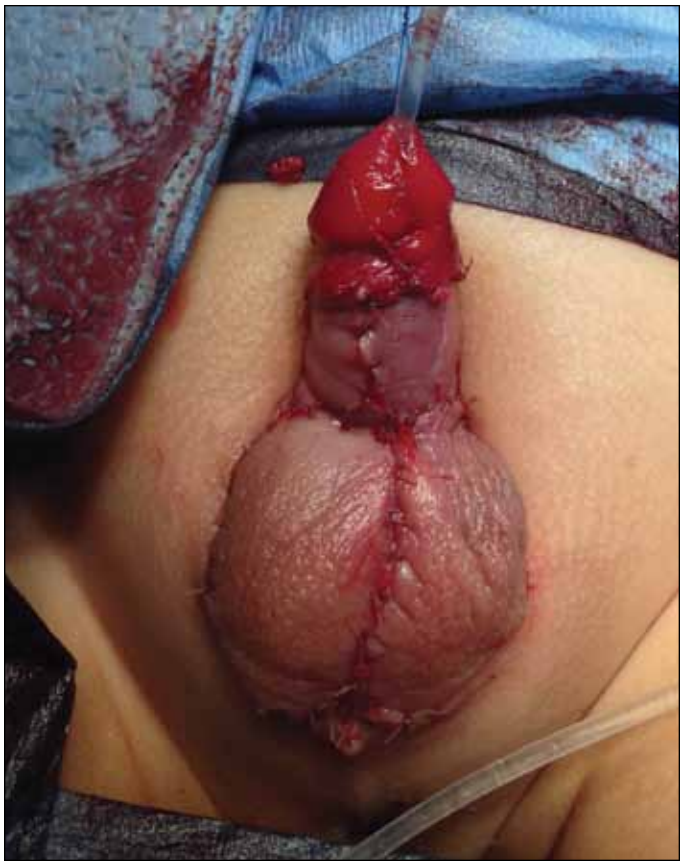

Fig. 5a. The final results after surgery: The anterior view.

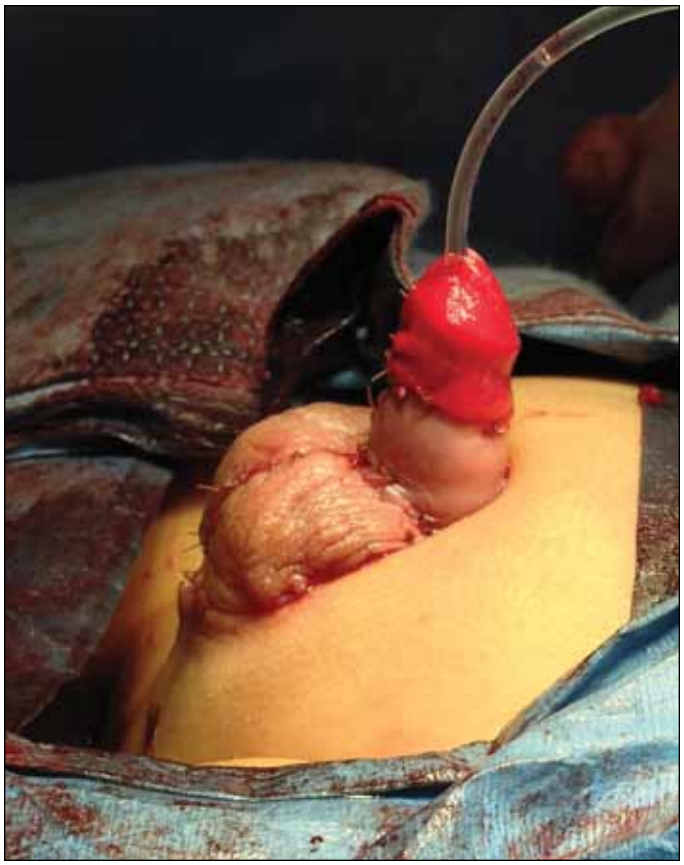

Fig. 5b. The final results after surgery: The lateral view.

Table 1. Descriptive analysis of prepubertally diagnosed cases of Klinefelter syndrome from the literature

Case report	Age of presentation	Karyotype	Associated malformations			
			Hypospadias	Chordee	Scrotal	Others
Lamy et al, 1962[20]	20 months	47XXY	Perineal			Unilateral undescended testis
Conen et al, 1964[21]	Newborn	47XXY	Penile	Severe	Transposition, bifid	
Rosenberg et al, 1972[22]	At birth	47XXY	Penoscrotal	Present	Bifid	
Moriyama et al, 1988[23]	3 years	47XXY	Penoscrotal			Bilateral undescended testis
Fuse et al, 1992[24]	5 years	48XXXY		Ventral	Complete transposition	
	9 months	46XY/47XXY	Proximal penile	Ventral	Complete transposition	Migrating testes
Sasagawa et al, 1992[25]	3 years	47XXY		Ventral		Left undescended testis
Lee et al, 2007[19]	At birth	47XXY	Perineal	Severe	Bifid	Micropenis
	Newborn	48XXXY		Severe		Micropenis and left undescended testis
	At birth	47XXY	Perineal		Bifid	Micropenis, bilateral undescended testis. And shallow vagina
	At birth	47XXY	Perineal		Transposition	
Kajbafzadeh et al, 2009[15]	7 years	47XXY	Penoscrotal	Ventral		Small testes
	Identical twin	47XXY		Severe		
Das et al, 2013[26]	6.5 years	47XXY	Type was not mentioned			Right congenital hydrocele and small penis
Our current patient		47XXY	Perineal	Severe	Complete transposition	

position is lower and may be associated with other renal anomalies, like renal agenesis.[16] However, there was no reported urinary tract anomaly in the present review, including our present case.

The presence of androgen receptors in temporal and prefrontal cortex can explain the underdevelopment of speech, language, intellectual, and reading function in Klinefelter patients.[17] Androgen deficiency can be a cause of psychosexual underdevelopment in these patients[18] and early prepubertal management with androgen can significantly improve their neurodevelopmental outcome.[17]

Following the standard recommendations of karyotyping according to Chicago Conesus Conference on Disorders of Sexual Differentiations can help in early diagnosis and management of Klinefelter patients whom are often undiagnosed before puberty.[19]

Conclusion

Penoscrotal malformations at birth are very rare in Klinefelter syndrome. Awareness of the current standard indications of Karyotyping can help early detection of these cases.

Competing interests: The authors declare no competing financial or personal interests.

This paper has been peer-reviewed.

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