GENITOPATELLAR SYNDROME: CASE REPORT OF A RARE SYNDROME

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ABSTRACT
Genitopatellar syndrome (GPS) is a rare syndrome comprising of scrotal hypoplasia, absent patellae, renal anomalies, facial dysmorphism, and mental retardation. It is an autosomal dominant condition caused due to mutation in KAT6B gene. It has several major and minor features. Very few cases have been reported worldwide till date. We present a further case in a new born with ambiguous genitalia, who was evaluated to look for other associated anomalies. Our patient had 5 major features of this rare syndrome, namely genital anomalies (Undescended testes and scrotal hypoplasia), absent patellae, renal anomalies (Hydronephrosis), flexion deformities (In the form of calcaneus feet with forefoot adduction) and dysgenesis of corpus callosum.

KEYWORDS
Genitopatellar Syndrome (GPS), KAT6B Mutation, Scrotal Hypoplasia, Dysgenesis of Corpus Callosum.


INTRODUCTION
Genitopatellar syndrome (GPS) is a rare syndrome comprising of scrotal hypoplasia, absent patellae, renal anomalies, facial dysmorphism, and mental retardation. Very few cases have been reported worldwide till date. It is associated with KAT6B mutation with an autosomal dominant inheritance and is predominantly seen in males. Another syndrome namely Say-Barber-Biesecker-Young- Simpson syndrome (SBBYS syndrome or Ohdo syndrome) is also associated with KAT6B mutation but can be differentiated from GPS by several features which are unique to each entity. Other entities associated with absent patella may be considered in differential diagnoses.

CASE REPORT
A full term male neonate from Non-consanguineous marriage, born by normal vaginal delivery was noted to have ambiguous genitalia. His birth weight was 2900g (25th to 50th centile) and head circumference was 33 cm (25th to 50th centile). The baby was active and feeding well and had passed urine and meconium on first day of life. On examination, both testes were not palpable in respective scrotal sacs with bilateral scrotal hypoplasia. Hypoplastic phallus was noted with penile length of ~ 1.5cm (Fig. 1a). There was facial dysmorphism with low set ears and high arched palate. There was pitting in the anterior aspect of both knees secondary to absent patellae (Fig. 1a).

There were bilateral calcaneus feet with forefoot adduction (Fig. 1b). The anus was patent. No obvious evidence of defects in the back or lumbosacral region. The patient was referred for ultrasound to localize testis and to rule out associated anomalies. Abdominal ultrasound revealed mild dilatation of bilateral pelvicalyceal system (Fig. 2a & b). Ureters were obscured by bowel gas. Other solid abdominal organs were within normal limits, including adrenals.

Scrotal ultrasound revealed absent testis in respective scrotal sacs (Fig. 3). The testes were not detected in bilateral inguinal regions and to the visualized extent of abdomen. There was hypoplastic phallus. As part of evaluation to rule out other associated anomalies (Based on clinical findings), ultrasound of knee joints and neurosonography were performed. Ultrasound of both knee joints revealed absent patellar cartilage (Fig. 4a & b). No obvious evidence of joint effusion noted. Neurosonography revealed severe thinning with abnormal morphology of corpus callosum and cerebral convolutions arising from third ventricle, consistent with dysgenesis of corpus callosum (Fig. 5a & b). Echocardiography done to look for any associated cardiac anomalies showed patent ductus arteriosus and patent foramen ovale.

Based on clinical and imaging findings, there were a constellation of anomalies namely, genital anomalies (Undescended testes and scrotal hypoplasia), absent patellae, renal anomaly (Hydronephrosis), Dysgenesis of corpus callosum and flexion deformities (In the form of calcaneus feet with forefoot adduction). This led to a search of syndromic association whereby genitopatellar syndrome was considered as diagnosis. Our patient had 5 major features and one minor feature of this rare syndrome, as described later in discussion. Karyotyping of the baby revealed normal 46XY.

Fig. 1(a): Photographs of baby showing scrotal hypoplasia with hypoplastic phallus. Fig. 1(b): Also note Dimple in the anterior aspect of both knees, secondary to absent patellae and bilateral club feet.
DISCUSSION
The first ever reported association of scrotal and patellar hypoplasia, renal anomalies, skeletal anomalies and mental retardation was from Goldblatt et al in 1988. This was followed by report of 7 cases with similar association by Cormier-Daire et al in 2000, who termed this association as Genito-patellar syndrome. It was distinct from many previously described entities associated with absent patella, including mosaic trisomy 8 syndrome, facio-genito-popliteal syndrome, nail-patella syndrome, the rapadilino syndrome and Coffin-Siris syndrome which were considered as differential diagnoses to genitopatellar syndrome.

There are very few reported cases (13, according to few studies) of genitopatellar syndrome till date. Their ages ranged from 15 days to 17 years. It is predominant in males, thought to be due to easier recognition of genital anomalies in males. Genitopatellar syndrome is known to be caused by distinct mutations in histone acetyl transferase KAT 6B gene and is inherited in an autosomal dominant manner. The karyotype in these cases is usually normal. The components of genitopatellar syndrome are: (1) Genital Anomalies: scrotal hypoplasia, cryptorchidism and hypoplastic phallus in males; hypoplastic clitoris & labia minora in females (2) Absent/Hypoplastic patellae (3) Skeletal anomalies: Arthrogryposis, contractures, brachydactyly, clubfoot (4) Craniofacial Anomalies: Microcephaly, abnormal skull shape, hypertelorism, broad nose with high nasal bridge, micrognathia (5) CNS anomalies: mental retardation, hypotonia, feeding difficulties, agenesis of corpus callosum and colpocephaly (6) Renal anomalies: Multicystic kidneys, hydronephrosis, fused kidneys, vesico-ureteric reflux (7) Cardiac anomalies: atrial and ventricular septal defects, patent ductus arteriosus, patent foramen ovale, abnormal aortic arch (8) Miscellaneous: Anal Atresia, Ectodermal Dysplasia, Pulmonary Hypoplasia & Apnoea and hearing loss.

Individuals with two major features or one major feature and two minor features are likely to have a KAT6B mutation. The major features include: genital anomalies, patellar hypoplasia/agenesis, flexion contractures at the hips and knees including club foot, agenesis of the corpus callosum with microcephaly, hydronephrosis and/or multiple renal cysts. The minor features include: congenital heart defect, dental anomalies, hearing loss, thyroid anomalies, anal anomalies, hypotonia and global developmental delay/intellectual disability.
Our patient had five major features namely: Genital anomalies (Undescended testes and scrotal hypoplasia), absent patellae, dysgenesis of corpus callosum, flexion deformities (In the form of calcaneus feet with forefoot adduction) and renal anomalies (Hydronephrosis). The minor feature in our patient was congenital heart anomalies (PDA & PFO). These features led to the diagnosis of genitopatellar syndrome (GPS) in our case.

Management includes educational and speech therapy beginning in infancy. Orthopaedic intervention is needed for contractures and club foot, with physical therapy to help increase joint mobility. Routine management of cryptorchidism, heart defects, dental & hearing problems, thyroid anomalies and ophthalmologic conditions are needed.3

The possible differentials to consider for cryptorchidism include retractile testes (Usually located anywhere along the normal path to the scrotum) and atrophic testes (Secondary to neonatal vascular ischemia). Ultrasound and MRI play an important role in localization of testicular tissue in these patients.9 Absent patella is associated with various differentials including Nail patella syndrome, Say-Barber-Biesecker-Young-Simpson syndrome (SBBYS syndrome or Ohdo syndrome), small patella syndrome, isolated patella aplasia hypoplasia, Meier-Gorlin syndrome and RAPADILINO syndrome.2

**Nail-patella syndrome (Or Fong disease)** is a rare autosomal dominant condition characterized by absent/hypoplastic nails with absent/hypoplastic patellae, bilateral posterior iliac horns, protuberant anterior iliac spines and radial head or capitellum hypoplasia. The SBBYS or Ohdo syndrome is also associated with mutations in KAT 6B gene. Features present only in SBBYSS include long thumbs, long great toes and lacrimal duct abnormalities in addition to intellectual disability, congenital heart defects, genital and patellar anomalies which are common to both entities.3 The small patella syndrome or ischiopatellar dysplasia is a rare autosomal dominant disorder comprising of aplasia/hypoplasia of the patellae and various anomalies of the pelvis and feet. Rappadilino syndrome is a rare autosomal recessive condition characterized by radial and patellar aplasia, cleft/high arched palate, short stature, limb anomalies, joint dislocations, diarrhea, long slender nose and normal intelligence. Short patella syndrome caused by TBX4 gene mutations, comprises of absent or hypoplastic patellae with knee contractures.2

**REFERENCES**