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Case Report

Bilateral Perinatal Testicular Torsion in a Newborn with Consequent Primary Endocrine and Exocrine Testicular Failure

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Received: January 22,2024; **Published:** January 31, 2024

Abstract

Testicular torsion is an emergency condition that results from twisting of the testis, and tissue ischemia. Prenatal testicular torsion "PTT" refers to a type of torsion that happens prenatally, or at any time within the first 30 days after delivery. PTT can be unilateral in most of the cases or bilateral which carries a devastating result of anorchia and its consequence of endocrine insufficiency and infertility.

We are reporting a rare case of a male newborn who presented with a synchronous bilateral testicular swelling immediately after birth without acute inflammatory signs. Doppler ultrasound demonstrated, an absent blood flow signal on the right testis and a questionable blood flow in the left testis, features consistent with bilateral PTT. Early exploration was done and intraoperative findings revealed the right testis was ischemic, gangrenous and unsalvageable. The left testis was found with extravaginal torsion, and de-torsion was done. Right orchidectomy and left orchidopexy were performed hoping that reserving the left testis might help to regain some its hormonal function in the future. The left testis was atrophied by the age of 3 months. Hormonal samples to assess the testicular function were collected soon after birth, during minipuberty, after hCG stimulation test, and beyond minipuberty confirmed the diagnosis of primary endocrine and exocrine testicular failure. Serial stretched penile length monitoring was done in the endocrinology clinic with a plan to give testosterone injections if there is inadequate growth. Till the last visit at age of 18 months he has a normal stretched penile length.

In conclusion, surgical exploration is the only way to confirm the diagnosis of PTT. Though still there is a lot of controversy in the management of bilateral PTT, orchidectomy of the most affected testis and orchidopexy of the contralateral side remains the most reasonable approach in a trial to maintain the testicular function even if the salvage rate is minimal.

Keywords: *Testicular Torsion; Prenatal Testicular Torsion; Neonate; Newborn; Bilateral Testicular Torsion; Testicular Swelling; Primary Gonadal Failure; Primary Testicular Failure; Endocrine Testicular Function; Exocrine Testicular Function*

Abbreviations

PTT: Perinatal Testicular Torsion; US: Ultrasound; LH: Luteinizing Hormone; FSH: Follicle-Stimulating Hormone; HPG: Hypothalamic-Pituitary-Gonadal; hCG: Human Chorionic Gonadotropin; SPL: Stretched Penile Length; AMH: Anti-Mullerian Hormone

Introduction

Testicular torsion occurs when the spermatic cord twists, resulting in the twisting of the testis. Twisting of the testis cuts off its blood supply, causing tissue ischemia which is an emergent condition. If that injury is not corrected within a narrow window of time, this will end up unfortunately with an atrophy of the affected testis, loss of its function, and future infertility [1]. Perinatal testicular torsion "PTT" refers to a type of torsion that happens during the prenatal stage, which means it occurs while the baby is still in utero and becomes apparent at the time of birth, or the baby will be born with normal testes and the torsion will occur at any time within the first 30 days after delivery [2]. This condition was reported in the newborn for the first time by Taylor in 1897 [3], a complete study about neonatal testicular torsion was published by Rigby and Howard in 1907 [4] then subsequently several prenatal testicular torsion case reports were described. PTT accounts for 10 to 12 percent of all cases of paediatric testicular torsions [5]. The reported incidence from the UK is 6.1 per 100,000 live births and could be even higher as some of these occur prenatally and can be asymptomatic.

Approximately 70% of PTT, present as prenatal torsion while 30% present in the postnatal period [2]. PTT is typically an extravaginal type, where the testis, epididymis, and tunica vaginalis twist around the spermatic cord [13]. 30 - 48% of PTT occur on the left side, 44 - 55% on the right, and 8 - 15% of cases are bilateral [7,8]. Bilateral torsion can be either synchronous with an incidence of 67% or asynchronous in 33% [9].

Management of bilateral PTT is still controversial as there is a very low probability of salvaging testes with each modality option. Though few cases of bilateral PTT have been published [10-12], it is rare to have synchronous bilateral prenatal testicular torsion at birth. We are reporting a newborn with bilateral testicular swelling presented immediately after birth without acute inflammatory signs. Doppler ultrasound demonstrated features of bilateral PTT, taken to an early exploration where right orchidectomy and left orchidopexy have been done and subsequent follow up showed atrophied left testicle with primary gonadal failure and normal stretched penile length.

Materials and Methods

Our case report and literature review from 1990-2021 through national library of medicine (PubMed https://pubmed.ncbi.nlm.nih.gov), a national center for biotechnology information, and from google scholar.

Consent

Written consent was taken from the parents for approval of case reporting and publishing.

Case Presentation

A full-term male newborn was born to 37 years old P4+5 woman after an uneventful pregnancy and assuring antenatal ultrasound, Apgar scores at 1 and 5 minutes were 9 and 10, respectively. The birth weight was 3.45 kg, length was 55 cm, and head circumference was 36 cm (all are appropriate for gestational age). The baby was noticed to have bilateral testicular swelling immediately after birth. Upon reviewing the history with the mother there was no history of preeclampsia or gestational diabetes, she had previous 3 abortions in the first trimester and two ectopic pregnancies. The baby has one sister and two brothers who had a hydrocele that resolved spontaneously and no family history of undescended testis, testicular disorders, or tumors. Delivery was smooth with no history of trauma and the baby was comfortable with no signs of respiratory distress. Examination in the well-baby nursery showed a newborn baby boy with no dysmorphic features with normal vital signs and normal systemic examination apart from bilateral asymmetrical testicular swelling. The right testis was larger with an estimated size of 4 by 3 cm, hard in consistency, and non-tender with a thick cord. The left testis was around 2 by 3 cm, firm in consistency, non-tender with no thickened cord. Both testes did not show transillumination with light. There was no skin discoloration or thickening of the scrotum on either side.

The initial impression was prenatal testicular torsion versus testicular tumors. Testicular ultrasound (US) showed enlargement of both testes with heterogeneous texture. Doppler US revealed enlarged right testis with heterogeneous echotexture and hypoechoic linear radiating foci. The right epididymis is markedly enlarged, with heterogenous echogenicity. No right testicular internal flow in the colour images and no arterial waveform could be depicted in the doppler images. The left testis also appears mildly enlarged and heterogeneous, with questionable internal flow on the color images.

Our impression based on the clinical presentation and US findings was perinatal bilateral testicular torsion that happened several days before delivery and unfortunately low probability of salvaging both testes is anticipated. An urgent meeting was conducted with the family by the attending neonatologist and pediatric surgeon where the condition was explained to them including the need for surgical exploration, the intervention that will be offered might be either orchidectomy or orchidopexy depending on the intraoperative finding, and the possibility of infertility in the future was raised. The patient was also referred to the pediatric endocrinologist to evaluate the testicular function. Blood samples were withdrawn for testicular tumor markers including beta hCG and alpha-fetoprotein as well as hormonal samples to assess the testicular function, including the levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and total testosterone. On the following day, the patient underwent early scrotal exploration. The intraoperative finding revealed the right testis was ischemic, (gangrenous), destructed, fragile and unsalvageable (Figure a-c). The left testis was found with extravaginal torsion, de-torsion was done and after opening the tunica, the left testis was found brown in color and destructed with no change in its color with warming (Figure d).

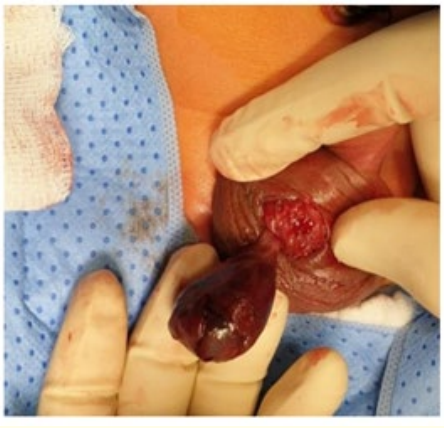

Figure a: *Right hemiscrotum, congested and enlarged.*

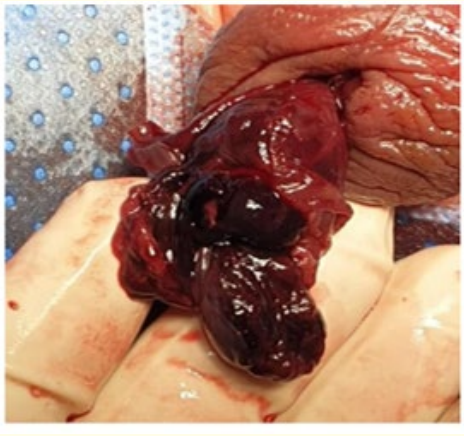

Figure b: *The right testis ischemic and fragile.*

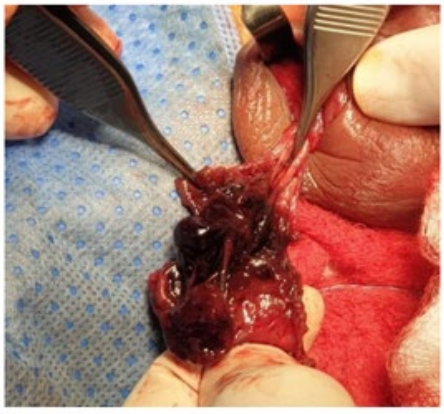

Figure c: *The right testis ischemic and fragile.*

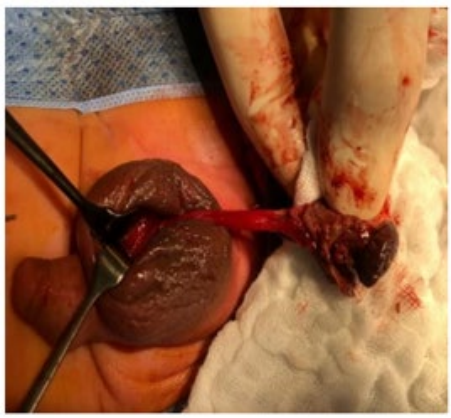

Figure d: *Left testis congested and extravaginally torted with preserved contours.*

Biopsy samples were taken from both testes, right orchidectomy and left orchidopexy were performed hoping that reserving the left testis might help to regain some of the hormonal function in the future. The patient had an unremarkable post-operative course. Examination at day 4 post-operation, showed a clean wound; the left testis was palpable, enlarged, and mildly tender. This is expected as the testis is ischemic and going to be atrophied. Results of blood investigations taken previously were as follows: beta-hCG was almost negative 5.75 mlU/ml (0 - 5). The alpha-fetoprotein level was highly elevated reaching 19500 ng/mL, which can still be a common finding in neonates and is insufficient to draw a conclusion about the etiology of the swelling. Hormonal levels taken on the second day of life revealed elevated concentrations of basal LH of 10.64 IU/L (normal value < 0.02 IU/L) and FSH of 15.26 IU/L (normal value < 0.16 IU/L). Both LH and FSH laboratory tests were performed using an immunochemiluminometric assay. The total testosterone level in the morning sample was in the low normal cut-off 8.54 nmol/L (normal value 8.5 - 29 nmol/L) compared to the concurrent gonadotropic stimulation. Bearing in mind that LH and FSH levels are typically low in a normal newborn due to the suppressive effects of high placental hormones, these results indicate a hypergonadotropic newborn boy and suggest an in-utero failure of the testosterone-secreting Leydig cells. The baby was discharged home with scheduled appointments with the paediatric surgeon and the paediatric endocrinologist.

Biopsy results came later with the following findings: right testicular parenchyma with hemorrhage, necrosis, and congested blood vessels, all are consistent with testicular torsion. Epididymis with hemorrhage, congested blood vessels, and necrosis. Granulation tissue, fibrin, and acute inflammation were seen as well as a viable spermatic cord with a focal area of hemorrhage and granulation. Left testicular parenchyma with hemorrhage and necrosis, consistent with testicular torsion.

The testicular endocrine function was re-evaluated post-operatively at the age of 3 weeks and showed more elevation in LH and FSH concentrations (LH of 46.75 IU/L and FSH of 72.02 IU/L) along with inappropriately low total testosterone level (0.59 nmol/L). These concentrations of LH and FSH exceed the adult male pubertal levels (adult male laboratory reference range for FSH, LH, and testosterone are 2 - 9 IU/L, 2- 9.2 IU/L, and 8.5 - 29 nmol/L respectively) while the patient's testosterone concentration is in the prepubertal reference range (< 0.7 nmol/L). All together are supporting our initial impression of Leydig cell failure.

On a three-month follow-up, the patient was thriving well; however, he had a very small palpable left testis, and the repeated US showed an empty scrotal sac. To explore the reproductive health of the remaining palpable tissue of the left testis, A further evaluation was conducted during the physiological mini-puberty phase, which is the natural activation of the hypothalamic-pituitary-gonadal (HPG) axis. Therefore, the basal hormone concentrations without stimulation tests were measured during the mini-puberty phase of this boy who is highly suspected to have a testicular failure after a longstanding bilateral torsion. The results came to show an extreme LH hormonal surge (LH of 43.01 IU/L and FSH of 153.4 IU/L) while testosterone level was low and barely detectable (0.2 nmol/L). At this point, A human chorionic gonadotropin (hCG) stimulation test was performed to establish the presence or absence of functional testicular tissue in the remaining part of the left testis.

A single-dose protocol of hCG stimulation test was followed, in which hCG 5000 IU/m^2 was injected intramuscularly and LH, FSH and testosterone levels were all repeated 72 hours post-stimulation to show LH of 88.45 IU/L, FSH of 185.7 IU/L and testosterone level of 0.48 nmol/L. Such a blunted testosterone response to the increase of gonadotropins was due to Leydig cell failure.

At age of five months, the stretched penile length (SPL) was assessed anticipating the possibility of the future need for testosterone injections. At that time, SPL was 3.5 cm and thus we did not intervene.

The function of Sertoli cells was evaluated by measuring the levels of two hormonal markers, serum anti-Mullerian hormone (AMH) and inhibin B. At nine months, both markers were present in almost negligible concentrations (AMH of 0.031 ng/mL and inhibin B of less than 10 pg/mL). These results are consistent with Sertoli cell failure.

After establishing the diagnosis of primary testicular failure based on the above-mentioned hormonal data, the results were fully discussed with the parents and a long-term follow-up by periodic physical examinations was planned to follow the penile growth, penile growth velocity and to ensure proper sex steroid hormonal replacement therapy whenever needed.

We continued to follow the stretched penile length and gonadotrophin secretion pattern in this child at 12 months and 18 months. Along with a persistently low testosterone level of 0.09 nmol/L, his LH and FSH levels started to decrease gradually but the LH decreased more readily than the FSH level. His LH level was 14.22 IU/L and his FSH level was 142.1 IU/L at 12 months. Later, his LH level decreased to 10.27 IU/L while his FSH level decreased to 108.4 IU/L at 18 months. In his last OPD visit at the age of 18 months which is just before publication of this report, his stretched penile length was 4.7 cm which corresponds to the mean value for stretched penile length for age. No intervention is needed for now but will be provided at any time as indicated by the clinical assessment.

Results and Discussion

Neonatal testicular torsion is a rare condition. especially if encountered bilaterally which carries devastating results of anorchia and its consequence of endocrine insufficiency and infertility. Experimental studies have shown that testicular torsion can cause irreversible

damage to spermatogenesis after 4-6 hours of ischemia, and prolonged ischemia of 10 - 12 hours can cause irreversible damage to the endocrine function of the testes [13].

Perinatal testicular torsion refers to a type of torsion that happens during the prenatal stage, which means it occurs while the baby is still in utero and becomes apparent at the time of birth, or the baby will be born with normal testes and the torsion will occur at any time within the first 30 days after delivery [2]. PTT can be classified either into intravaginal or extravaginal type and it is almost always extravaginal in the neonatal period where the testis, epididymis, and tunica vaginalis twist around the spermatic cord [13]. 30 - 48% of PTT occur in the left side, 44-55% in the right while 8-15% of cases are bilateral [7,8]. Bilateral torsion can be either synchronous with an incidence of 67% or asynchronous in 33% [9].

The exact etiology behind PTT is not yet well established with risk factors including intrauterine stress, birth trauma, and genetic predisposition [3,4]. Exposure to an extreme cremasteric reflex during delivery or in utero may cause torsion due to hypermobility of the tunica vaginalis within the scrotal sac. This may explain why most torsions occur in winter and are related to extravaginal torsions rather than intravaginal ones [13]. According to Cubillos., *et al*. genetic predisposition may play a role in the development of PTT and about 10% of cases are familial. Mutations in RAF1, INSL3 hormone, and its receptor and RXLF2 genes have been identified as markers or linked to PTT [12].

Diagnosing PTT clinically can be challenging as the clinical signs depend on the time that a PTT takes place [12]. A wide range of differential diagnoses including hydrocele, hernias, traumatic vaginal delivery, meconium periorchitis, and neoplasms. Ultrasound with doppler color may be used as an adjunct to aid the diagnosis of PTT by demonstrating the lack of detected blood flow to the affected testis. In addition, the presence of a heterogeneous parenchymal echogenicity resembling rim-like hyperechoic area (calcifications) between testis and tunica albuginea, suggests a torsion event and testicular nonviability [15,16].

Management approaches currently include watchful waiting, delayed ipsilateral orchidopexy with contralateral orchidopexy, and emergent exploration [11]. The Advocates of the first management option claim that most of these events occur in utero and the testes are never salvageable. Therefore, emergent intervention is only reserved for postnatal cases in which the event occurs acutely, and salvageability exists. [5]. The latter group who was in favour of delayed orchidopexy, weighed out the risks and benefits of delaying the procedure until the baby can tolerate anaesthesia better where bradycardia and postoperative apnoea are more tolerable with no change in the outcome of the testis. Fernandez reported a case in which they used regional anaesthesia as a safe alternative approach with minimal effect on hemodynamic stability and respiratory depression [15].

Surgical exploration on both sides can increase the chance of successful treatment to 20%. Delayed fixation of the tunica vaginalis to the scrotal wall can put both testes at risk of torsion. This could happen within hours and may not show any symptoms.

Management of bilateral synchronous PTT has more consensus with early exploration with orchidopexy being most frequently advocated. As Leydig cells are more tolerant to ischemia, there is an increasing chance of maintaining endogenous production of testosterone, though this could increase the risk of abscess formation and wound infection [11]. regardless of the management approach prompt diagnosis is essential which can only be achieved by exploration [11].

Bilateral neonatal testicular torsion may pose a significant risk to subsequent fertility and sex steroid synthesis and secretion. One must not take lightly the hefty burden of a diagnosis like primary testicular failure and its life-long implications on the patient and the family. The diagnosis was made after a careful examination of this infant over four physiological stages, namely, soon after birth, during minipuberty (Table 1), after hCG stimulation test, and beyond minipuberty to measure infantile AMH and inhibin B (Table 2). The family were counselled on future consequences like need for hormonal replacement and infertility.

	At birth		Minipuberty	
	Normal boy	**Our patient**	**Normal boy**	**Our patient**
FSH	Low	high	High	High
LH	Low	high	High	High
Testosterone	Low	Inappropriately normal	High	Low

Table 1: *The hormonal profile of this patient compared to normal boys are showing Leydig cell dysfunction.*

	During infancy	
	Normal boy	**Our patient**
Inhibin B	high	Undetectable
AMH	high	Undetectable

Table 2: *The hormonal profile of this patient compared to normal boys are showing Sertoli cell dysfunction.*

In a normal male newborn, the gonadal axis is inactive at birth, which explains the low blood concentrations of LH, FSH and testosterone from birth till the first week of life [17]. Minipuberty is the transient activation of the hypothalamic-pituitary-gonadal axis starting after the first week of life and may extend till the age of 6 months, resulting in elevated concentrations of blood gonadotropins and testosterone as well as testicular and penile growth [18]. At 3 months of age, boys experience elevated levels of FSH, LH, and testosterone during this normal physiological phase. Upon evaluation of our patient, we did not miss the opportunity to assess his gonadal hormonal activity at this physiological stage.

There is a growing interest in using serum AMH and inhibin B levels to measure Sertoli cell function and to indirectly assess spermatogenesis and future fertility. Both hormones peak after six months of age and remain elevated during infancy, then gradually decrease during childhood [19,20]. Therefore, the best time to assess AMH and inhibin B levels in our patient is during infancy as demonstrated in table 2. At 9 months old, he had undetectable levels of AMH and Inhibin B, unlike normal male infants at this age. These findings all together are confirming the diagnosis of primary endocrine and exocrine testicular failure.

Most patients with primary testicular failure require testosterone replacement in adolescence and adulthood. Replacement in these patients during minipuberty might have some potential benefits, but it is still experimental [21].

Conclusion

Neonatal testicular torsion is a rare entity especially if encountered bilaterally with minimal clinical evidence thus bilateral surgical exploration is still recommended approach in order to improve the chances of saving the testis and preserving its both endocrine and exocrine functions.

Conflict of Interest

No conflict of interest exists.

Funding Support

None.

Ethical Approval

The Institutional Review Board (IRB) approved this study (QCH-SERCO 69/2023). Written informed consent was obtained from the patient's father for the publication of this case report and all accompanying images.

Contribution of Authors

All the authors were involved in the writing and editing of the manuscript. All the authors read and approved the final manuscript.

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