Clinical Case Reports

Brazilian Journal of Case Reports

Neonatal hypogonadism due to rare testicular atrophy with congenital contralateral torsion: case report

Bruno Antunes Contrucci [1]*, Gustavo Rogério Pinato [1], Camila Manzati Galvani [1], Isabela Claudino Altomari [1], Sebastião Camargo Schmidt Neto [1], Júlia Moraes Castro [1], Bruna Belone Garcia [1], Henrique Mendes Farinazzo [1], Giulia Fiuza Tambellini [1], Maria Fernanda Lomba Corsini [1], Pedro Henrique Leite Beneli [1], Raquel Cristina Bortolozzo [1]

[1] Department of Pediatric Endocrinology, Children's Hospital and Maternity/Faculdade de Medicina de São José do Rio Preto (HCM/FAMERP - SP), São José do Rio Preto – São Paulo.

** Corresponding Author: Bruno Antunes Contrucci. Hospital da Criança e Maternidade / Hospital de Base da Faculdade de Medicina de São José do Rio Preto. Av. Brigadeiro Faria Lima, 5416, Vila São Pedro, São José do Rio Preto – São Paulo. CEP: 15090-000. Email: bruno_acontrucci@hotmail.com.*

Research Ethics Committe Aproval: The Research Ethics Board approved the research (CAAE - 51157521.8.0000.5415).

Received on: Mar 29, 2022. Accepted on: Abr 26, 2022. Available online: May 2, 2022.

Abstract

The process of sexual differentiation involves genetic, hormonal and anatomical factors, and there may be several disorders evident at birth. Congenital testicular torsion associated with atrophy contralateral gonad in phenotypically male newborns, without alteration in development of the internal and external genital organs, is a rare condition and little reported in the literature. Thereby, we sought to report and discuss the clinical case which the presence of both clinical conditions was diagnosed in the perinatal period. Hormonal production of testicular androgens is confirmed by the development of the male genital system, both internal and external. It isn't possible to determine whether the atrophic testis was caused by extrinsic compression of the vascular bundle due to torsion of contralateral testis, or by testicular regression syndrome, in which there in involution of the organ in utero as part of presentation of gonadal dysgenesis. The twisted testicle may have been regression, without hormone production by it, or there was hormonal production of congenitally atrophied testicle and later regressed. Regardless of this fact, early diagnosis is the cornerstone of the clinical condition, since it will invariably evolve with hypergonadotropic hypogonadism, with need for multidisciplinary follow-up.

Keywords: Testicular Torsion; Sex Differentiation; Gonadal Dysgenesis; Hypogonadism.

Introduction

During the early fetal period, the gonads have a dual potential for transformation, coexisting Muller's and Wolf's ducts, precursors of the female and male internal reproductive organs, respectively. The male embryogenic development, as early as the 7th week, the differentiation of Sertoli cells begins,

ISSN: 2763-583X. doi: 10.52600/2763-583X.bjcr.2022.2.2.141-148.

responsible for the production of anti-Mullerian hormone (AMH) [1,2].

In this early period, the secretion of this hormone occurs independently and prior to steroidogenesis, having direct relationship with the gene expression of the typical male karyotype, including the SRY gene (sex-determining region Y). It exerts its action of inhibition and regression of the Muller's ducts in addition to organization of the testicular interstitial cells, culminating the development, mainly, of the internal male reproductive tract [2-4].

Upon initial production of testicular androgen, its action occurs on primarily undifferentiated external genitalia, promoting differentiation into the male phenotype, in addition to migration from the testicle to the scrotum. This entire complex process depends on both anatomical and hormonal factors, and any abnormality results alterations in the formation and migration of the gonad, including testicular torsion, associated or not with other contralateral alterations [5-8].

This condition is defined by the interruption of blood supply to the organ due rotation of the spermatic cord on its own axis. About 5% cases of testicular torsion can occur in the perinatal period, mainly in the prenatal period, representing around 70% of these cases. Unlike the torsion that occurs in adolescent age group, the genesis of the perinatal results from the anomalous testicular migration, either due to anatomical or hormonal causes [9,10].

Clinically, it presents at the opposite extreme of the advanced age group, with a firm, regular and painless scrotal mass. Unilateral enlargement of the testicular pouch associated with dark purple color, due to the presence of bloody fluid, can be observed at birth or referred by parents in the first weeks of life, presenting itself as differential diagnosis of hydrocele and incarcerated inguinal hernia [10,11].

The diagnostic approach through surgical exploration is immediate upon clinical suspicion, with the main objective of returning blood flow to the organ. However, in the vast majority of cases, the torsion of the testicle occurs in utero, presenting ischemia at the first evaluation [11,12].

Another function of the surgical analysis is the valuation of other abnormalities in the testis and contralateral scrotum, occurring sporadically or causally. Testicular atrophy, for example, has been little reported in the literature in association with testicular torsion. Such a condition may be associated with both extrinsic compression of the vascular bundle, resulting from significant locally generated edema, and hormonal changes from the fetal moment, characterizing the unilateral testicular regression syndrome [10-13].

Thereby, due to the very low incidence of this association, we sought to report the clinical case of a neonate

diagnosed with testicular torsion and atrophy of the contralateral testicle in the first days of life, making evident the need for long-term follow-up.

Case Report

Primiparous mother, without complications, comorbidities, infections or use of teratogenic substances during pregnancy, gave birth to a term newborn, adequate weight and anthropometric parameters for gestational age (50th percentile of Intergrowth-21st), with no need for neonatal resuscitation at birth [14]. At the initial physical examination in the birth room, presented with phenotypically male genitalia, with tumor of the right testicular pouch, hardened appearance, clinically painless, without local phlogistic signs, with negative translumination test.

In the topography of the left testis, there was reduction in testicular volume and in the pouch, demonstrating significant asymmetry (Figure 1). There was no change in labioscrotal fusion, anogenital proportion and positioning of the external urethral meatus. In addition, plhallic size was adequate for gestational age [15].

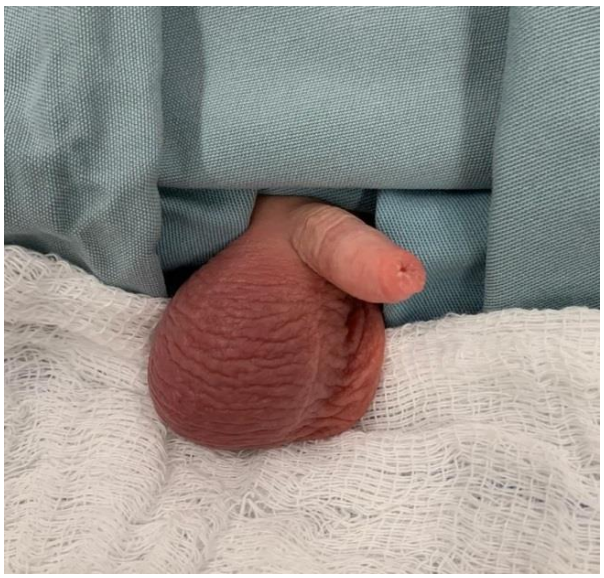

Figure 1. Phenotypically male genitalia, Right testicular bag with greater volume in relation to the contralateral on, presenting an asymmetrical shape with a hardened and edematous aspect. Left testicular pouch with reduced volume, apparently with reduced content inside. Absence of other abnormalities on ectoscopy, with centralized exnternal urethral meatus, no hypospadias or epispadias, no changes in scrotum fusion.

The newborn was active and reactive, with atypical facies, without respiratory distress, hemodynamically stable, with an unaltered abdominal examination and an umbilical stum containing two arteries and one vein. Ultrasound examination of the scrotal region and lower abdomen was requested on the 1st day of life, showing an increase in volume of the right

testicle, with diffusely heterogeneous, echotexture, predominantly hypoechogenic with anechoic areas, with no sign of vascular flow.

Left testis reduced in volume, with irregular contours, with limited assessment of blood flow. Abdominal ultrasound did not show any structure suggesting embryonic remnants of the Muller's ducts and urogenital sinus.

During surgical exploration by the Pediatric Surgery team, right testicular necrosis was evidenced due to extravaginal torsion, and an orchiectomy was performed. When evaluating the contralateral testicular pouch, it was possible to notice significant atrophy of the left gonad, with significant volumetric reduction, and fixation was performed in the scrotum due to the risk of future rotation (Figure 2).

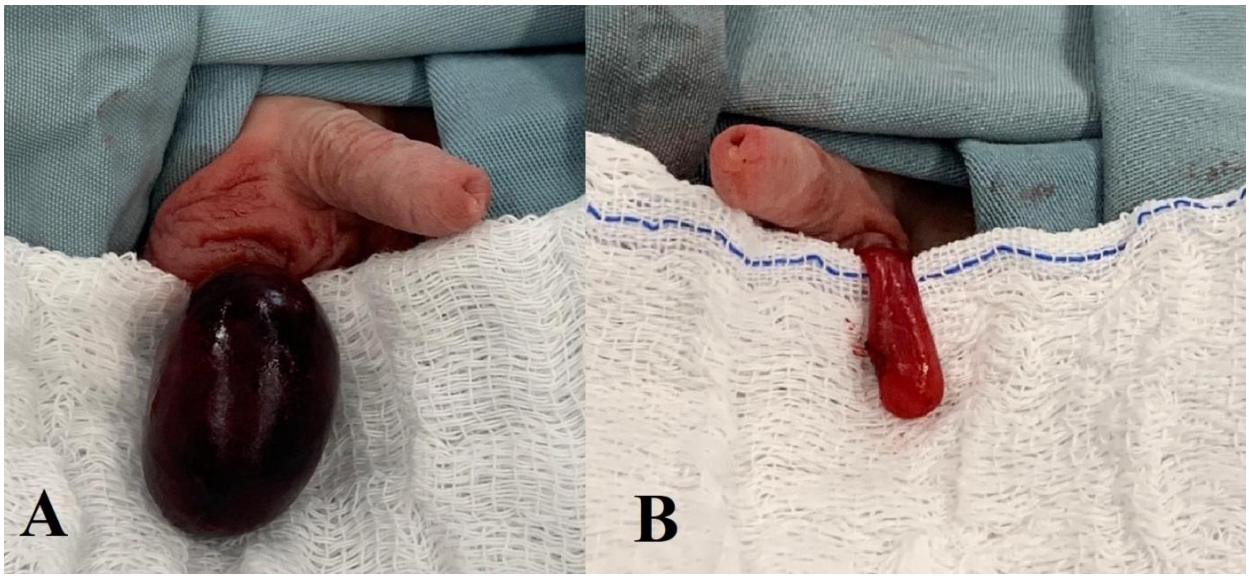

Figure 2. Moment of surgical exploration of testicular pouch. Figure A demonstrates right gonad with ischemia due to testicular torsion, with evident necrosis, and orchiectomy was performed. Figure B demonstrates the left testis with reduced volume, with an atrophic appearance together with other structures, and its fixation was performed in the ipsilateral scrotum.

In an evaluation with Pediatric Endocrinology during the 1st month of life, the patient presented with supraphysiological levels of follicle stimulating hormone (FSH) and luteinizing hormone (LH), in addition to reduced levels of circulating total testosterone, indicating hypergonadotropic hypogonadism resulting from testicular atrophy. The family was duly oriented about the clinical, prognosis and long-term management of the presented condition.

Discussion and Conclusion

During the fetal period, the migration of the male gonad to the scrotum is a complex process,

dependent on hormonal and anatomical factors, as well as the formation of the external genital organ. The association of testicular torsion during intrauterine time associated with atrophy of the contralateral testis, with a typically male phenotype is extremely rare.

There is no report or consensus in the literature at the time of exploration regarding testicular torsion associated with contralateral atrophy, which is evidenced in ultrasound and confirmed at the operation moment.

Due to the fact that bilateral testicular torsion is urgently recommended as a way to ensure tissue viability, and more recently also unilateral torsion in order to avoid apoptosis and contralateral dysgenesis, an early approach was chosen, as reported [16-18].

It is notable that there was fetal production of androgenic hormones of testicular origin as well suppression of Muller's ducts by anti-Mullerian hormones, clinically confirmed by male phenotyping, testicular migration to the scrotum and normality of abdominal ultrasound, respectively [19-22].

Nevertheless, it is no possible to determine whether the testicular atrophy was caused by torsion of the contralateral testicle, through edema and compression extrinsic to the anatomy of the vascular bundle, since surgically there was no suggestive sign. However, such an atrophic testicle may be due to the unilateral testicular regression syndrome, one of the types of gonodal dysgenesis reported in the literature, with the testicle twisted at birth, responsible for androgen production during the prenatal period [23,24].

It is not possible to determine which testicle was responsible for hormone production. The twisted testicle may have been responsible for hormone production prior to its torsion associated with contralateral testicular regression, without hormone production by it, or there was hormonal production of the congenitally atrophied testicle and later regressed.

Unlike occurs in congenital hypogonadotropic hypogonadism unrelated to testicular torsion, gonadal stimulation must be guaranteed by exogenous administration of gonodatropins in the first months of life, causing the mini-puberty phase. Started in the third semester of pregnancy and characterized by a transient increase in testicular gonadotropins and androgens, it is important for the maintenance of testicular integrity in the long term [25].

However, because the reported case did not presente with functional testes due to testicular torsion and contralateral atrophy, confirmed by low levels of androgens and high levels of gonadotropins, their exogenous administration is not supported by the literature.

Regardless of the cause, the need for long-term and multidisciplinary follow-up is evident, as there was permanent secondary hypergonadotropic hypogonadism. The replacement of androgenic hormones in greater quantity will be necessary in the pubertal period, since in pre-pubertal androgens of adrenal origin are

responsible for child development, being independent of gonodal integrity.

With exogenous androgen replacement, serial monitoring of serum levels if of fundamental importance to ensure quality of life for the patient, in addition to allowing metabolic and bone balance with lower risk of future complications and psychosocial impact results from irreversible infertility.

Ensuring that the Family is aware of the need for regular and lifelong follow-up due to such a clinical condition is the cornerstone for successful long-term health promotion and quality of life.

References

[1] Xu H, Zhang M, Zhang H, Alpadi K, Wang L, Li R, Qiao J. Clinical Applications of Serum Anti-Müllerian Hormone Measurements in Both Males and Females: An Update. Innovation (N Y). 2021 Feb 9;2(1):100091. doi: 10.1016/j.xinn.2021.100091.

[2] Wilhelm D, Yang JX, Thomas P. Mammalian Sex Determination and Gonad Development. Curr Top Dev Biol. 2013;106:89-121. doi: 10.1016/B978-0-12-416021-7.00003-1.

[3] Eggers S, Sadedin S, van den Bergen JA, Robevska G, Ohnesorg T, Hewitt J, et al. Disorders of sex development: insights from target gene sequencing of a large international patient cohort. Genome Biol. 2016;17(1):243. doi: 10.1186/s13059-016-1105-y.

[4] Kim JH, Kang E, Heo SH, Kim GH, Jang JH, Cho EH, Lee BH, Yoo HW, Choi JH. Diagnostic yield of targeted gene panel sequencing to identify the genetic etiology of disorders of sex development. Mol Cell Endocrinol. 2017 Mar15;444:19-25.

[5] Johannsen TH, Main KM, Ljubicic ML, Jensen TK, Andersen HR, Andersen MS, Petersen JH, Andersson AM, Juul A. Sex Differences in Reproductive Hormones During Mini-Puberty in Infants With Normal and Disordered Sex Development. J Clin Endocrinol Metab. 2018 Aug 1;103(8):3028-3037. doi: 10.1210/jc.2018-00482.

[6] Castets S, Nguyen KA, Plaisant F, Prudon MB, Plotton I, Kassai B, Roche S, Ecochard R, Claris O, Nicolino M, Villanueva C, Gay CL. Reference values for the external genitalia of full-term and pre-term female neonates. Arch Dis Child Fetal Neonatal Ed. 2021 Jan;106(1):39-44.

[7] de la Calle CM, Kim S, Baskin LS. Diagnosis and treatment of the intra-abdominal gonad in the pediatric population: Testes, ovaries, dysgenetic gonads, streaks, and ovotestes. J Pediatr Surg 2020; 55:2480. doi: 10.1016/j.jpedsurg.2020.02.014.

[8] Loch Batista R, Inácio M, Prado Arnhold IJ, Gomes NL, Diniz Faria JA, Rodrigues de Moraes D, Frade Costa EM, Domenice S, Bilharinho Mendonça B. Psychosexual Aspects, Effects of Prenatal Androgen Exposure, and Gender Change in 46,XY Disorders of Sex Development. J Clin Endocrinol Metab. 2019 Apr 1;104(4):1160-1170. doi: 10.1210/jc.2018-01866.

[9] Tanaka K, Ogasawara Y, Nikai K, Yamada S, Fujiwara K, Okazaki T. Acute

scrotum and testicular torsion in children: a retrospective study in a single institution. J Pediatr Urol. 2020 Feb;16(1):55-60.

[10] Feng S, Yang H, Lou Y, Ru W, Wang A, Liu W. Clinical Characteristics of Testicular Torsion and Identification of Predictors of Testicular Salvage in Children: A Retrospective Study in a Single Institution. Urol Int. 2020;104(11-12):878-883. doi: 10.1159/000506236.

[11] Laher A, Ragavan S, Mehta P, Adam A. Testicular Torsion in the Emergency Room: A Review of Detection and Management Strategies. Open Access Emerg. Med. 2020;12:237–246. doi: 10.2147/OAEM.S236767.

[12] Taghavi K, Dumble C, Hutson JM, Mushtaq I, Mirjalili SA. The bell-clapper deformity of the testis: The definitive pathological anatomy. J Pediatr Surg. 2021 Aug;56(8):1405-1410. doi: 10.1016/j.jpedsurg.2020.06.023.

[13] Flück C, Nordenström A, Ahmed SF, Ali SR, Berra M, Hall J, Köhler B, Pasterski V, Robeva R, Schweizer K, Springer A, Westerveld P, Hiort O, Cools M. Standardised data collection for clinical follow-up and assessment of outcomes in differences of sex development (DSD): recommendations from the COST action DSDnet. Eur J Endocrinol. 2019 Nov;181(5):545-564. doi: 10.1530/EJE-19-0363.

[14] Villar J, Cheikh Ismail L, Victora CG, Ohuma EO, Bertino E, Altman DG, Lambert A, Papageorghiou AT, Carvalho M, Jaffer YA, Gravett MG, Purwar M, Frederick IO, Noble AJ, Pang R, Barros FC, Chumlea C, Bhutta ZA, Kennedy SH; International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st). International standards for newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-Sectional Study of the INTERGROWTH-21st Project. Lancet. 2014 Sep 6;384(9946):857-68. doi: 10.1016/S0140-6736(14)60932-6.

[15] Feldman KW, Smith DW. Fetal phallic growth and penile standards for newborn male infants. J Pediatr 1975; 86:395.

[16] Pogorelić Z, Jukić M, Škrabić V, Mrklić I, Fridl Vidas V, Jurić I, Furlan D. Bilateral Simultaneous Testicular Torsion in a Newborn: Report of a Case. Acta Medica (Hradec Kralove). 2017;60(3):120-123.

[17] Mellick LB, Sinex JE, Gibson RW, Mears K. A systematic review of testicle survival time after a torsion event. Pediatr Emerg Care. 2019;35:821–825. doi: 10.1097/PEC.0000000000001287

[18] Nelson CP, Kurtz MP, Logvinenko T, Venna A, McNamara ER. Timing and outcomes of testicular torsion during the COVID-19 crisis. J Pediatr Urol. 2020;16:841.e1-e5.

[19] Bay K, Main KM, Toppari J, Skakkebæk NE. Testicular descent: INSL3, testosterone, genes and the intrauterine milieu. Nat Rev Urol. 2011 Apr;8(4):187-96.

[20] Koskenniemi JJ, Virtanen HE, Wohlfahrt-Veje C, Löyttyniemi E, Skakkebaek NE, Juul A, Andersson AM,

Main KM, Toppari J. Postnatal Changes in Testicular Position Are Associated With IGF-I and Function of Sertoli and Leydig Cells. J Clin Endocrinol Metab. 2018 Apr 1;103(4):1429-1437. doi: 10.1210/jc.2017-01889.

[21] Johannsen TH, Main KM, Ljubicic ML, Jensen TK, Andersen HR, Andersen MS, Petersen JH, Andersson AM, Juul A. Sex Differences in Reproductive Hormones During Mini-Puberty in Infants With Normal and Disordered Sex Development. J Clin Endocrinol Metab. 2018 Aug 1;103(8):3028-3037. doi: 10.1210/jc.2018-00482.

[22] Harrison SM, Bush NC, Wang Y, Mucher ZR, Lorenzo AJ, Grimsby GM, Schlomer BJ, Büllesbach EE, Baker LA. Insulin-Like Peptide 3 (INSL3) Serum Concentration During Human Male Fetal Life. Front Endocrinol (Lausanne). 2019Sep4;10:596.

[23] Sharma D, Sagar N, Khurana N. Testicular regression syndrome: A series of 22 cases at a tertiary care hospital. Trop J Pathol Microbiol. 2020;6(2):191-197. doi: 10.175111/jopm.2020.i02.12

[24] Canales-Ramos NM, Burgos-Ortega NI, Grana-Santini AJ, Colon-Castellano JM, Gracia-Ramis A, Nieves-Rivera F, Alvarado M, Gonzalez-Rodriguez LA, Ramirez-Vick M. SUN-027 Testicular Regression Syndrome, an Underdiagnosed Cause of Hypergonadotropic Hypogonadism. J Endocr Soc. 2020 May 8;4(Suppl1):SUN-027.

[25] Swee D, Quinton R. Current concepts surrounding neonatal hormone therapy for boys with congenital hypogonadotropic hypogonadism. Expert Review Endocrin Metabol. 2022;17(1):47-61.

Conflict of interest: The author declares no conflicts of interest.

Acknowledgements: None.

Funding: None.

How to cite this article: Contrucci BA, Pinato GR, Galvani CM, Altomari IC, Schmidt Neto SC, Castro JM, Garcia BB, Farinazzo HM, Tambellini GF, Corsini MFL, Beneli PHL, Bortolozzo RC. Neonatal hypogonadism due to rare testicular atrophy with congenital contralateral torsion: case report. Brazilian Journal of Case Reports. 2022 Jan-Mar;02(2):141-148.