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Case report

Bilateral testicular Leydig cell hyperplasia presented incidentally: A case report

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ABSTRACT

Introduction: Leydig cell hyperplasia or tumor represents less than 3% of all testicular tumors. It can be defined as an increase in the size and number of Leydig cell within the testicles. These cells are responsible for the production of testosterone in human males.
Case presentation: Our patient is a forty-eight-year-old male presented with erectile dysfunction and decreased libido for the past six months. Ultrasound of the scrotum show bilateral hypoechoic testicular masses larger on the left size thus left orchidectomy was performed. Histopathology confirmed our diagnosis.
Discussion: Leydig cell hyperplasia (LCH) is a rare and mostly benign entity that affects both children and adults. In adults, it might be associated with variety of condition including Klinefelter's syndrome, exogenous human chorionic gonadotropin (hCG) therapy, and many others but it mostly occurs idiopathically. Scrotal ultrasound and tumor markers can be used to diagnose most of the patients with LCH.
Conclusion: LCH should be differentiated from Leydig cell tumor to avoid unnecessary and sometimes harmful intervention in the future.

1. Introduction

In general population, the overall incidence of testicular tumors is low, as it affects two men in every one hundred thousand. In males aged 20–30 years-old, testicular neoplasms account for 20% of all tumors [1]. From all testicular tumors, less than 3% can be classified as Leydig cell tumor or hyperplasia [2]. Leydig cell hyperplasia (LCH) is an extremely rare but benign condition that should be discriminated from testicular neoplasms [3]. LCH is characterized by an increase in the number and size of Leydig cells of the testicles accompanied by high nucleoli count and reduced lipofuscin and smooth endoplasmic reticulum [4]. This unusual entity troubles adults (75%) way more than children (25%) [5]. In adults, gynecomastia, erectile dysfunction, and infertility are one of the usual presentations of LCH, in spite of the fact that most adult patients are asymptomatic. Although a testicular mass may be palpable, but it is an atypical complaint of patients with LCH [6,7]. On the other hand, LCH may manifest as a premature pseudopuberty and androgen secretion in children [8].

By using a combination of the patient history, radiological features and tumors marker, a diagnosis of LCH can be assembled and excisional biopsy should be executed [9]. Here we present a rare case report of a LCH in a 48 years-old male patient. To the best of our knowledge, the presented case is the first case reporting a Leydig cell hyperplasia in Jordan [10]. To the best of our knowledge, the presented case is the first case reporting a Leydig cell hyperplasia in Jordan.

2. Case presentation

A Forty-eight-year-old male, nonsmoker patient presented at our urology clinic complaining from gradual onset erectile dysfunction and decrease libido of 6 months duration, associated with loss of morning erection. The patient is a father of three children and had no history of infertility. There was no significant past medical or surgical history. On physical examination the patient had normal secondary sexual characteristics. Genitalia exam showed small both testes with no tenderness or palpable masses. Hormonal profile was done which showed low total

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and free testosterone with normal follicular stimulating hormone (FSH) and luteinizing hormone (LH).

A scrotal ultrasound was done and showed small both testes and bilateral hypoechoic intratesticular lesions larger in the left testicle with left testicular microlithiasis (Fig. 1).

To get clearer image about these lesions, a testicular Magnetic Resonance Imaging (MRI) was ordered and showed an intratesticular lesion on the left testicle measuring about 5 × 4 mm which has an intermediate signal intensity in T1 and slightly decreased signal intensity in T2 weighted MRI images relative to testicular tissue. Following contrast administrations theses lesions showed enhancement with suspicious of malignancy (Fig. 2).

Tumor markers (beta – human chorionic gonadotropin, alpha fetoprotein, and lactate dehydrogenase) all were within normal ranges.

After discussing laboratory and radiological investigations with the patient and because of the concern regarding a multifocal germ cell tumor, the patient underwent a successful left radical orchidectomy. The patient recovered well and was discharged on the same day of the operation. Histopathology came back showing variable atrophy of seminiferous tubules with nodular Leydig cell hyperplasia, no evidence of malignancy. After three months, follow-up ultrasound was performed and showed no signs of recurrence or complications of the left testicle. Also, the right testicular lesions maintained the same size and character. A follow-up with a serial ultrasound every 6-months is planned to evaluate the size and characteristic of the right testicular lesions.

3. Discussion

Leydig cells are located between seminiferous tubules within the testicular parenchyma's interstitium. They are responsible for testosterone production, and they are normally observed as a single cell or in small aggregates. Reinke crystals, which are crystalloid inclusion with the shape of a rod, are occasionally seen within the cytoplasm of testicular Leydig cells [11]. The count of Leydig cells within the testicle may be variable in different condition. For instance, in Leydig cell hypoplasia or agenesis the number of Leydig cells is decreased or absent respectively, whereas Leydig cell count will be high in Leydig cell hyperplasia (LCH). Differentiation between LCH and Leydig cell tumor (LCT) is still on debate as it is unclear whether LCT is a neoplastic proliferation of LCH or not [12].

In children, primary LCH is more common. Furthermore, it can be classified as idiopathic or associated with familial male-limited precocious puberty (FMLPP) [3,4]. LCH in a 4 years-old or older children with negative genetic association or family history is most likely to be idiopathic. On the other hand, FMLPP-Leydig cell hyperplasia typically occurs in younger boys with family history of precocious puberty [13,14]. McCune–Albright syndrome, congenital adrenal hyperplasia, hepatoblastoma or germ cell tumors all have been accompanying secondary LCH in children [15–17].

In adults, most cases of LCH are believed to be benign and idiopathic. Interestingly, hyperplasia of Leydig cells has been documented in adult with increasing rates, and this was assumed to be due to the use of biopsy and ultrasound to investigate infertility [18]. Prostate cancer antiandrogen therapy, Klinefelter's syndrome, alcoholism, cachexia, exogenous hCG therapy, and tuberculosis, all are identified as associations with LCH in adults. Also, LCH can be caused by local conditions, such as chronic compression of the spermatic cord, stricture of the vas deferens and chronic diseases of the bladder and prostate [15].

There is a controversy whether LCH can progress to Leydig cell tumor, or it represents separate benign clinical entity [6]. In general, adults with LCH are asymptomatic. However, patients may present with signs of adult feminization including painful gynecomastia and decreased libido that infrequently precedes the appearance of testicular swelling, pain, and infertility [6,19].

Diagnostic workup of LCH includes endocrine evaluation by obtaining urinary and serum steroid profiles, (testosterone, dehydroepiandrosterone, androstenedione, urinary 17-ketosteroids and 17-hydroxy progesterone levels). Nevertheless, a normal result of urinary and serum steroid profiles does not rule out the diagnosis of LCH. Moreover, serum tumor marker levels such as Alpha Fetoprotein (AFP) and human chorionic gonadotropin (hCG) can be also used to exclude other pathologies. Scrotal ultrasound of LCH often shows homogenous hyperechoic regions with hypoechoic intervening tissue representing extensive fibrosis. Moreover, LCH typically appears as solid hypointense lesions on T2-wieghted MRI with mild contrast enhancement [3,4]. In contrast, LCT appears as a low signal intensity on T1-wighted and high signal intensity on T2-wieghted MRI. [20] Histologic examination may be needed and is considered the most accurate method of diagnosis accompanying microscopic evaluation of the entire mass [21,22].

The management of LCH can vary depending on the presentation and ultrasonographic findings, it can range from observation with serial physical and ultrasonographic examinations to obtaining testicular excisional biopsy under intraoperative ultrasonographic guidance with frozen section or performing radical inguinal orchidectomy. In the absence of endocrinological manifestation combined with negative laboratory workup, conservative medical management with consecutive MRIs is a useful treatment option, avoiding the patient undergoing unnecessary operation [22,23].

4. Conclusion

Though testicular Leydig cell hyperplasia is a rare benign testicular lesion, it should be kept in mind in the differential diagnosis of bilateral and multifocal testicular lesions. Our patient is a Forty-eight-year-old male diagnosed with bilateral testicular Leydig cell hyperplasia (LCH) and underwent successful left radical orchidectomy. We hope this case study will spot the light on differentiating between LCH and other testicular tumor thus avoiding unnecessary and sometimes harmful intervention in the future.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the

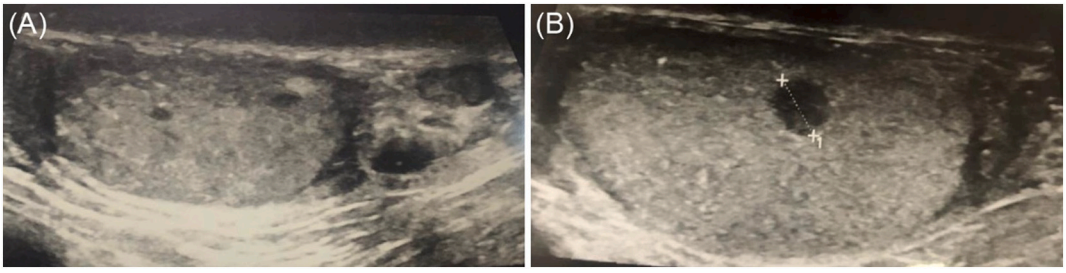

Fig. 1. (A) Ultrasound of scrotum showing two well defined solid hypoechoic focal nodules in the right testicle measuring about 3 × 3 mm and 2 × 2 mm, and (B) another larger nodule in the left testicle measuring about 5 × 4 mm. No hydrocele or varicocele was observed.

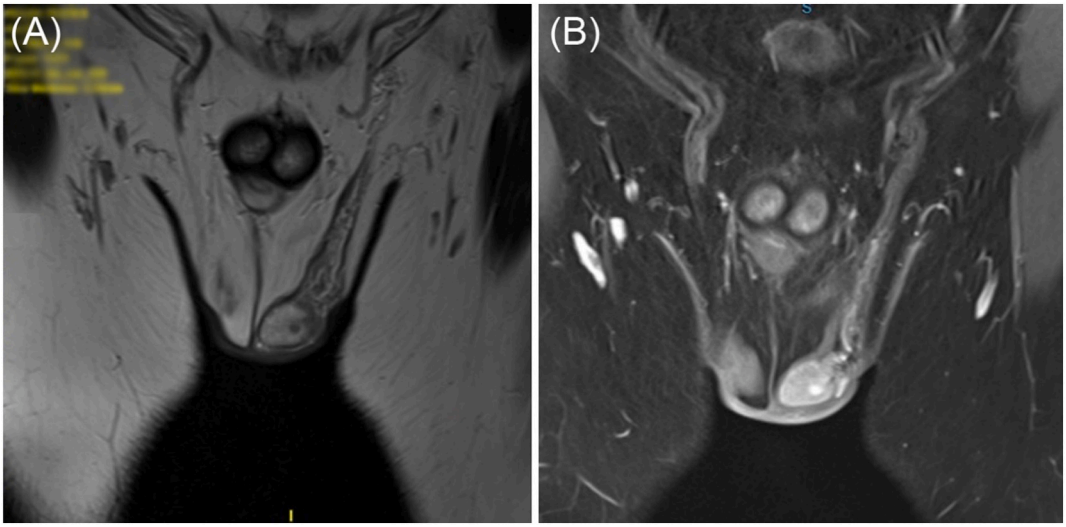

Fig. 2. T2-weighted (A) and post contrast T1-wieghted (B) MRI of the scrotum showing a left intra-testicular lesion measuring about 5 × 4 mm which has an intermediate signal intensity in post contrast T1 and slightly decreased signal intensity in T2 weighted MRI.

written consent is available for review by the Editor-in Chief of this journal on request.

Provenance and peer review

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Ethical approval for case reports and case series are waived according to the ongoing regulations of Yarmouk University.

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Guarantor

Mohammad Al-zubi.

Research registration number

This case report is not eligible for obtaining a research registry since it only contains a report of a known entity with no new surgical or medical interventions.

CRediT authorship contribution statement

Conceptualization: M.A.Z, M.A, S.A.S, S.A.Q. Methodology: M.A.Z, M.A. Validation: M.A.Z, M.A, S.A. Investigation: M.A.Z, M.A, S.A.S. Writing—original draft preparation: M.A.Z, M.A, S.A.S, S.A.Q, S.A, B.M.E. Writing-review and editing: M.A.Z, M.A, T.S.Q. Supervision: M.A.Z. All authors have read and agreed to the published version of the manuscript.

Declaration of competing interest

All authors declare that they have no conflict of interest.

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References

[1] J.P. Dilworth, G.M. Farrow, J.E. Oesterling, Non-germ cell tumors of testis, Urology 37 (5) (1991) 399–417.
[2] M.F. Tazi, S. Mellas, M.J. El Fassi, M.H. Farih, Leydig cell hyperplasia revealed by gynecomastia, Rev.Urol. 10 (2) (2008) 164–167.
[3] C.K. Naughton, R.B. Nadler, J.W. Basler, P.A. Humphrey, Leydig cell hyperplasia, Br. J. Urol. 81 (2) (1998) 282–289.
[4] L.R. Carucci, A.T. Tirkes, E.S. Pretorius, E.M. Genega, S.P. Weinstein, Testicular Leydig's cell hyperplasia: MR imaging and sonographic findings, AJR Am. J. Roentgenol. 180 (2) (2003) 501–503.
[5] I. Kim, R.H. Young, R.E. Scully, Leydig cell tumors of the testis. A clinicopathological analysis of 40 cases and review of the literature, Am. J. Surg. Pathol. 9 (3) (1985) 177–192.
[6] S.L. Asa, T.A. Bayley, K. Kovacs, E. Horvath, Leydig cell hyperplasia due to a testicular embryonal carcinoma producing human chorionic gonadotropin, Andrologia 16 (2) (1984) 146–155.
[7] E.D. Clegg, J.C. Cook, R.E. Chapin, P.M. Foster, G.P. Daston, Leydig cell hyperplasia and adenoma formation: mechanisms and relevance to humans, Reprod.Toxicol. (Elmsford, NY). 11 (1) (1997) 107–121.
[8] A.C. Leung, S.J. Kogan, Focal lobular spermatogenesis and pubertal acceleration associated with ipsilateral leydig cell hyperplasia, Urology 56 (3) (2000) 508–509.
[9] J. Sterbis, T. E-Nunu, Leydig cell hyperplasia in the setting of Klinefelter syndrome, BMJ Case Rep. 2015 (2015), bcr2015209805, https://doi.org/10.1136/bcr-2015-209805.
[10] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, A. Kerwan, A. Thoma, et al., The SCARE 2020 guideline: updating consensus surgical CAse REport (SCARE) guidelines, Int. J. Surg. 84 (2020) 226–230.
[11] S.M. Wu, E.W. Leschek, O.M. Rennert, W.Y. Chan, Luteinizing hormone receptor mutations in disorders of sexual development and cancer, Front Biosci 5 (2000) D343–D352.
[12] N.S. Lakis, K.A. Lombardo, S. Mangray, G.J. Netto, D. Salles, A. Matoso, INSL3 expression in Leydig cell hyperplasia and Leydig cell tumors, Appl. Immunohistochem.Mol. Morphol. 27 (3) (2019) 203–209.
[13] A. Richter-Unruh, H.T. Wessels, U. Menken, M. Bergmann, K. Schmittmann-Ohters, J. Schaper, et al., Male LH-independent sexual precocity in a 3.5-year-old boy caused by a somatic activating mutation of the LH receptor in a Leydig cell tumor, J. Clin. Endocrinol. Metab. 87 (3) (2002) 1052–1056.
[14] N. Mennie, S.K. King, M. Marulaiah, P. Ferguson, Y. Heloury, C. Kimber, Leydig cell hyperplasia in children: case series and review, J. Pediatr. Urol. 13 (2) (2017) 158–163.
[15] M. Colecchia, M. Nistal, P. Gonzalez-Peramato, L. Carmignani, R. Salvioni, N. Nicolai, et al., Leydig cell tumor and hyperplasia: a review, Anal. Quant. Cytol. Histol. 29 (3) (2007) 139–147.
[16] A.W. Root, A.M. Bongiovanni, W.R. Eberlein, A testicular-interstitial-cell-stimulating gonadotrophin in a child with hepatoblastoma and sexular precocity, J. Clin. Endocrinol. Metab. 28 (9) (1968) 1317–1322.
[17] R. Coutant, S. Lumbroso, R. Rey, N. Lahlou, M. Venara, S. Rouleau, et al., Macroorchidism due to autonomous hyperfunction of sertoli cells and G(s)alpha gene mutation: an unusual expression of McCune-albright syndrome in a prepubertal boy, J. Clin. Endocrinol. Metab. 86 (4) (2001) 1778–1781.
[18] L. Carmignani, R. Salvioni, F. Gadda, M. Colecchia, G. Gazzano, T. Torelli, et al., Long-term followup and clinical characteristics of testicular leydig cell tumor: experience with 24 cases, J. Urol. 176 (5) (2006) 2040–2043, discussion 3.
[19] M. Nistal, P. González-Peramato, R. Paniagua, Congenital leydig cell hyperplasia, Histopathology 12 (3) (1988) 307–317.

[20] K. Okamura, T. Yoshizako, R. Yoshida, A. Araki, S. Kyo, H. Kitagaki, Diagnosis of a small leydig cell tumor by dynamic contrast-enhanced and diffusion-weighted magnetic resonance imaging, Radiol.Case Rep. 15 (7) (2020) 875–878.
[21] S. Cooper, A. Richman, T. Carpenter, AJJouim Rosenfield, in: Scrotal Ultrasonography in Leydig Cell Hyperplasia 8, 1989, pp. 689–692 (12).
[22] H.G. Rushton, A.B. Belman, Testis-sparing surgery for benign lesions of the prepubertal testis, Urol.Clin. N. Am. 20 (1) (1993) 27–37.
[23] A. Koni, H.S. Ozseker, E. Arpali, E. Kilinc, H.S. Dogan, A. Akyol, et al., Histopathological evaluation of orchiectomy specimens in 51 late postpubertal men with unilateral cryptorchidism, J. Urol. 192 (4) (2014) 1183–1188.