Cent. Eur. J. Med. • 9(5) • 2014 • 653-656
DOI: 10.2478/s11536-013-0317-8

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Central European Journal of **Medicine**

Sertoli-Leydig tumor and male pseudohermaphroditism discovered during inguinal hernia surgery

Case Report

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Received 21 January 2013; Accepted 5 November 2013

Abstract: The diagnosis of inguinal hernia is usually clinical and it is performed with high sensitivity and specificity. Very occasionally, it may be confused with other diseases (lymphadenopathy, testicular pathology,etc). We report a rare case of a 80-year-old woman with a clinical diagnosis of hernia, which was underwent surgery and a tumor from the hernia orifice was found. After histological analysis we discovered that the misdiagnosed hernia was actually a tumor on a rudimentary testis. After radiological, gynecological and cytogenetic assessment we obtained an unexpected diagnosis: Male psheudohermaphroditism and Sertoli-Leydigtumor (SLCT) development on the testis. Diagnostic guidance for disorders of sexual development is based almost entirely on pediatric experience and very few guidelines are available for adults. Male pseudohermaphroditism is an intersex condition in which the carriers show a phenotype that includes external female genitalia, but a male genetic and gonadal sex. SLCT are sex-cord stromal tumors which develop in ovary and very rarely in the testis, representing 0.1-0.5% of ovarian tumors and less than 0.2% of testicular tumors. Thus far 24 case have been reported in the literature in which SLCT tumor has developed on testis.

Keywords: *Male pseudohermaprhoditism • Sertoli-Leydig tumor • Inguinal Hernia*

1. Introduction

Fetal sexual development consists of three sequential stages: a) an undifferentiated stage, in which identical primitive structures become XY and XX embryos, b) gonadal differentiation into testes or ovaries and c) the differentiation of the internal and external genitalia [1]. The human embryo is sexually ambiguous until the seventh week of pregnancy, a period in which, without the expression of the SRY gene on the Y chromosome, embryo tends to develop as a female [2]. For male differentiation the production of testicular AMH is also required, thus inducing regression of Mullerian structures (in the upper 2/3 of the vagina, uterus and fallopian tubes) and secretion of testosterone, which allows the Wolff ducts to progress, forming the vas deferens, epididymides and seminal vesicles, and allowing the development of external genital structures [1,3].

Male pseudohermaphroditism is an intersex condition in which the carriers show a phenotype that includes external female genitalia, but a male genetic and gonadal sex, with risk of malignancy in these gonads [4-8].

2. Case report

We report a case of an 80-year-old patient with a history of hypertension who underwent elective surgery for right inguinal hernia. During surgery a tumor was identified

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protruding through the hernia orifice, which initially appeared to be a pelvic tumor. The tumor was removed and sent for histological analysis and hernioplasty was completed.

The tumour specimen was a multinodular, measuring 11.5 x 10cm with a tubular pattern and hyaline fibrous stroma compatible with a well-differentiated Sertoli-Leydigtumor (SLCT) or a tumor likely to be of Wolffian origin (Figure 1). Immunohistochemical analysis was positive for inhibin, CD 99 and calretinin, and negative for keratins, CAM 5.2,7, EMA, CD10 and chromogranin A. These results established the diagnosis of well- differentiated SLCT as a first option. Upon review of the patient›s medical history a complete gynecological and radiological assessments were recommended.

The patient recalled a gynecological examination many years before due to amenorrhea and sterility. We performed gynecological ultrasound, which identified a cystic mass measuring 22x21x10cm suggestive of a mesenteric cyst or an ovarian cyst. In view of this finding, abdominal CT was conducted which revealed a unilocular cystic abdominal mass, absence of uterus and a tumor in the left inguinal area (Figure 2 and 3). The testosterone, progesterone and estradiol analysis was normal and cytogenetic analysis showed a 46,XY karyotype without structural alterations.

With the differential diagnosis of male pseudohermaphroditism or pure gonadal dysgenesis, including cyst of uncertain origin and a left inguinal mass, a second surgical intervention was performed.

In the second intervention, a left adnexal cyst of 30cm was observed and two tumors were seen in both inguinal orifices measuring around 5cm compatible with the left gonad and remains of the right (Figure 4). The cystic tumor was removed, along with the two gonads and uterine remnant en bloc.

The final histology results confirmed that the left inguinal tumor was an atrophic testis (Figure 4). The right inguinal mass was composed of fibrous tissue, acute and chronic inflammatory cells, and clusters of histiocytes with multinucleated giant cells of foreign body type in relation to the suture material without residual testicular parenchyma. In both structures smooth muscle tissue was identified, which corresponded to a rudimentary uterus. The cyst was filled with abundant serous fluid and covered by a monolayer of cuboidal epithelial cells with cilia, which were positive for cytokeratin 7 and

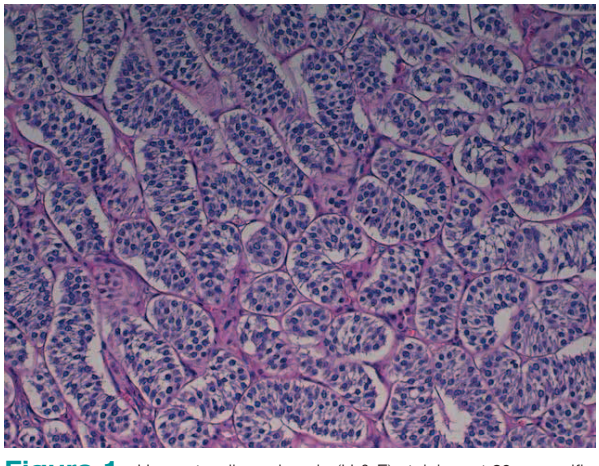

Figure 1. Haematoxylin and eosin (H & E) staining, at 20x magnification, of Sertoli-Leydigtumor with tubular pattern, with the two types of cells and hyalinized fibrous stroma

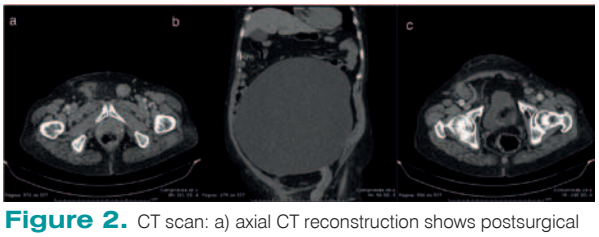

Figure 2. CT scan: a) axial CT reconstruction shows postsurgical changes in the right inguinal region and solid mass in the left inguinal region; b) coronal CT reconstruction shows cystic abdominal mass and left inguinal mass; c) axial CT reconstruction shows absence of uterus

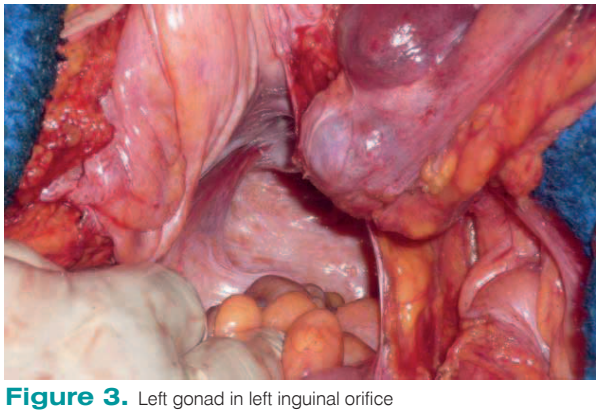

Figure 3. Left gonad in left inguinal orifice

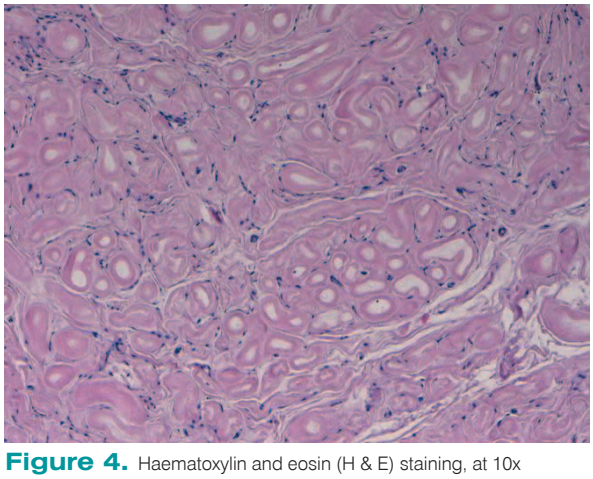

Figure 4. Haematoxylin and eosin (H & E) staining, at 10x magnification. Atrophic left testicle. Fibrous and hyalinized seminiferous ducts without spermatogenesis

negative for calretinin and CD10, supporting the notion of this being a paramesonephric cyst.

The postoperative period was uneventful. In view of the patient's age, and given that the SLCT was well-differentiated, no adjuvant treatment was given. The patient has been followed up periodically upon hospital discharge.

3. Discussion

The diagnostic guidance for disorders in sexual development is based almost entirely on pediatric experience, whereas very few guidelines are available for adults [10]. These genetic disorders have a variety of causes, such as SRY gene mutations, resulting in cases of pure gonadal dysgenesis [11], steroidogenic factor mutations (NR5A1) and mutations of the genes encoding the androgen receptor, such as 17β- hydroxysteroid dehydrogenase-3 and 5α-reductase-2, which form a poorly defined clinical group known as partial androgen insensitivity syndrome (PAIS) [5,7,9,10]. Morris syndrome or testicular feminization is the most common form of PAIS [4], and is the form that we strongly believe our patient presented with. This condition is typically diagnosed during puberty, due to primary amenorrhea and lack of body hair, but given the presence of external genitalia and normal breast development, the diagnosis in postmenopausal patients is rare [5,7,9]. In these patients it is crucial to find the rudimentary male gonads and to remove them surgically, due to risks of malignant degeneration [6,7–9).

Our patient presented with a Sertoli-Leydigtumor, developing on the testis. Only 24 such cases have been reported in the literature so far [12]. SLCTs are sex-cord stromal tumors, which develop in the ovaries and very rarely in the testis, representing 0.1-0.5% of ovarian tumors and less than 0.2% of testicular tumors [13-18]. The age of onset is between the second and third decade of life whereas only 10% appear after the age of 50 and they are usually unilateral [13,17]. In some cases these tumors are functional, and those developing on the ovaries may cause menstrual disorders and virilisation. In other cases they may not be functional or present clinical symptoms of abdominal pain nor mass effect [13]. The Meyer classification is still being used for the SLCTs (well, moderately and poorly differentiated), but two subtypes of SLCT have recently been described: heterologous and retiform [14,17]. SLCTs have slow growth and low rates of metastatic lymph node dissemination [12]. The prognosis is good although factors influencing prognosis are tumor stage, differentiation, tumor rupture and younger age [16].

The standard treatment for SLCT is surgery, performing a bilateral gonadectomy with radical lymphadenectomy. The role of adjuvant therapy is still inconclusive. Although its effectiveness in preventing recurrence of the disease has not been demonstrated [12,17], some authors recommend adjuvant chemotherapy and long-term follow-up in patients with risk factors for recurrence [19]. Conservative surgery may be acceptable for young patients who wish to preserve fertility, although the tendency of poorly differentiated tumors to reappear is an issue that should be borne in mind [19,20].

Conflict of interest statement

Authors state no conflict of interest.

References

[1] Rey RA, Grinspon RP. Normal male sexual differentiation and aetiology of disorders of sex development. Best Pract Res ClinEndocrinolMetab 2011; 25(2):221-238

[2] Liao X, Liang D, Li Y, et al. Mutation analysis of the SRY, NR5A1 and DHH genes in six Chinese 46.XY women. J MaternFetalNeonaltal Med 2011;24(6):863-866

[3] Larson A, Nokoff NJ, Travers S. Disorders of sex development: clinically relevant genes involved in gonadal differentiation. Discov Med 2012;14(78):301-309

[4] Manrique-Hurtado H, Calderón-Ticona J, Medina-SánchezC,etal.Pseudohermafroditismomasculino: insensibilidadandrogénicacompleta. Reporte de uncaso. Rev Soc Peru Med Interna 2007;20(1):26-28

[5] Jarzabek K, Philibert P, Koda M, et al. Primary amenorrhea in a young Polish woman with complete androgen insensitivity syndrome and sertoli-leydig cell tumor: identification of a new androgen receptor gene mutation and evidence of aromatase hyperactivity and apoptosis dysregulation within the tumor. Gynecological Endocrinology 2007;23(9):499-504

[6] Kriplari A, Savithrisowmya S, Argwal N, et al. A rare case of large epididymal cyst in androgen insensitivity syndrome removed laparoscopically. J Minim Invasive Gynecol 2009;16(4)504-506

[7] Rutger JKL. The case reported as bilateral Sertoli-Leydig cell tumor in a 61-year old woman with uterine apalasia may instead represent complete androgen insensitivity syndrome. Int J GynecolPathol 2011;30:395

[8] Dell'Edera D, Malvasi A, Vitullo E, et al. Androgen insensitivity syndrome (or Morris Syndrome) and other associated pathologies. Eur Rev Med PaharmacolSci 2010;14(11):947-957

[9] Subramaniam A, Singh R, Tilak P, et al. Androgen insensitivity syndrome: ten years of our experience. Front Brosci 2013; 5:779:84

[10] Berra M, Williams EL, Muroni B, et al. Recognition of 5α-reductasa-2 deficiency in an adult female 46XY DSD clinic. Eur J Endocrinol 2011;164(6):1019-1025

[11] Paliwal P, Sharma A, Birla S, et al. Identification of novel SRY mutations and SF1 (NR5A1) changes in patients with pure gonadal dysgenesis and 46,XY karyotype. Mol Hum Reprod 2011;17(6):372-378

[12] Pérez-Becerra R, Santana-Ríos Z, Hulda-Graus S, et al. Tumores del Estroma Gonadal Sertoli- Leydig en el Hospital General Dr Manuel GeaGonzález. Rev MexUrol 2009;69(3):174-177

[13] Metzinger DS, Webb MJ. Surgical management of Sertoli-Leydig cell tumors of the ovary. CME J GinecolOncol 2002;7:140-142

[14] Young RH. Sex cord-stromal tumors of the ovary and testis: their similarities and differences with consideration of selected problems. Modern Pathology 2005;18:S81-S98

[15] Caringella A, Loizzi V, Resta L, et al. A cause of Sertoli-Leydig cell tumor in a postmenopausal woman.Int J Gynecol Cancer 2006;16:435-438

[16] Sachdeva P, Arora R, Dubey C, et al. Sertoli-Leydig cell tumor : a rare ovarian neoplasm. Case report and review of littérature.GynecolEndocrinol 2008;24(4):230-234

[17] Lou W, Cao D, Yang J, et al. RetiformSertoli-Leydig cell tumor of ovary in a 9-year-old girl : case report and review of the literature. Int J ClinOncol 2011;16(6):705-708

[18] Guo L, Yang X, Zun H, et al. Sertoli-Leydig cell tumor presenting hyperestrogenism in a postmenopausal woman: a case report and review of the literature. Taiwan J ObstetGynecol 2012;51(4):620-624

[19] Gui T, Cao D, Shen K, et al. A clinicopathological analysis of 40 cases of ovarian Sertoly-Leydig cell tumors.GynecolOncol 2012;127(2):384-389

[20] Xiao H, Li H, Zuo J. Ovarian Sertoli-Leydig cell tumor: a report of severe cases and a review fo the literature. GynecolEndocrinol 2012 DOI: 10.3109/09513590.2012.738723 [Epub ahead of print]