Clinical Case

Secondary Leydig cell hyperplasia as bilateral testicular tumor: a case report


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Keywords
Leydig cell hyperplasia; Bilateral testicular tumor

Abstract

Background: Leydig cell hyperplasia is a rare benign condition characterized by small, multifocal testicular nodules that are frequently bilateral. Its form can be primary or secondary. The former produces precocious puberty in boys and the latter presents as a testicular mass and produces gynecomastia in approximately 30% of the patients as a result of idiopathic supraphysiologic hormone stimulation, and has clinical manifestations similar to those of Leydig cell tumors.

Clinical case: A 30-year-old man with an unremarkable past history, the father of two children, was seen at a primary care hospital for pain and swelling of the right testis that was resolved with nonsteroidal antiinflammatory drugs. Ultrasound study revealed bilateral testicular tumor. The patient had no palpable testicular mass or gynecomastia or other relevant signs or symptoms. The ultrasound finding was confirmed by magnetic resonance imaging and retroperitoneal activity was ruled out from tomography scan results. Exploration of the right testis was carried out with the inguinal approach. The incisional intraoperative biopsy revealed a millimetric mass protruding from the healthy parenchyma. It was reported as undetermined in the intraoperative study and so radical orchiectomy was completed. The definitive histopathology study stated Leydig cell hyperplasia. The patient refused any invasive diagnostic procedure in the contralateral testis. His postoperative progression was favorable with no changes in imaging studies in the contralateral testis during follow-up.

Conclusion: This was a case of atypical secondary Leydig cell hyperplasia whose definitive diagnosis was made through the final histopathology study of the specimen, the only manner in which to accurately rule out a Leydig cell tumor.

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Hiperplasia secundaria de células de Leydig como tumor testicular bilateral: reporte de un caso

Resumen
Antecedentes: La hiperplasia de células de Leydig es una condición benigna infrecuente caracterizada por nódulos testiculares pequeños, multifocales y frecuentemente bilaterales, y puede presentarse de forma primaria, produciendo pubertad precoz en niños varones o secundaria, como una masa testicular con ginecomastia en aproximadamente el 30% de los pacientes, con manifestaciones clínicas similares a las de los tumores de células de Leydig, lo anterior como resultado de una estimulación hormonal suprarafisiológica idiópatica de los testículos.

Caso clínico: Presentamos el caso de un hombre de 30 años de edad sin antecedentes relevantes, padre de 2 hijos, atendido en el primer nivel de atención por presentar dolor y aumento del volumen del testículo derecho, que resolvieron con antinflamatorios no esteroideos, con hallazgo ecográfico de un tumor testicular bilateral, no obstante sin masa testicular, asimismo sin ginecomastia u otros síntomas o signos físicos relevantes. Se confirma el hallazgo por resonancia magnética y se descarta actividad retroperitoneal por tomografía; se realiza exploración testicular derecha por abordaje inguinal, con biopsia incisional transoperatoria de una masa milimétrica que sobresalía del parénquima sano, reportada como indeterminada en el estudio transoperatorio, por lo que se completó la orquiectomía radical con reporte histopatológico definitivo de hiperplasia de células de Leydig. El paciente no aceptó algún procedimiento diagnóstico invasivo en el testículo contralateral, evolucionó favorablemente en el postoperatorio sin cambios por imagen en el testículo contralateral durante el seguimiento.

Conclusions: Se trata de una presentación atípica de hiperplasia secundaria de células de Leydig cuyo diagnóstico solo pudo realizarse de manera definitiva al realizar el estudio final de la pieza, siendo esta la única forma de excluir con certeza un tumor de células de Leydig.

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Introduction

Leydig cell hyperplasia (LCH) is a rare benign condition characterized by the presence of small, multifocal, testicular nodules that are frequently bilateral. In the primary form, it can present as precocious puberty in boys. The secondary form is the more frequent in adults and presents as a testicular mass with the development of gynecomastia in approximately 30% of the patients.1 Leydig cell tumors have 2 incidence peaks: in patients between 5 and 10 years of age and between 25 and 35 years of age, and the appearance of a tumor or Leydig cell hyperplasia is a rare event in puberty.2 The primary form is caused by either familial mutation that activates the luteinizing hormone (LH) receptor, causing an elevation in serum testosterone and resulting in precocious puberty in males, or a congenital stimulation of placental human chorionic gonadotropin (hCG) to the testes. Moreover, secondary Leydig cell hyperplasia is usually idiopathic and results from supraphysiologic hormone stimulation of the testes that may be due to a transitory or sustained increase in LH or hCG, a reduced production of testosterone, or unknown paracrine testicular growth factors. The precise mechanism is not understood,3 but expositional factors have been analyzed in experimental studies,3 in addition to being a frequent finding in patients with lepromatous leprosy together with testicular damage,4 which is believed to play a counter-regulating role in the preservation of bone volume in these patients.5 The clinical presentation of LCH can be similar to that of Leydig cell tumors: endocrinologic signs of feminization in adults, including painful gynecomastia and reduced libido can result in the production of estrogens by the Leydig cells. These cells can also produce testosterone, giving rise to precocious puberty in boys. The patients can present with a testicular mass or infertility, but the most common presentation is increased testicular volume with gynecomastia. Twenty-five percent of patients have a decrease in libido or sexual potency.6 Scrotal ultrasound is characterized by hyperechogenic testicular regions with hypoechogenic or have mixed echogenicity.2,7 It is known that up to 45% of focalized testicular lesions smaller than 2 cm are benign and Leydig cell hyperplasia can correspond to up to 6% of them.8 Microsurgical techniques have been described for the approach to suspicious testicular lesions in patients with compromised fertility.9 Nevertheless, accurate diagnosis can be difficult without the performance of a radical surgical procedure.4

Case presentation
A 30-year-old man, the father of 2 children, had no hereditary or family pathologic or expositional past history.
He presented with the symptoms of pain and an enlarged right testis that improved with nonsteroidal anti-inflammatory drugs. Testicular ultrasound revealed findings related to bilateral testicular tumor and the patient was referred to tertiary care. Directed physical examination found a comparatively slightly enlarged right testis and pain in the lower pole upon palpation. Masses consistent with cysts were palpated in both epididymides. Alpha-fetoprotein, beta fraction hCG, and lactate dehydrogenase tests were ordered and their results were negative. Hormone profile was normal with no increase in LH. Semen parameters showed oligospermia (8 million sperm per ml) with no other alterations. A new testicular ultrasound was done that showed diffuse vascularized hypoechochogenic areas in both testes (fig. 1). The computed tomography scan showed no evidence of retroperitoneal lymph node activity or distant activity (fig. 2). Due to the absence of a palpable tumor, the decision was made to carry out testicular magnetic resonance that reported bilateral neoplasia vs. dilation of the rete testis (fig. 3). Exploration of the right testis (because it was the most affected side in the imaging studies) through the inguinal approach produced the intraoperative finding of an approximately 7 mm hardened, light brown mass that protruded from the testicular parenchyma at the edge in the direction of the epididymis. The incisional biopsy of the mass for intraoperative study was nonspecific. Because of the imaging findings of uncircumscribed infiltration of the testicular parenchyma, radical orchiectomy, rather than the partial procedure, was performed (fig. 4). Likewise, due to the datum of oligospermia and the explicit wish of the patient, biopsy of the contralateral testis was not performed. The definitive histopathology report stated Leydig cell hyperplasia. The patient had a satisfactory postoperative period and after receiving the news of the nature of his condition decided against further invasive diagnostic procedures in the contralateral testis. He was released with indications for clinical surveillance and imaging studies.

Discussion

The clinical case presented herein had atypical manifestations that made the diagnostic approach difficult. The patient had no past history related to the diagnosis (extragonadal seminoma, cryptorchidism, exposures, leprosy). The initial symptoms were pain and an enlarged testis with no palpable masses that were resolved with analgesics and were not perceived after symptom resolution. In a study involving 1,320 patients with different urologic symptoms that was carried out to evaluate the incidence of benign testicular neoplasias, focal testicular lesions were found in 27 (2%) patients. Of them, only one patient presented with Leydig cell hyperplasia in the final histopathologic study. In addition, during the approach to
our patient, no endocrine abnormalities such as those described in the literature were found. In regard to oligospermia, it is known that the severity to which spermatogenesis is affected is associated with serious morphologic and functional alterations in the compartment containing the Leydig cells. However, our patient had no fertility problems and only one sperm parameter study reported oligospermia.

Regarding the imaging study findings, the heterogeneous, infiltrating, and diffuse appearance in the contrast-enhanced ultrasound differed from the characteristic aspect of benign lesions. Multinodular complex cystic lesions of the rete testis have been reported that are similar to intratesticular Leydig cell neoplasias, concurring with the differential diagnosis of the magnetic resonance report. However, these cases are infrequent and insufficient for ruling out malignant neoplasia.

Finally, upon opting for an inguinal exploration of the most affected testis with an intraoperative study, it is important to point out that techniques for cold-section histopathologic analysis have been validated for selecting patients for conservative surgery. However, the characteristics of the sample must be adequate. On the other hand, in case of doubt, accurate diagnosis can only be made with the study from the radical orchiectomy specimen.

**Conclusion**

Secondary Leydig cell hyperplasia is a benign condition that is a diagnostic challenge. The approach should be centered on an extensive medical history and the systematic study of the patient in order to avoid unnecessary procedures that can compromise reproductive and sexual function, but especially that do not miss the diagnosis of a malignant neoplasia.

**Ethical responsibilities**

Protection of persons and animals. The authors declare that no experiments were performed on humans or animals for this study.

Data confidentiality. The authors declare that they have followed the protocols of their work center in relation to the publication of patient data.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

**Financial disclosure**

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**Conflict of interest**

The authors declare that there is no conflict of interest.

**References**