

Primary carcinoid tumor of the testis: A rare case

Testisin karsinoid tümörü: Nadir bir olgu

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Abstract

Neuroendocrine tumors most commonly occur in the gastrointestinal tract, lungs and pancreas. Primary testicular neuroendocrine tumors are rare, constituting 0.23% of all testicular tumors. A 35-year-old man presented to urology department with a painless left scrotal mass. He had no history of trauma. Scrotal Doppler ultrasonography revealed a 2x1.5 cm, well-circumscribed, solid lesion. Tumor marker levels were normal and staging computed tomography demonstrated no evidence of metastasis. The patient subsequently underwent left radical orchiectomy. The orchiectomy material, grossly showed a 1.4x1.2 cm, well-circumscribed, yellow, solid mass. On histopathologic examination, primary testicular carcinoid tumors cannot be distinguished from well-differentiated neuroendocrine carcinoma. The diagnosis of a primary testicular carcinoid tumor was made after ruling out an extratesticular neuroendocrine tumor using clinical and radiological data. This rare case is presented with clinical, morphological and immunohistochemical features.

Keywords: Testis, carcinoid tumor, neuroendocrine tumors.

Öz

Nöroendokrin tümörler, sıklıkla gastrointestinal sistem, akciğer ve pankreas gibi organlarda görülmektedir. Primer testiküler nöroendokrin tümörler son derece nadir olup, tüm testis tümörlerinin %0.23'ünü oluşturur. 35 yaşındaki hasta, sol skrotumda ağrısız şişlik şikayeti ile üroloji kliniğine başvurdu. Hastada travma hikayesi bulunmamaktaydı. Skrotal Doppler ultrasonografisinde sol testis alt polde 2x1.5 cm boyutlarında düzgün sınırlı solid kitle izlendi. Tümör markerları ve bilgisayar tomografi taramaları normaldi ve hastada metastaz izlenmedi. Hastaya sol radikal orşiektomi uygulandı. Orşiektomi materyali, makroskopik olarak 1.4x1.2 cm boyutlarda düzgün sınırlı, sarı solid kitle olarak izlendi. Histopatolojik incelemede primer testiküler karsinoid tümör, iyi diferansiye nöroendokrin karsinomdan ayırt edilemedi. Primer testiküler karsinoid tümör tanısı, klinik ve radyolojik olarak ekstratestiküler nöroendokrin tümör dışlanarak yapıldı. Bu nadir olgu, morfolojik ve immunhistokimyasal özellikleri ile sunulmuştur.

Anahtar Sözcükler: Testis, karsinoid tümör, nöroendokrin tümörler.

Introduction

Neuroendocrine tumors (NETs) were first described by Langhans (1) in 1867. These tumors are usually seen in the gastrointestinal tract, lungs, and pancreas. Primary NETs rarely present in the testis, constituting 0.23% of all testicular tumors.

Simon et al. (2) reported the first primary testicular carcinoid tumor (TCT) in 1954, more than 60 cases of TCT have been reported, although it remains an uncommon disease (3).

In this report, we describe a rare case of a primary carcinoid tumor of the testis

Case report

A 35-year-old man with no trauma history presented to urology clinic with a painless left scrotal mass. He denied any weight loss, hematuria or systemic

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symptoms. Physical examination revealed that the scrotal mass was indurated. Serum lactate dehydrogenase (LDH), β -human chorionic hormone (β -HCG), and alpha-fetoprotein (AFP) levels were within the normal ranges. Scrotal Doppler ultrasonography revealed a 2.0 \times 1.5 cm, well-circumscribed, solid lesion. Computed tomography demonstrated no evidence of metastasis. The patient subsequently underwent left radical orchiectomy.

Grossly, the orchiectomy material showed a 1.4 \times 1.2 cm well-circumscribed, yellow solid mass. The tumor reached the tunica albuginea but did not invade it, nor did the tumor invade the rete testis or epididymis. On histopathologic examination, the tumor displayed features typical of a carcinoid tumor and the adjacent testicular parenchyma showed no germ cell neoplasia in -situ. The tumor cells were arranged in insular and nesting patterns. The cells had abundant granular, eosinophilic cytoplasm. The nuclei were round-to-oval-shaped with a "salt and pepper" chromatin pattern (Figure-1).

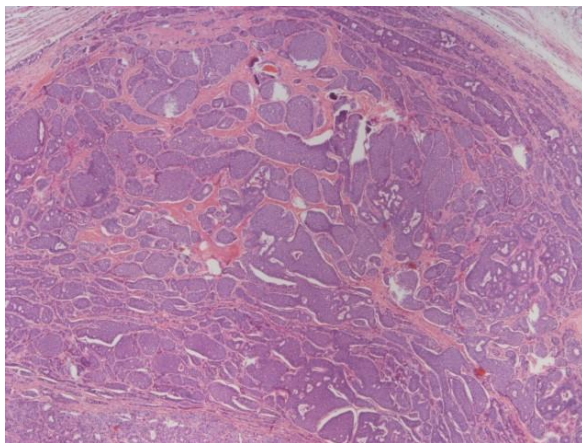


Figure-1. The nucleus is characterized by "salt and pepper" chromatin pattern without evidence of marked cytologic atypia or mitotic activity (H&E, \times 200).

One mitosis per 10 high-power fields (HPFs) were observed on phospho-histone H3 (pHH3) immunohistochemical staining. No teratomatous elements were identified. Immunostaining was positive for neuroendocrine markers (chromogranin, synaptophysin, and CD56), supporting the diagnosis of a carcinoid tumor. Immunohistochemistry showed negative staining for placental alkaline phosphatase, D2-40, SALL-4, CD30, OCT-4, AFP, SOX-2, inhibin α , and calretinin. The Ki67 proliferation index was 1%. As the patient had no NETs in other regions, the final diagnosis was a primary testicular carcinoid tumor.

Written informed consent was obtained from the patient for publishing the individual medical records.

Discussion

In 1907, a German pathologist named Oberndorfer explored the term carcinoid (karzinoide) to distinguish a group of tumors found in the small intestine (1). The first case of a primary TCT was reported by Simon et al. (3) in 1954. The histogenesis of neuroendocrine neoplasms of the testis remains unclear, although several hypotheses have been proposed. Abbosh et al. (4) suggested that TCTs typically occur in the background of a teratoma. They found that isochromosome 12p and 12p over-representations were present in both the carcinoid tumor cells and in the cells of the co-existing mature teratoma. Mai et al. (5) proposed that TCTs arise from Leydig cells, which may be new members of the diffuse neuroendocrine system. In addition, using immunohistochemical methods, Davidoff et al. (6) found neuronal and neuroendocrine cell substances in the cytoplasm of the interstitial Leydig cells of human testes. These findings support the hypothesis that both carcinoid tumor cells and Leydig cells may have the same cell origin in the primary TCT.

Tumor grade is used as the basis for prognostic classification systems, including those proposed by the European Neuroendocrine Tumor Society (ENETS) and the World Health Organization (WHO) (7,8). In 2010, the revised WHO classification of neuroendocrine neoplasm defined three tumor grades based on either the mitotic rate (mitoses per 10 HPFs) or the Ki67 index (%):

Grade 1 (NET G1): 2 mitoses/10 HPFs or Ki67 index $<$ 2%

Grade 2 (NET G2): 2-20 mitoses/10 HPFs or Ki67 index 3–20%

Grade 3 (NET G3): $>$ 20 mitoses/10 HPFs or Ki67 index $>$ 20%.

The term *carcinoid tumor* is used for NET G1.

In 2016, testis carcinoid tumors were identified as well-differentiated NETs, as part of the WHO classification for tumors of the urinary system and male genitalia. The cases may be pure primary neoplasm as well as with teratomas or epidermoid/dermoid cysts. Most primary TCTs have a benign clinical behavior, regardless of association with teratomas or epidermoid/dermoid cysts. However, lesions with the morphology of an atypical carcinoid can occasionally display metastatic spread. Atypical carcinoid tumors have either coagulative necrosis or increased mitotic

activity, with 2-10 mitoses per 10 HPFs. In a series of 29 cases, 1 of the 3 atypical carcinoid tumors had aggressive behavior, with a lymph node metastasis and a lung metastasis (9).

In this case study, the patient's tumor showed a mitotic rate of 1 mitosis per 10 HPFs by using phospho-histone H3 (pHH3) immunohistochemical stain and a ki67 proliferation index of 1%. There was no necrosis. So that pathological diagnosis was NET G1.

The most common presentation of a TCT is a painless testicular enlargement, followed by testicular pain and the presence of a hydrocele. Carcinoid syndrome occurs in 10-20% of all carcinoid tumors. No carcinoid syndrome was observed in this case.

Grossly, the tumors appear to be yellow/tan-colored and solid, with a firm, cut surface due to desmoplasia. The average tumor size is 4.6 cm (ranging from 1.0 cm to 9.5 cm). On histopathologic examination, there are insular, trabecular patterns of monotonous neoplastic cells, with abundant eosinophilic cytoplasm, round-to-oval nuclei, and a distinct nuclear membrane

displaying a "salt and pepper" chromatin pattern. The tumor shows positive immunostaining for chromogranin, synaptophysin, and CD56, and negative immunostaining for placental alkaline phosphatase, CD30, β -HCG, AFP, and epithelial membrane antigen. The Ki67 proliferation index is <1% in tumor cells.

Morphologically, primary TCTs cannot be distinguished from well-differentiated neuroendocrine carcinoma. The diagnosis of a primary TCT was made after ruling out extratesticular NET, using both clinical and radiology data. The treatment course decided was radical orchiectomy. While carcinoid tumors usually have an excellent prognosis, factors such as large tumor size, the presence of carcinoid syndrome, and distant metastases can worsen the prognosis (10).

The primary carcinoid tumor of the testis is a rare tumor, and this case will contribute to the literature. It should be excluded the metastasis of TCT, because the primary tumor is indistinguishable from the metastatic ones with the morphological and histological characteristics.

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