Case Report

Primary neuroendocrine tumor of the testis

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Abstract Testicular neuroendocrine tumor is rare. It accounts for less than 1% of all testicular neoplasms. More than 60 cases have been published in the literature. A 27-year-old man presented with left testicular mass and underwent radical orchidectomy. Histological examination showed neuroendocrine tumor, confirmed by immunohistochemistry and electron microscopy. The patient showed no evidence of metastasis over 1-year follow-up post-orchidectomy in spite of extensive tumor necrosis.

Key Words: Neuroendocrine tumor, orchidectomy, testis

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INTRODUCTION

Neuroendocrine tumors are more frequently arisen from the embryonic gut. Testicular neuroendocrine tumor can occur as a primary or as metastases. Primary neuroendocrine tumors of the testis are rare. The cell of origin of testicular neuroendocrine tumor is unknown. Here, we report a case of primary testicular neuroendocrine tumor in a young man. The national data of such a tumor is extremely limited. The morphological findings and biological behavior of this rare tumor are discussed.

CASE REPORT

A 27-year-old man presented with a history of painless swelling of the left testis mass for 7 months. Physical examination revealed nontender firm testicular mass. Scrotal ultrasound revealed a well-defined oval heterogenous hyperechoic hypervascularized mass in the left testis measuring 3.7 × 2.7 cm, associated with mild hydrocele [Figure 1]. The right testis appeared normal. Chest X-ray and CT scan of the abdomen were normal. Laboratory investigations showed: Quantitative beta-HCG <3.0 (normal <5.0) U/L, AFP 3.0 (normal <15.0) micro g/L. The patient underwent surgery for exploration and possible radical orchidectomy. Intraoperative consultation was considered and wedge biopsy was sent for frozen section examination which showed a round cell tumor with neuroendocrine features associated with extensive necrosis. Therefore, radical orchidectomy was performed.

Macroscopically, the tumor showed multiple yellow confluent nodules measuring up to 6.2 cm, associated with foci of necrosis. The epididymis and spermatic cord were unremarkable.

Microscopically, the tumor cells were arranged in nests and solid islands with rosettes formation. Extensive tumor necrosis was present [Figure 2]. Tumor cells were round with mild pleomorphism and had eosinophilic cytoplasmic granules [Figure 3]. The mitosis was rarely seen.

There were no invasion to tunica albuginea and no intratubular germ cell neoplasia. The tumor mass was submitted entirely, and showed no teratomatous elements.

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On immunohistochemistry, the tumor was positive for chromogranin, synaptophysin, and neuron-specific enolase (NSE). MIB-1 proliferative index was less than 1%. Ultrastructural examination of the tumor cells by transmission electron microscope (TEM) revealed the multiple intracytoplasmic neurosecretory granules [Figure 4].

DISCUSSION

Neuroendocrine tumor commonly arises from intestinal and respiratory epithelium. Neuroendocrine tumor of the testis is a rare tumor and accounts for less than 1% of all testicular neoplasms.[1] More than 60 cases have been reported to date.[2,3] The first case reported in Saudi Arabia and Middle East was in 1997.[4]

The reported cases ranged from 10 to 83 years of age with higher incidence in the fifth and sixth decade of life.[2,4] Most patients present with unilateral painless testicular mass. 16% of patients present with symptoms of neuroendocrine tumor syndrome.[3,5] Eleven percent of primary testicular neuroendocrine tumors are associated with metastasis.[6]

The neuroendocrine tumors of the testis occur as a primary testicular neuroendocrine tumor; or metastatic neuroendocrine tumor to the testis. The primary testicular neuroendocrine tumor can be further divided into: 1) primary pure testicular neuroendocrine tumor; and 2) associated with teratoma or dermoid/epidermoid cysts.[2,4,7] Once a testicular neuroendocrine tumor has been found, a metastatic neuroendocrine tumor to the testis should be excluded.[3,8] The presence of teratomatous elements sufficiently excludes the primary site outside the testicles. So, it is important to submit the tumor mass entirely and look for any additional lineage of differentiation. Twenty-five percent of primary testicular neuroendocrine tumors are associated with teratoma.[9]

Histogenesis of pure neuroendocrine tumor of the testis remains

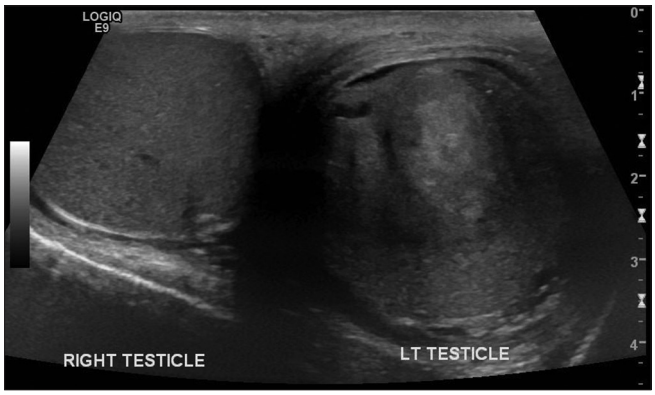

Figure 1: Testicular ultrasound showing heterogenous mass in the left testicle

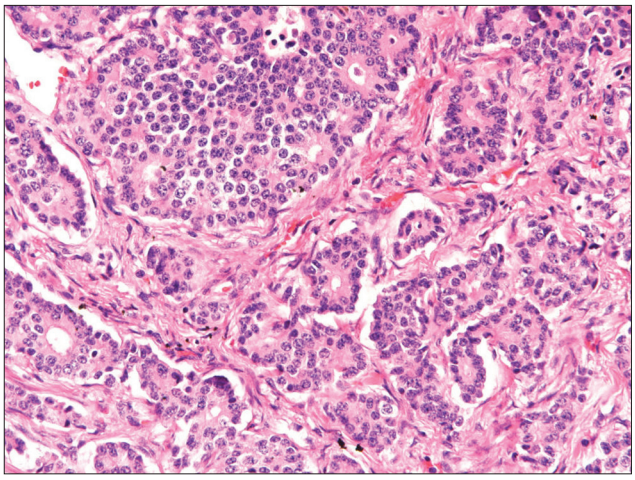

Figure 3: Photomicrograph (original magnification ×40; Hematoxylin and eosin stain) showing tumor cells arranged in sheet of polygonal cells with moderate cytoplasm and fine stippled chromatin patten

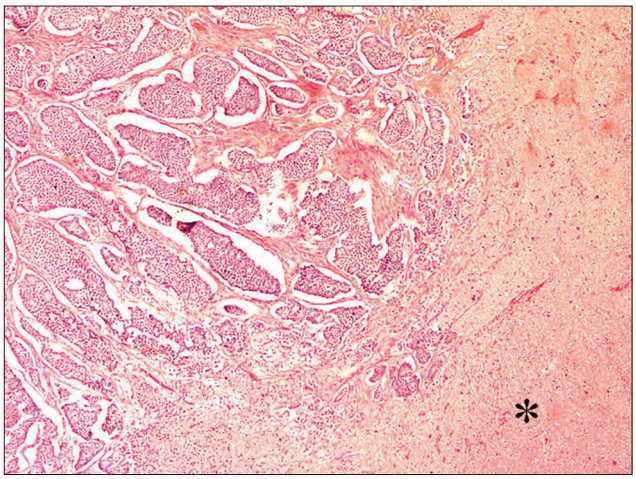

Figure 2: Photomicrograph original magnification ×20; Hematoxylin and eosin stain) showing nests of neuroendocrine tumor with extensive necrosis (asterisk)

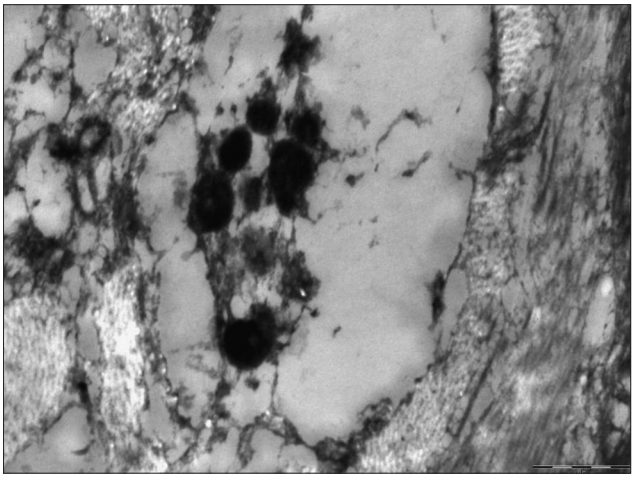

Figure 4: Electron micrograph showing intracytoplasmic neurosecretory granules

unclear. Two theories have been implicated regarding the mode of origin; derived from teratoma (germ cell origin) or arising in argentaffin cells located in crypts of Lieberkühn.[8,10] The later also present in gastrointestinal tract and bronchial mucosa. However, in a study involved three pure testicular neuroendocrine tumors suggested that pure testicular neuroendocrine tumor might have different genetic background other than germ cell tumor.[11]

Histologically, neuroendocrine tumor is characterized by presence of nests of small round cells with uniform nuclei forming small acini and rosettes or sheets. The cells have eosinophilic granules in the cytoplasm and granular chromatin within the nuclei. The tumor cells stained positively for neuroendocrine markers like chromogranin and synaptophysin.

In our case the frozen section showed round tumor cells with neuroendocrine features associated with extensive necrosis. The presence of necrosis does not correlate with the malignant behavior of the tumor and doesn't predict the propensity for metastases.[5]

Radical orchidectomy is the treatment of choice; however, the need for adjuvant therapy depending on histological grading remains unclear.[2,7] Octreotide analog can improve the neuroendocrine (carcinoid) syndrome and stabilize the tumor.[3]

The rarity of testicular neuroendocrine tumor is a limiting factor to understand the biological behavior of the tumor on which a modern classification and prediction of prognosis can be reached. However, the localized testicular neuroendocrine tumor has excellent prognosis after surgery.[2,3,7] Neuroendocrine tumor can develop metastasis 7 years after the initial treatment.[3] Few cases reported metastases 5 and 19 years later.[4] 50% of testicular neuroendocrine tumor with carcinoid syndrome metastasized and the larger tumor the higher risk for metastasis.[5] The association with teratoma has a prognostic value depending on the age; Postpubertal teratomatous neuroendocrine has advert prognosis.[2]

Because a metastatic potential exists, long-term follow-up is indicated. Regular physical examination, urinary 5-HIAA, abdominal CT scan, and gastrointestinal contrast can be exercised for follow-up evaluation.[2,3,4,7,12]

CONCLUSIONS

Primary testicular neuroendocrine tumor is very rare. It is crucial to submit the entire gross specimen for histopathologic examination to rule out an existing of other germ cell elements. The patient showed no evidence of metastasis over 1-year follow-up post-orchiectomy in spite of presence of extensive tumor necrosis. Long-term follow-up is warranted for such a testicular neoplasm.

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