Primary pure carcinoid tumor of the testis: Radiology, pathology and molecular correlation

Gang Wang a, *, Wei Xiong b, Tracy Tucker a, Henry Tran c, Lucia Nappi d, Ren Yuan e

a Department of Pathology, British Columbia Cancer Vancouver Centre, Vancouver, BC, Canada
b Department of Pathology, St. Paul’s Hospital, Vancouver, BC, Canada
c Department of Urology, St. Paul’s Hospital, Vancouver, BC, Canada
d Department of Medical Oncology, British Columbia Cancer Vancouver Centre, Vancouver, BC, Canada
e Department of Radiology, British Columbia Cancer Vancouver Centre, Vancouver, BC, Canada

ARTICLE INFO

Keywords:
Testicle
Carcinoid tumor
Pathological
Radiological

ABSTRACT

We describe a case of a primary carcinoid tumor of the testis in a 35-year-old man as an incidental finding. Testicular ultrasound showed a 1.1 cm hypoechoic/isoechoic mass with some calcification in the left testicle. The pathology examination of the radical orchiectomy demonstrated a pure carcinoid tumor, with the adjacent coarse calcification. Fluorescence in situ hybridization showed 35% of the tumor cells had one additional chromosome 12p11.21 signal. This case adds to the rare reports in the literature of a primary pure carcinoid tumor of the testis, and provides additional insight into the radiological and pathological correlation of this disease.

1. Introduction

Testicular carcinoid tumors are rare neoplasms, accounting for 0.2–1% of all testicular tumors. 1 Although since 1930, more than 100 cases of testicular carcinoid have been reported, it remains a very rare diagnosis. Testicular carcinoid tumors can be divided into four subgroups: (1) primary pure testicular carcinoid; (2) primary carcinoid tumor associated with teratoma; (3) primary with epidermoid or dermoid cysts; and (4) metastatic carcinoid tumor to the testis.2 In this report, we describe a case of a primary carcinoid tumor of the testis with a focus on radiology, pathology, and molecular correlation.

2. Case presentation

The patient was a 35-year-old man who presented with abdominal pain and left testicular discomfort. He underwent a CT scan to rule out the presence of kidney stones. However, there was a suspicious mass in the left testicle. He underwent an ultrasound which showed a 1.1 × 1.1 × 1 cm hypoechoic/isoechoic mass with some calcification (Fig. 1A) and moderate internal vascularity in the left testicle (Fig. 1B). Tumor markers (LDH, alpha-fetoprotein, and beta-hCG) were all negative.

He underwent a left radical orchiectomy. The pathology demonstrated nests of monotonous tumor cells with relatively abundant eosinophilic cytoplasm, round to oval nuclei, a distinct nuclear membrane with "salt and pepper"-like chromatin (Fig. 2A–C). The adjacent coarse calcification present (Fig. 2B). Immunohistochemistry showed the tumor cells are positive for synaptophysin (Fig. 2D), chromogranin, and cytokeratin AE1/AE3 and negative for PLAP, CD30, b-HCG, AFP, and CD117. Ki-67 labeling index was <2% of tumor cells. The tumor was unifocal, limited to the testis, with no lymphovascular invasion identified. The possibility of an extratesticular carcinoid tumor was ruled out with negative esophagogastroduodenoscopy and colonoscopy. Fluorescence in situ hybridization (FISH) showed 35% of the tumor cells had one additional chromosome 12p11.21 signal relative to the 12q21.33 signal (Fig. 2E), but was not consistent with the expected signal pattern for an isochromosome 12p, or reached the threshold for 12p overrepresentation. There was no evidence of other germ cell tumor components or germ cell neoplasia in situ identified. The final diagnosis was a primary pure well-differentiated neuroendocrine tumor (G1)/carcinoid tumor of the testis. The tumor was staged as pT1 N0 M0 per the American Joint Committee on Cancer (AJCC) TNM staging for testicular cancers. The patient is in six months of follow-up with no evidence of recurrence.

* Corresponding author. Department of Pathology, British Columbia Cancer Vancouver Centre, 600 West 10th Avenue, Vancouver, British Columbia, VSZ 1H5, Canada.
E-mail address: gang.wang1@bccancer.bc.ca (G. Wang).

https://doi.org/10.1016/j.eucr.2021.101787
Received 2 July 2021; Accepted 21 July 2021
Available online 21 July 2021
3. Discussion

Patients with testicular carcinoid tumors usually present with a self-detected testicular mass or testicular ache (as occurs with common testicular tumors) or, rarely, carcinoid syndrome (red-hot flushing, diarrhea, abdominal pain, palpitations, and bronchospasms) if there is metastasis to the liver or lungs.

The diagnosis should begin with a physical examination of the scrotum, followed by a Doppler ultrasound. The tumor is usually well-circumscribed, hyperemic, isoechogetic solid, or mixed cystic and solid, with increased vascularity. Interestingly, a few reported cases with Doppler ultrasound available showed large calcified foci, as we see in the current case. Whether the particular pattern of the calcification seen in these cases is associated with the testicular carcinoid tumors
worth exploring further. Upon detecting a testicular carcinoid tumor, a multimodal approach should be taken to exclude the possibility of metastasis from another organ. A staging CT scan is used for detecting metastasis.

Microscopically, tumor cells are composed of monotonous polygonal-shaped cells with eosinophilic cytoplasm and finally dispersed chromatin within the uniform, bland nuclei. The neoplastic cells can be found to have different architectural arrangements, but trabecular and insular patterns predominate. The necrosis can be seen in large size tumors. The tumor cells are immune-reactive for the neuroendocrine markers, including synaptophysin and chromogranin, and negative for the germ cell tumor markers such as CD117, Oct3/4, CD30, or PLAP. The neuroendocrine neoplasms are currently defined into three groups by WHO/European Neuroendocrine Tumor Society (ENETS). The classification is based on the immunostaining of Ki-67 or mitotic count – Neuroendocrine Tumors G1 (NET) G1: Ki-67 < 2 %, NET G2: Ki-67 3–20 %, NET G3: Ki-67 > 20 %. The term “carcinoid” is used for NET G1.

The histogenesis of pure testicular carcinoid has not been well established. It was described that testicular carcinoids typically occur in the background of teratoma (a germ cell neoplasm), giving the rationale that testicular carcinoid tumor can be of germ cell origin, which was further supported by FISH used by Abbosh et al. They found that Isochromosome 12p and 12p overrepresentations were present in both the carcinoid tumor cells as well as in the cells of co-existing mature teratoma. However, not all testicular carcinoid tumors had Isochromosome 12p11.21 or 12p overrepresentation. In the current case, although FISH results did not show typical Isochromosome 12p or reach the threshold for 12p overrepresentation (12p to 12q ratio > 1.5), there were 35 % of the tumor cell nuclei containing additional chromosome 12p (2–3 12p and 1–2 12q). The significance of this pattern of chromosome abnormality needs to be further explored.

Radical orchiectomy is the treatment of choice. Symptomatic treatment, such as octreotide, should be given to patients with carcinoid syndrome. The carcinoid tumors, in general, have an excellent prognosis due to their indolent course. In the literature, approximately 16 % of primary testicular carcinoid tumors have exhibited malignant behavior. However, this number may be overrepresented as there may be a selection bias to publish case reports with malignant behavior as opposed to the benign lesion in which long-term disease-free follow-up would be expected before reporting the case. Nonetheless, close follow-up is essential, as there are isolated cases of testicular carcinoid tumors with a prolonged apparent interval free of disease that precedes an aggressive metastatic course. Moreover, multidisciplinary discussion and primary retroperitoneal lymph nodes dissection (RPLND) in experienced centers should also be considered in light of the poor sensitivity to chemotherapy of these rare subsets of testicular tumors.

4. Conclusion

This case adds to the rare reports in the literature of a primary pure carcinoid tumor of the testis. It provides additional insight into the radiological and pathological correlation of this disease. It is essential to exclude metastasis in testicular carcinoid tumors, and molecular study may provide evidence of the germ cell origin but not for all the cases. Primary testicular carcinoid tumors have a good prognosis, but the metastatic potential exists and may be delayed; hence a long-term follow-up is warranted.

References

1. Wang WP, Guo C, Berney DM, et al. Epstein JI: primary carcinoid tumors of the testis: a clinicopathologic study of 29 cases. Am J Surg Pathol. 2010;34(4):519–524.
2. Hosking DH, Bowman DM, McMorris SL, Ramsey EW. Primary carcinoid of the testis with metastases. J Urol. 1981;125(2):255–256.
3. Abou Zahr R, Chalhoub K, Mansour E, Chouairy C, Ghazal G, Nohra J. Primary carcinoid tumor of the testis: a case report and review of the literature. Case Rep Urol. 2018;2018, 3614387.
4. Neely D, Gray S. Primary carcinoid tumour of the testis. Ulster Med J. 2011;80(2):79–81.
5. Abbosh PH, Zhang S, Maclellan GT, et al. Germl cell origin of testicular carcinoid tumors. Clin Canc Res. 2008;14(5):1393–1396.