A unique case of a sarcoma arising in a testicular non-seminomatous mixed germ cell tumour with a predominant yolk sac component

Luke T. Lavallée, MD;[*] Nicolas LD Roustan Delatour, MD;[†] Ilias Cagiannos, MD, FRCSC;[*] Eric C Bélanger, MD, FRCPC;[†] Kien T. Mai, MD, FRCPC[†]

[*]Division of Urology, Department of Surgery, The Ottawa Hospital, University of Ottawa, Ottawa, ON; [†]Division of Anatomical Pathology, Department of Pathology and Laboratory Medicine, The Ottawa Hospital, University of Ottawa, Ottawa, ON

Cite as: *Can Urol Assoc J* 2011;5(1):E81-E83; DOI:10.5489/cuaj.10069

Abstract

We present a unique case of a sarcoma arising in a testicular non-seminomatous mixed germ cell tumour with a predominant yolk sac tumour (YST) component. This is the first case reported in which a sarcoma is linked to YST of the testis in a patient not having undergone prior chemotherapy. This finding confirms the ability of YST to contain sarcoma; it underlies its importance for urologists, oncologists and pathologists to be aware of this phenomenon and to modify treatment strategies appropriately.

Introduction

Despite its incidence, testicular cancer represents only 0.1% of cancer deaths as current treatment regimens are highly effective. The presence of a sarcomatous component in testicular germ cell tumours, although very rare, has been reported as a predictor of poor outcomes.[1,2] Treatment strategies following orchiectomy vary and are largely dependent on the cell types contained within the primary tumour. The presence of a sarcomatous component may necessitate altering the surgical and chemotherapeutic approach as these cells are often chemoresistant, therefore careful identification of all cellular components is paramount to ensure optimal outcomes.[2,3]

Case presentation

A 28-year-old man presented to hospital with an acutely painful and enlarging right-sided testicular mass. Ultrasonography of the abdomen and scrotum was obtained followed by a computed tomography scan of the abdomen and pelvis revealing a large, complex, heterogeneous, partially enhancing mass, with solid and cystic components, originating from the right testicle. We also identified a 5 × 5-cm fullnesss in the right inguinal canal, several small para-aortic lymph nodes and multiple lesions suspicious for malignancy in the liver. Serum tumour markers revealed a beta-human chorionic gonadotropin (β-hCG) of 1 IU/L, lactate dehydrogenase (LDH) of 240 U/L and alpha fetoprotein (AFP) of 3000 μg/L. The patient underwent radical orchiectomy.

Pathologic examination of the surgical specimen revealed a 20 × 13 × 9-cm primarily solid heterogeneous mass, containing tan-yellow and white areas with focal necrosis, hemorrhage and myxoid change. Of note, hemorrhage within the tumour was thought to have contributed to the mass acutely enlarging and to the patients' new onset of pain on presentation. The mass had a large defect measuring 6.5 × 5.5-cm in size which likely hemorrhaged and corresponded to the fullness noted in the inguinal canal. The mass was grossly penetrating the tunica albuginea and involved the spermatic cord. Histological examination revealed a mixed germ cell tumour containing primarily a yolk sac component (85%), as well as sarcoma (sarcomatous) component (10%), embryonal carcinoma (4%) and mature teratoma (1%) components. The sarcomatous component consisted of atypical spindle cells with hyperchromatic and often bizarre nuclei, as well as frequent mitotic figures (Fig. 1). It was thought to originate from the yolk sac tumour (YST), as there seemed to be areas of transition between them, and the presence of numerous spindle cells was noted throughout the YST component. There was no sarcomatous component closely associated with teratomatous components. Lymphovascular invasion and spermatic cord involvement were identified. Immunohistochemical stains displayed strong positivity for low molecular weight keratin (cam 5.2) and AFP in the yolk sac component. Octamer ¾ (Oct ¾), cluster of differentiation 30 (CD30) and β-hCG were negative in the yolk sac component. Areas of transition between the yolk sac

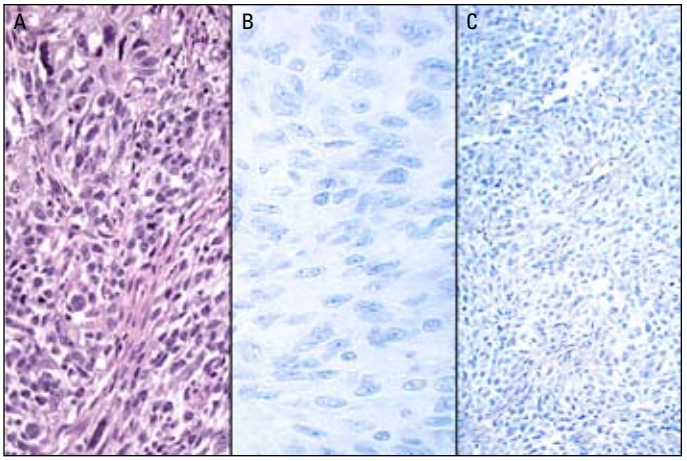

Fig. 1. Sarcomatous transformation. A: Photomicrograph showing atypical spindle cells with marked pleomorphism, and frequent mitotic figures (H&E, ×40); B: Immunohistochemical stain showing negative staining for AFP (×60); C: Immunohistochemical stain showing negative staining for cam 5.2 (×20).

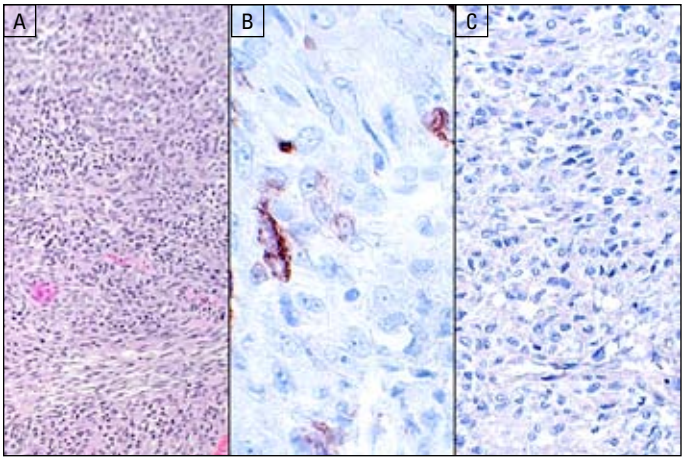

Fig. 2. Transitional areas. A: Photomicrograph showing bland spindle cells arranged in fascicles (H&E, ×20); B: Immunohistochemical stain showing rare single cell positivity for AFP (×60); C: Immunohistochemical stain showing negative staining for cam 5.2 (×20).

elements and the bizarre spindle cells of the sarcomatous component displayed positivity for AFP in rare single cells, and negativity for cam 5.2. In the sarcomatous component, both AFP and cam 5.2 were negative (Fig. 2).

Complete metastatic workup revealed bulky stage IIIC testicular cancer involving the liver and lungs bilaterally. The patient received 4 cycles of bleomycin, etoposide and cisplatin (BEP) chemotherapy. He demonstrated full normalization of his tumour markers; however, there was evidence of metastatic disease in the liver and lungs. A liver biopsy revealed a sarcomatous component which upon review was identical to that seen in the primary tumour. Significant consideration was given to additional, sarcomatous-like systemic chemotherapy, with either azomycin, ifosfamide or gemcitabine; however, the patient's poor clinical status and compromised liver status limited this option. The patient died 6 months later.

Discussion

Germ cell tumours represent a diverse group of neoplasms, including classic seminoma, spermatocytic seminoma, embryonal carcinoma, YST, choriocarcinoma, teratoma and mixed tumours containing variable amounts of the aforementioned tumour types. On rare occasions, these tumours have demonstrated differentiation into non-germ cell (somatic) tumours, such as sarcomas and various types of carcinomas.[2] The type of tumour identified on pathologic examination is important with regards to treatment and prognosis.[1,2]

Previous authors have reported on the ability of germ cell tumours to contain sarcomatous components.[2,4-7] Sarcomatous cells have been found in primary testicular tumours, their metastases and in primary extragonadal germ cell tumours originating intracranially, retroperitoneally and in the mediastinum.[1] About 6% of spermatocytic seminoma tumours undergo sarcomatous transformation; the sarcomatous component is responsible for cases of metastases in these tumours.[1] Sarcoma has also been described as a component of ovarian germ cell tumours.[8]

Most sarcomatous components have been associated with teratomas, and have been hypothesized to result from a malignant transformation of mesenchymal cells.[2] Ulbright and colleagues reported 11 cases of YST demonstrating sarcomatous components in patients with late recurrence all of whom underwent prior chemotherapy.[4] Authors have suggested that this occurrence could be the result of transformation of the blastematous stroma (undifferentiated connective tissue) in YST and of a chemoselection of the spindle cells in YST, allowing subsequent overgrowth and creation of a true sarcomatous component from YST.[2,4,7] Chemoselection refers to a process in which chemotherapy targets one component of a tumour but is not able to neutralize another, effectively selecting the resistant component by allowing only it to survive. Malagon and colleagues reported one case of rhabdomyosarcoma associated with a YST of the mediastinum, but not of the testis.[2]

To our knowledge, we report the first documented case of a sarcoma originating from the YST component of a primary germ cell tumour of the testis in a patient not having received prior chemotherapy. This differs from the sarcomatous pattern of YST due to the lack of myxoid stroma, presence of a storiform pattern and the more striking cytologic atypia, as seen in our case. The histological analysis clearly revealed spindle cells throughout the YST component of the neoplasm, as well as areas of transition from YST to sarcoma. This transition was demonstrated by the conversion of cytokeratin and AFP positivity in YST component to cytokeratin and AFP negativity in the sarcomatous component, further suggesting that the YST was the origin of the sarcomatous

component. It is possible that the rapid growth of the sarcomatous component may account for the clinical symptoms urging the patient to seek the medical attention.

This finding may be significant because the presence of a sarcomatous component in a patient with a germ cell tumour changes the prognosis and treatment strategy.[2,7] Malagon and colleagues reported a statistically significant difference in survival ($p \leq 0.001$) for a cohort of patients having a sarcomatous component in their germ cell tumour when compared to a cohort of age-matched and stage-matched controls.[2] In his cohort, Malagon and colleagues found that 32 of 40 patients (80%) were either deceased or alive with advanced, progressive disease at 5 to 40 months follow-up.[2] Most authors advocate for full surgical excision of the tumour masses when an active sarcomatous component is identified, as this component is not susceptible to chemotherapeutic agents employed in the treatment of germ cell tumours.[2,4,7]

This case demonstrates the importance of thorough analysis of YST to rule out the presence of a sarcomatous component.

Competing interests: None declared.

This paper has been peer-reviewed.

References

1. Bahrami A, Ro JY, Ayala AG. An overview of testicular germ cell tumours. *Arch Pathol Lab Med* 2007;131:1267-80.
2. Malagon HD, Valdez AM, Moran CA, et al. Germ cell tumours with sarcomatous components: a clinicopathologic and immunohistochemical study of 46 cases. *Am J Surg Pathol* 2007;31:1356-62.
3. Michael H, Ulbright TM, Brodhecker CA. The pluripotential nature of the mesenchyme-like component of yolk sac tumour. *Arch Pathol Lab Med* 1989;113:1115-9.
4. Ulbright TM, Michael H, Loehrer PJ et al. Spindle cell tumours resected from male patients with germ cell tumours. A clinicopathologic study of 14 cases. *Cancer* 1990;65:148-56.
5. True LD, Otis CN, Delprado W, et al. Spermatocytic seminoma of testis with sarcomatous transformation. A report of five cases. *Am J Surg Pathol* 1988;12:75-82.
6. Manivel C, Wick MR, Abenoza P, et al. The occurrence of sarcomatous components in primary mediastinal germ cell tumours. *Am J Surg Pathol* 1986;10:711-7.
7. Michael H, Lucia J, Foster RS, et al. The pathology of late recurrence of testicular germ cell tumours. *Am J Surg Pathol* 2000;24:257-73.
8. Kabukcuoglu F, Sungun A, Senturk BA, et al. Mixed germ cell tumour of the ovary with sarcomatous component. *Pathol Oncol Res* 2001;7:60-2.

Correspondence: Dr. Kien T Mai, Professor of Pathology, Division of Anatomical Pathology, Department of Pathology and Laboratory Medicine, The Ottawa Hospital and University of Ottawa, 501 Smyth Road, Ottawa, ON K1H 8L6; ktmai@ottawahospital.on.ca