Oncology

Primitive Neuro Ectodermal Tumor Arising in a Testicular Teratoma with Retroperitoneal Metastasis: A Case Report and Review of Literature

Guodong Hu, Andrew Wang, Xiu Wang, Leilei Xia, Benjamin L. Taylor, S. Buce Malkowicz, Priti Lal, Julia R. Maisel

The Second Department of Urology, Shenyang Red Cross Hospital, Shenyang, LN, China
Eastern Virginia Medical School, Norfolk, VA, USA
Department of Anesthesia, The Fourth Affiliated Hospital of China Medical University, Shenyang, LN, China
University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA
Department of Urology, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA
Department of Pathology, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA

A R T I C L E   I N F O
Article history:
Received 30 September 2016
Accepted 25 November 2016

Keywords:
Testicular tumor
Mixed germ cell tumor
Primary neuroectodermal tumor
Teratoma
Retroperitoneal lymph node dissection
Adjuvant chemotherapy

A B S T R A C T
A 38-year-old man presenting with left testicular mass and extensive retroperitoneal lymphadenopathy underwent radical orchiectomy and specimen showed a germ cell tumor of primarily primitive neuroectodermal tumor mixed with mature teratoma. He then underwent RPLND, followed by adjuvant CAV (cyclophosphamide, doxorubicin, vincristine) and IE (ifosfamide, etoposide) alternating chemotherapy given the high rate of recurrence and high rate of response to the PNET-specific chemotherapy.

Introduction
Teratomas make up about 4% of testicular germ cell tumors and follow a heterogeneous clinical progression. While some teratomas may be inert or only locally aggressive, 3–8% of the testicular teratomas have the potential for malignant transformation along endodermal, ectodermal, or mesodermal lines. There are rare cases of malignant transformation of teratomas to Primitive Neuro Ectodermal Tumor (PNET) reported in the literature. We report a rare case of mixed germ cell tumor with PNET metastasis and the role of adjuvant chemotherapy.

Case presentation
A previously healthy 38-year-old male who was noted to have a left testicular mass during a routine medical evaluation by occupational health presented to the emergency department for further work-up. Physical exam revealed an oval-shaped mass measuring 20 × 18 × 6 cm. Ultrasound of the scrotum (Fig. 1) showed a markedly enlarged left testis with heterogeneous and complex hydrocele concerning for testicular neoplasm. The apparent decrease in blood flow in the left testis was indeterminate since the doppler settings had changed between the evaluation of two testes. Testicular tumor markers were within normal limits: β-human chorionic gonadotrophin (β-HCG), <5 mIU/mL, lactate dehydrogenase (LDH), 211 U/L, alpha-fetoprotein (AFP), 1 IU/mL. Chest computed tomography (CT) revealed no evidence of metastatic disease. CT of the abdomen and pelvis (Fig. 2) demonstrated a low-attenuating, non-enhancing and para-aortic lymph node of 2.2 × 2.6 cm and a conglomerate of two para-aortic lymph nodes measured up to 2.6 × 4.4 cm. Prominent lymph nodes were also noted in the left common iliac chain and more distally in the left external iliac chain, measuring...
0.9 × 1.4 cm and 1 cm in the long axis, respectively. Patient underwent initial left radical orchiectomy under a working diagnosis of left non-seminomatous germ cell testicular tumor. Pathologic evaluation revealed a malignant mixed germ cell tumor primarily composed of a small round blue cell tumor with pseudorosettes, morphologically consistent with Primitive Neuro Ectodermal Tumor (PNET) admixed with teratomatous components (Fig. 3). The tumor involved the epididymis, rete testis, hilar fat, and spermatic cord. No other germ cell tumor components including yolk sac, embryonal or choriocarcinoma were identified in this extensively sampled specimen. Germ cell neoplasia in situ was present. Extensive lymphovascular invasion was noted. Immunohistochemical stains were performed for CD99, FLI-1, WT-1, CD57, synaptophysin, chromogranin, S100, desmin and myogenin. Fluorescent in situ hybridization study for EWS-FLI1 was negative. PNETs arising in the background of malignant mixed germ cell tumors are known to be negative for this translocation.

As there was no metastatic disease evident elsewhere, we decided to proceed with bilateral template retroperitoneal lymph node dissection (RPLND) with pelvic extension and appendectomy.

Figure 1. Ultrasound of the scrotum showing enlarging and heterogeneous echotexture and cystic spaces within the left testicle.

Figure 2. Abdomen CT demonstrating moderate para-aortic lymphadenopathy, with smaller pre-aortic and aortocaval lymph nodes.

Figure 3. A malignant mixed germ cell tumor primarily composed of a small round blue cell tumor with pseudorosettes, morphologically consistent with Primitive Neuro Ectodermal Tumor (PNET) admixed with teratomatous components.

Intraoperatively, due to serious adhesion and the fact that unresectable malignant transformation of teratoma to PNET bears a poor prognosis, left nephrectomy was performed in order to resect retroperitoneal lymphadenopathy as entirely as possible. The surgery was otherwise uncomplicated. Pathology revealed a 14.0 cm periaortic metastatic PNET tumor with intra-aortic caval node involvement. No tumors were found in the resected appendix or left kidney. The patient received adjuvant chemotherapy with a Ewing’s sarcoma type regimen of Cyclophosphamide + Doxorubicin + Vincristine (CAV) followed by Ifosfamide + Etoposide (IE) for a total of 4 cycles. Sperm cryopreservation was offered before chemotherapy. Follow-up is on-going.

Discussion

Mixed germ cell tumors (MGCTs) of the testis represent about one-third of all testicular germ cell tumors (GCTs). Various combinations of neoplastic elements exist, e.g. seminoma and teratoma, embryonal carcinoma and teratoma, seminoma and embryonal carcinoma, choriocarcinoma and teratoma, or a combination of several elements. Metastatic mixed germ cell tumor we reported was made up of Primitive Neuro Ectodermal Tumor (PNET) with mature teratoma. Rarely, primary or metastatic testicular germ cell tumors may involve PNET, a pathologic diagnosis that are classically divided into central PNET as in medulloblastoma or medulloepithelioma and peripheral PNET as in Ewing sarcoma. As making a definitive diagnosis of PNET is difficult given its deviation from elements of GCT and non-specific pathologic findings, our pathologist did not make such a distinction between the subtypes.

Surgical resection is the mainstay of treatment for PNET, although it has a high rate of recurrence in patients who undergo RPLND. In contrast to metastatic germ cell tumors, PNET is rarely chemoresponsive to cisplatin-based therapy. However, chemotherapy regimens traditionally used for Ewing’s sarcoma, cyclophosphamide + doxorubicin + vincristine (CAV) alternating with ifosfamide + etoposide (IE), as adjuvant therapy has shown high response rate in patients who undergo RPLND for resection of PNET. Disease response will be monitored in subsequent follow-ups.

Conclusion

Primitive Neuro Ectodermal Tumor is a rare and malignant transformation of testicular teratoma. PNET-specific adjuvant chemotherapy should be used after RPLND due to high chemosensitivity to this regimen to potentially increase disease free survival.
Conflicts of interest

The authors have no conflicts of interest.

References

1. Ulbright TM. Germ cell tumors of the gonads: a selective review emphasizing problems in differential diagnosis, newly appreciated, and controversial issues. *Mod Pathol.* 2005;18:S61–S79.

2. Fletcher CDM, Bridge AJ, Hogendoorn P, Mertens F, eds. *WHO Classification of Tumours of Soft Tissue and Bone* Vol 4. International Agency for Research on Cancer; 2013.

3. Dunne RF, Sahasrabudhe DM, Messing EM, et al. A case series of transformation of teratoma to primitive neuroectodermal tumor: evolving management of a rare malignancy. *Rare tumors.* 2014, Jan 23;6(1):5268.

4. Ganjoo KN, Foster RS, Michael H, et al. Germ cell tumor associated primitive neuroectodermal tumors. *J Urol.* 2001;165:1514–1516.

5. Al-Hader AA, Jain A, Al-Nasrallah N, Einhom LH. Metastatic malignant transformation of teratoma to primitive neuroectodermal tumor (PNET): results with PNET-based chemotherapy. *Am J Clin Oncol.* 2015;38(4):364–366.