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Case report

Transformation of Testicular Teratoma to Aggressive Primitive Neuroectodermal Tumor (PNET): A Case Report

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Abstract

Introduction: Most testicular cancers have over 95% survivability. Non-seminomatous Germ Cell Tumor (NSGCTs) make up 5% of testicular cancers. Clinical stage I of NSGTs can often be cured with orchiectomy; the challenge is identifying high recurrence risks.

Case Presentation: We present a case of a 36 year-old male found to have a Nonseminomatous Germ Cell Tumor (NSGCT) initially treated with orchiectomy. Two years post orchiectomy, lytic bone lesions were discovered on surveillance CT. Subsequent bone marrow biopsy (BMB) showed neural differentiation, consistent with metastatic Primitive Neuroectodermal Tumor (PNET) arising from prior testicular germ cell tumor. Treatment included vincristine, doxorubicin, cyclophosphamide, and ifosfamide/ etoposide mesna. Additionally he received tandem autologous stem cell transplant with carboplatin/etoposide conditioning and adjuvant etoposide. PET/CT scan showed treatment response.

Conclusion: There is no established guideline on the treatment for malignant transformation of testicular teratoma into PNET. The regimen for our patient yielded promising results. Our aim is to highlight a regiment that can be utilized for this rare aggressive neoplasm.

Introduction

Testicular neoplasms are one of the most common solid malignancies in males between ages 15-35; however, it only represents 1% of all solid tumors in males (1). Up to 95% of testicular tumors are of germ cell origin. Germ cell tumors are derived from germ cell neoplasia in situ which are further subtyped into pure seminomas and nonseminomatous germ cell tumors. The clinical behavior of Germ cell tumors varies from benign to aggressive where careful histological classification is required to determine the most appropriate treatment and staging. Afterall, testicular cancers are one of the most curable neoplasms.

Teratomas are germ cell tumors with at least 2 germ layers (ectoderm, mesoderm, or endoderm). In contrast to ovarian counterparts, teratomas in the post pubertal testis are always considered malignant (3). Transformation of teratoma to malignant Primitive neuroectodermal tumors (PNET) is documented only in a small number of patients; approximately 3-6% of metastatic germ cell tumor (GCT) cases (4-5). Among these transformations, the shift from teratoma to primitive neuroectodermal tumor (PNET), occurring specifically within ectodermal cell lines, is an even more infrequent occurrence that is more commonly seen in children and young adults.

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Case reports describing the treatment of PNET in adults are few. The 5-year survival rate of adults with local PNET is low at 35% and for cases with metastatic disease the 5-year survival rate is close to 0% (6). Adults, age 26 and up, with metastatic disease are at highest risk of death. Treatment and therapies that have been outlined so far consist of chemotherapy in combination with surgery. Here we report the case of a patient with Non-Seminomatous Germ Cell tumor (NSGCT) that transformed into PNET, highlighting the treatment regimen and response. The CARE checklist has been completed by the authors and can be found in online supplementary material.

Case Presentation

A 36 year-old male was referred to our clinic for left testicular swelling. Initial laboratory testing resulted normal lactate dehydrogenase (LDH) levels, elevated Alpha fetoprotein (AFP) of 737.9 ng/mL (< 8.8 ng/mL), and elevated beta HCG (B-hCG) of 692 IU/L (0 - 3 IU/L). Abdominal and pelvic computed tomography (CT) did not show any evidence of metastatic disease. Patient underwent a left radical orchiectomy. Our patient's radical orchiectomy revealed a malignant mixed germ cell tumor with three different subtypes: Embryonal Carcinoma 20%, Yolk Sac Tumor 20%, and Teratoma 60% teratoma. No tumor involvement was identified at the margins or lymphovascular structures. Although post-operative labs showed normalized beta HCG and LDH levels, the AFP level were persistently elevated at 74 ng/mL for three months. Chemotherapy regimen consist of Bleomycin, Etoposide and Platinum (BEP) was recommended as the patient was at high risk of recurrence given the presence of teratoma and embryonal components in addition to delayed lowering of tumor markers (AFP). Patient was monitored closely.

As part of surveillance scans (CT A/P), lytic bone lesions were found 1.5 years post orchiectomy. The ordered nuclear medicine bone scan showed abnormal uptake in the periacetabular region and calvarium concerning for osseous metastasis. Shortly after, patient was admitted to the hospital with new onset anemia, thrombocytopenia, transaminitis, and lytic bony lesions. Patient also endorses mild hip pain and fatigue but denies any fevers/chills, unintentional weight loss, chest pain, or shortness of breath. Vital signs were stable, and the physical exam was unremarkable. Laboratory findings reveal an elevated LDH of 1524 U/L but stable AFP and beta HCG levels. CT head was unremarkable. CT of the chest showed scattered tiny lung nodules. Scrotal ultrasound (US) demonstrated an unremarkable right testicle. Bone marrow biopsy is significant for the presence of Primitive Neuroectodermal Tumor (PNET), likely due to prior testicular cancer. Tumor cells were positive for synaptophysin, chromogranin, and CD56 (Figure 1) while negative for keratin, CD99, desmin, and myogenin. Overall, the bone marrow findings are consistent with involvement by a small round blue cell tumor with neural differentiation.

Treatment was initiated with 1 cycle of vincristine, doxorubicin (Adriamycin), and cyclophosphamide/ ifosfamide and etoposide (VDC/IE) chemotherapy. Bone

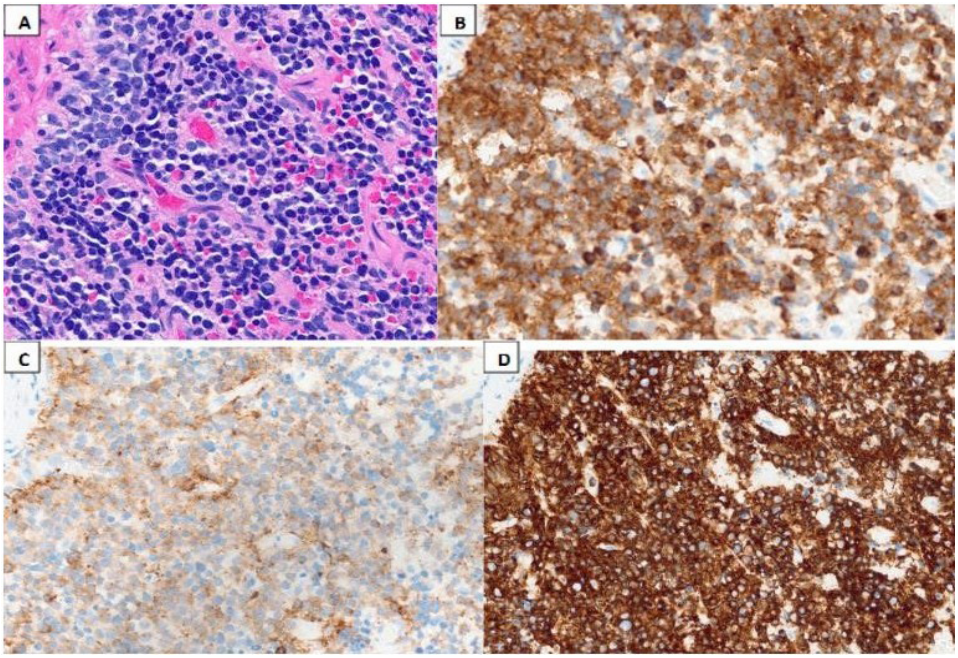

Figure 1: The histological section shows near complete effacement of the normal hematopoietic elements of the marrow by sheets or cords of small round blue cells (A) with high nuclear to cytoplasmic ratio and scant eosinophilic cytoplasm. These neoplastic cells have round nuclear contours, finely dispersed chromatin, and one or more inconspicuous nucleoli. These small round blue cells show expression of (B) synaptophysin, (C) chromogranin, and (D) CD56.

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marrow biopsy 2 months after the start of chemotherapy marrow elements with rare scattered CD56, chromogranin, synaptophysin positive cells raising a suspicion for minimal residual tumor cells. An autologous transplant option was considered as it could afford him a better quality of life compared to 14 cycles of VAC/IE. He completed four cycles of chemo then underwent tandem autologous transplants. Patient has recovered well from treatments thus far. His most recent PET/CT scan after two autologous stem cell transplants showed a decrease in FDG avidity.

Discussion

Most of the testicular cancers are of the germ cell tumor (GCT) types, which represent one of the most curable types of solid neoplasms and have a survivability of over 95%. On the other hand, NSGCTs comprise only 5% of testicular cancers, and treatment modalities include a radical inguinal orchiectomy for diagnosis followed by chemotherapy, especially in those that have elevated serum tumor markers following orchiectomy. Majority of patients that are in clinical stage I of NSGTs are cured with the orchiectomy alone, however, it is challenging to identify which of the patients have a high risk for recurrence and will benefit from receiving neoadjuvant therapy. (7)

Our patient, who had a NSGCT, specifically a mixed germ cell tumor, with 60% characteristics of a teratoma, was an interesting case and rare event as it transformed 1.5 years post orchiectomy into a PNET – his tumor lab markers started trending up and surveillance scan later revealed bone metastasis. PNET is known to be an extremely aggressive tumor with a poor prognosis, given its limited responsiveness to standard chemotherapy using platinum-based drugs. (8) Our patient underwent VDC/IE chemotherapy. Further, given significant bone involvement, the patient was considered for an autologous stem cell transplant to replace damaged bone marrow after the cycles of high-dose chemotherapy.

This case represents a rare transformation from a Teratoma to a PNET of the bone after 1.5 years of orchiectomy of the NSGCT. Currently there is no established guideline on the ideal treatment for malignant transformation of testicular teratoma into PNET. The treatment regimen for our patient yielded promising results as shown in the repeat bone marrow biopsy 2 months after the first cycle of chemotherapy. This case aims to shed light on a treatment regimen that can be utilized in other patients with this rare condition.

Statement of Ethics: Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of this case report and any accompanying images

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Data Availability Statement: All data analyzed in this study are included in the article. Further inquiries can be directed to the corresponding author.

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