Case Report

Primitive neuroectodermal tumor transformation of testicular teratoma

Anastasios Karatzas, Vasileios Papadopoulos[1], Vagianna Katsiouli[1], Louis Pisters[2], Christos Papandreou[1], Vassilios Tzortzis

Departments of Urology and [1]Medical Oncology, Faculty of Medicine, School of Health Sciences, University of Thessaly, Larissa, Greece, [2]Department of Urology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Abstract

Malignant transformation of teratoma develops in a small subset of testis cancer patients. Primitive neuroectodermal tumor represents a highly malignant component of testicular germ cell tumors. It is a rare clinical entity which is characterized by a high risk of disease progression and death. Surgical resection plus chemotherapy appears to be the therapy of choice.

Keywords: Germ cell tumor, malignant transformation of teratoma, primitive neuroectodermal tumor, retroperitoneal lymph node dissection

Address for correspondence: Dr. Anastasios Karatzas, Department of Urology, Faculty of Medicine, School of Health Sciences, University of Thessaly, Biopolis, Larissa 41110, Greece.
E-mail: karatzas@med.uth.gr
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INTRODUCTION

Germ cell tumors (GCTs) can be differentiated into somatic elements. Teratomas may undergo transformation (malignant transformation of teratoma [MTT]) into malignant non-GCTSs. Primitive neuroectodermal tumor (PNET) results from the malignant transformation along the ectodermal lines and is rare.[1] Unlike conventional GCTs, PNET-MTT is highly aggressive, with poor prognosis. Surgical resection is the mainstay of therapy for the localized disease, because PNET-MTTs are considered to be resistant to radiation and systemic chemotherapy.[2] Effective therapeutic strategies targeted to MTT are needed. A case of PNET-MTT treated according to a combined modality is presented.

CASE REPORT

A 26-year-old male underwent radical inguinal orchiectomy for left testicular cancer. Pathology revealed immature teratoma (40%), PNET cells (60%) plus seminomatous morphology with syncytiotrophoblast giant cells, and infiltration of the spermatic cord.

Abdominal computed tomography (CT) imaging revealed multiple scattered hypodense lesions in the liver (diameter<1cm), multiple enlarged lymph nodes on the right para-aortic field (maximum lymph node diameter = 3.5cm), enlarged lymph node block on the left para-aortic field (6.6 cm × 5.9 cm × 12.9 cm), and external bilateral iliac lymph nodes and inguinal nodes (<1.5 and <1.2 cm of diameter, accordingly) [Figure 1]. Laboratory findings revealed normal tumor markers (carcinoembryonic antigen [CEA] = 2.4 ng/ml [<3.4]), alpha-fetoprotein (aFP) = 1.6 ng/ml (<10), beta-human chorionic gonadotropin (bHCG) = 0.1 (0–2 mIU/ml), and increased neuron-specific enolase (NSE) (1280 ng/ml, normal <16.3)

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and LDH (1897 U/L, normal 135–225 U/L). Tumor, node, metastasis staging was $PT_3N_3M_{1b}S_3$ (Stage IIIC). The patient received four courses of etoposide, 100 mg/m^2/day, and cisplatin, 20 mg/m^2/day (five consecutive days/every 21 days) and continued with ifosfamide, 1500 mg/m^2/day; paclitaxel, 200 mg/m^2/day; and cisplatin, 25 mg/m^2/day. Due to imaging and tumor marker findings, abdomen CT showed nodular metastasis involving the left para-aortic lymph nodes (1 cm) and the right para-aortic lymph nodes (1.5 cm) and tumor markers were as follows: CEA = 1.13 ng/ml, aFP = 1.98 ng/ml, bHCG = 2.70 mIU/ml, and NSE = 10.2 ng/ml, and the patient was considered eligible for retroperitoneal lymph node dissection (RPLND). Histopathology revealed PNET infiltration in 10/36 dissected lymph nodes.

Three months later, follow-up abdomen CT revealed liver metastases, enlarged retroperitoneal lymph nodes that were blocking both ureters, and enlarged left iliac lymph nodes [Figure 2]. Due to patients' complaints of headache and bone pain, somatostatin receptor scintigraphy (positron emission tomography [PET]) was scheduled. PET-CT confirmed the bone metastases at the facial skeleton, at the temporal and occipital bones, at the superior scapular angle, at the thoracic vertebral bodies, and at the para-aortic and iliac lymph nodes (Krenning score 3). Tumor markers were also impaired (NSE = 1490 ng/ml and LDH = 3873 UI/L) The patient received salvage chemotherapy with gemcitabine, 1000 mg/m^2, and oxaliplatin, 130 mg/m^2, every 21 days. After receiving one cycle, therapy was halted due to headache, strabismus, and vomiting. Brain MRI showed a metastatic lesion (3.6-cm diameter) at the subdural space, causing elevated intracranial pressure [Figure 2]. Radiotherapy was scheduled, but the patient deceased.

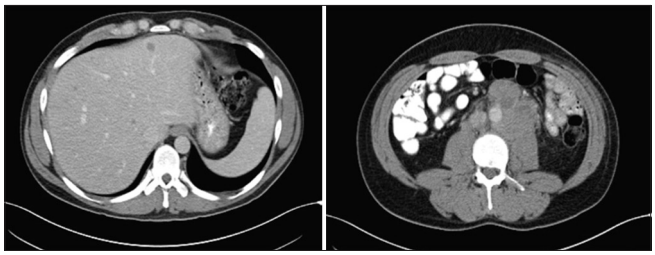

Figure 1: Multiple liver metastatic lesions (left). Enlarged para-aortic lymph node block (right)

DISCUSSION

Teratomas may undergo malignant transformation and represent a relatively rare entity (3%–6% of metastatic testicular GCTs). The most frequent malignant components are sarcomas, squamous cell or adenocarcinomas, carcinoid, PNET, nephroblastoma, and osteosarcoma.[3]

PNET arising from GCT is infrequent. It develops from the MTT along ectodermal lines and varies greatly in size from a few centimeters up to 30 cm.[2] The appearance of these tumors varies, making the histopathological identification, as a component of malignant testicular teratoma or mixed GCTs, difficult.[1] In our case, pathology revealed aggregation of immature neuroepithelium that formed anastomosing neural tubules. Mitotic figures were easily found in the tubules, including along the luminal border.

Unlike conventional GCTs which respond well to platinum-based chemotherapy,[4,5] MTT is a highly aggressive tumor. Surgical resection plus chemotherapy appears to be the therapy of choice.[6] Patients who had complete resection of MTTs had significantly better overall survival.[7] PNET-specific chemotherapy combined with surgical resection has been effective in metastatic PNET, resulting in long-term disease-free survival. PNET-specific chemotherapy has also been used as adjuvant therapy for patients who underwent RPLND for resection of PNET, since it is resistant to cisplatin-based therapy.[8]

PNET has a high probability of relapse after RPLND, mainly due to the remaining microscopic PNET. Constant surveillance after surgery is compulsory, since chemotherapy is ineffective and repeat resection may be additive to therapy. The poor prognosis seen in these patients is largely due to the chemoresistance of MTT, emphasizing the need for alternative therapeutic strategies.[9]

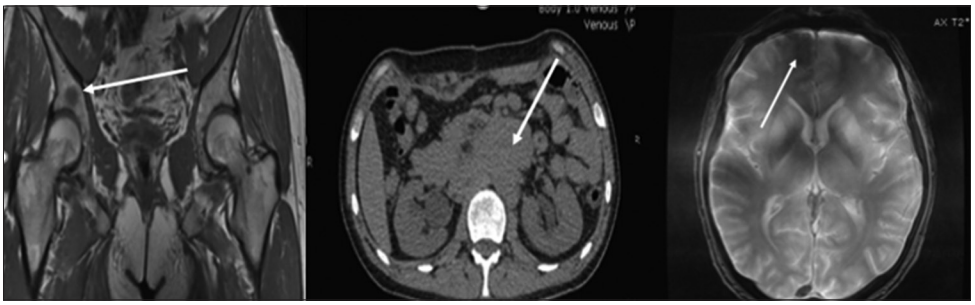

Figure 2: Bone metastasis (left arrow). Para-aortic lymph node relapse (middle arrow). Metastasis at the subdural space (right arrow)

CONCLUSION

Contrary to conventional GCTs, which have an excellent response to platinum-based chemotherapy with overall cure rates of over 90%, PNET-MTT is highly aggressive, with poor prognosis. This case illustrates the need for a multimodality therapy access for PNET-MTT, since this tumor has high mortality rates. PNET-MTT is resistant to radiation and systemic chemotherapy. Thus, we underline RPLND as the cornerstone of every therapeutic strategy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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