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Benign Neck Metastasis of a Testicular Germ Cell Tumor

Haim Gavriel, Stephen Kleid

Department of Surgical Oncology, Peter MacCallum Cancer Institute, Melbourne, Australia

Germ cell tumors (GCTs) are relatively rare neoplasms considered to be curable malignancies since the introduction of cisplatin. The presence of neck metastasis has been reported, with fewer reports of metastatic mature teratoma. In this study, 3 cases of "benign neck" metastasis in patients with GCT between 1998 and 2010 were reviewed retrospectively. In all 3 cases the presenting clinical sign was a left lower neck mass, leading to the diagnosis of the primary site in the testis. All had surgical salvage following chemotherapy, with benign lesions or mature teratoma in histopathology of the neck mass. Chemotherapy was followed by salvage lower-half neck dissection showing benign features in the neck specimen, even though malignancy was proven histologically in other areas. Only 1 patient had a postoperative chyle leak, which resolved spontaneously after several days. Neck dissection is recommended in those patients because malignancy cannot be excluded.

Key words: Germ cell tumor – Metastasis – Neck – Teratoma

Teratoma comes from the Greek words *terato*, meaning "a monster," and *onkoma*, meaning "swelling or mass." Both teratomas and germ cell tumors (GCTs) arise from postmeiotic germ cells and may occur in both gonadal and extragonadal locations. GCTs are relatively rare neoplasms that account for 0.8% of all cancers in males, and they comprise 95% of testicular neoplasms.[1] GCTs are the most common malignancy among men ages 15 to 44 years, with a peak incidence between the age of 25 and 35 years.[2,3] GCTs have been considered to be curable malignancies, even in the advanced stage, since the introduction of cisplatin,[4] and a dramatic improvement has been shown by using a treatment protocol of neoadjuvant cisplatin-based chemotherapy followed by surgical resection of residual tumor mass, with a complete response rate of 70% to 80%.[5]

Testicular teratomas may present in both prepubertal and adult males. The prognosis differs greatly between these two groups. In children, teratomas most often occur before the age of 4 years, and they have a benign behavior in this age group. In adults,

Corresponding author: Haim Gavriel, Department of Surgical Oncology, Peter MacCallum Cancer Institute, Melbourne, 3002 Australia.
Tel.: +972 8 6716259; E-mail: haim.ga@012.net.il

teratomas are usually part of mixed GCTs and have the potential to metastasize. The presence of neck metastasis in patients with testicular GCT is a rare but known phenomenon and has been reported to be present in up to 5% of cases.[6,7] Metastatic disease from the testis first involves the retroperitoneal lymph nodes, and then the tumor spreads via the thoracic duct to its emptying site near the junction of the left internal jugular and subclavian veins. Hence, the left supraclavicular region is one of the possible places where testicular teratomas can metastasize.[8,9] Because testicular carcinoma is the most common malignancy in men ages 20 to 30 years, a left supraclavicular mass in this age group should raise suspicion for a concomitant testicular mass.

Our literature search has shown few reports of mature teratomas in patients who had been treated for GCT with neoadjuvant chemotherapy and surgical resection.[10–13] We present here our experience with 3 patients who were treated with neoadjuvant chemotherapy and surgical resection of highly malignant lesion, followed by surgical resection of a metastasis in the left lower neck, with benign histology.

Patients and Methods

Three cases of neck metastasis from testicular GCT were reviewed retrospectively from 2001 to 2010 in our institute, operated by the senior author (S.K.). The 3 patients were male, ages 26, 32, and 33 years. All patients had computed tomography (CT) and/or magnetic resonance imaging, and some had a positron emission tomography (PET)/CT scan. Serologic tumor markers, including human chorionic gonadotropin (HCG) and/or α-fetoprotein (AFP), were available for monitoring and detecting GCT in all patients.

Surgical salvage was reserved for patients who presented with imaging suggestive of residual tumor, and/or for those having high levels of serologic tumor markers.

All patients underwent a selective neck dissection that included levels 3, 4, and 5b of the involved side, which was the left side in all 3 patients in our group. A low horizontal incision was used on the left neck, followed by subplatysmal flap elevation. The spinal accessory nerve was identified in the posterior triangle of the neck, and the lower sternocleidomastoid muscle was divided horizontally and either excised, or repaired after tumor excision. Care was taken to preserve the phrenic nerve, brachial plexus, and subclavian vein. Leakage from the thoracic duct or branches was ligated.

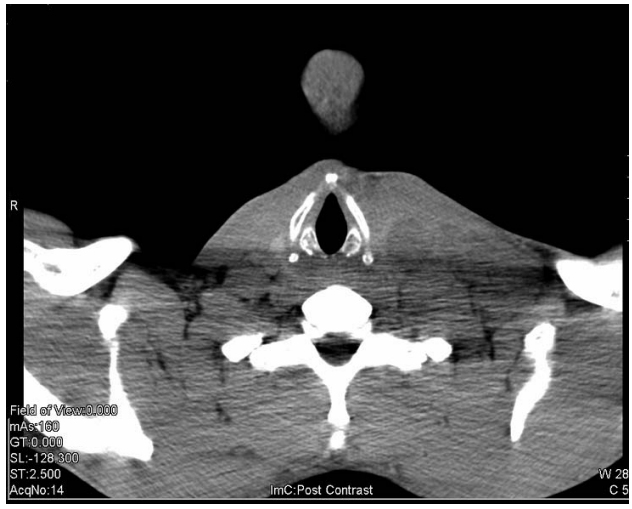

Fig. 1 Neck CT scan demonstrating Lt neck mass.

Results

Patient 1: RA

A 33-year-old man presented with left neck nodes, and after open biopsy he was found to have a nonseminoma of the left testis, with abdominal, mediastinal, and cervical nodes. He received 2 cycles of Taxol and ifosfamide, followed by 3 doses of high-dose carboplatin and etoposide, and a fourth cycle of ifosfamide, because of a temporary response of his left neck nodes. He had a good response to treatment, with CT scan showing improvement of all of his lymphadenopathy and a PET scan showing just minor [18F]-fluorodeoxyglucose uptake in the left neck nodes. Serum tumor marker levels also returned to normal.

Follow-up imaging a month after completion of chemotherapy showed about a 4-cm mass just below the left renal hilum consistent with residual disease, and some residual disease also in the mediastinum and the neck (Fig 1).

He therefore had a retroperitoneal lymph node dissection revealing residual metastatic teratoma up to 25 mm in size, involving 3 of 5 lymph nodes in the left para-aortic lymph nodes. Subsequent to that he underwent a left lower neck dissection, with the pathologic report in keeping with multiple nodular deposits of hyaline fibrosis and xanthomatous change, but no viable tumor. Postoperative chyle leak was diagnosed on postoperative day 1, which was of low volume and resolved after 3 days of

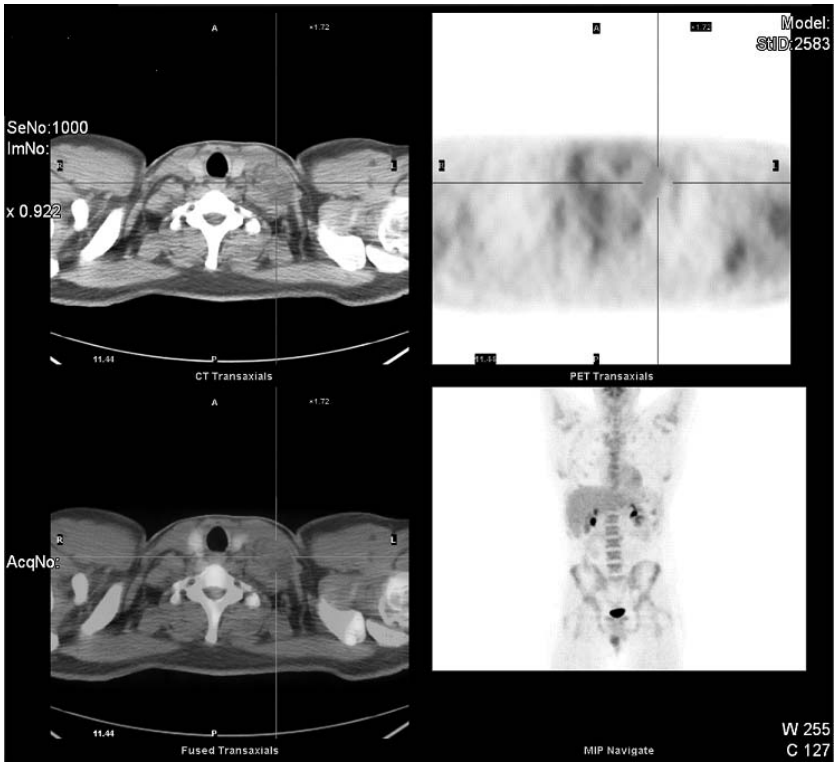

Fig. 2 PET/CT scan demonstrating cold left neck mass.

conservative treatment (suction drainage and medium-chain fatty acid diet). Further mediastinal surgical clearance revealed metastatic nonseminomatous GCT, with components of teratoma (90%) and embryonal carcinoma (10%) 58 mm in diameter, with close margins.

Patient 2: RM

A 32-year-old man presented with a left lower neck lump. Physical investigation revealed left supraclavicular lymphadenopathy, and an incisional biopsy revealed a nonseminomatous GCT. Further investigation revealed a left testicular mass, a large retroperitoneal mass, and multiple pulmonary metastases. His tumor markers at the time were elevated, with a HCG at diagnosis of 66,500 U/L and an AFP of 99 μg/L. His LDH was also elevated at 743 IU/L. He had a left orchidectomy and then chemotherapy with four cycles of bleomycin, etoposide and cisplatin (BEP).

The patient's tumor markers fell and were within the normal range following his third cycle of chemotherapy, and a CT scan revealed an improvement in his supraclavicular lymphadenopathy and complete resolution of his intrathoracic disease (Fig. 2). However, his retroperitoneal mass remained extensive. Follow-up HCG levels rose to 38, and he underwent a bilateral retroperitoneal lymph node dissection. The pathology showed mature teratoma alone, and all the margins were clear. Lower neck dissection was then performed, with the histology showing 4 nodules of mature teratoma with hyalinizing features, which suggest treatment effect but no malignancy.

His follow-up tumor markers show a normal beta-HCG level, but his AFP level was marginally elevated at 11.

Patient 3: TN

A 26-year-old man presented with a left neck mass, which was biopsied, showing a GCT. His markers were abnormal, with a markedly elevated AFP of 3420. Further examination revealed left testicular tumor, and the patient underwent left orchidectomy, with pathology in keeping with mixed nonseminomatous GCT, mostly mature teratoma but with some seminoma and embryonal carcinoma and much background atrophy. A CT scan of the chest, abdomen, and pelvis showed no chest abnormality but did confirm his left neck mass, a retrocrural

right nodal mass, and a large mass of tumor extending from the level of the left renal vein to the bifurcation of the aorta. Subsequently, he had 4 cycles of BEP and became marker negative and free of any symptoms. However, CT scan demonstrated persistent disease in his left retroperitoneum, right retrocrural area, and left neck. He therefore underwent retroperitoneal lymph node dissection, which showed mature elements of teratoma, and then left lower neck dissection, which showed necrotic tissue. His serum tumor markers were normal on follow-up.

A year later, the patient developed a 1-cm lump in the left lower neck. Excision biopsy showed an intranodal cyst with high suspicion to represent recurrent mature teratoma. Normal serum tumor markers were found, and a CT scan from neck to pelvis showed no other evidence of disease. Follow-up CT scan and blood tests showed no abnormality

Discussion

Teratoma is a chemoresistant, nonseminomatous GCT composed of somatic cell type from more than two germ layers. It is derived from a totipotential, malignant precursor cell, which might be either an embryonal carcinoma or a yolk sac tumor. Mature teratoma is a possible histologic finding in metastases of nonseminomatous testicular GCT after chemotherapy. Although teratoma is a benign tumor, in the setting of being a nonseminomatous testicular GCT metastasis, its biologic potential is unpredictable.[5]

Histopathologic evidence of scars and calcifications in the adjacent parenchyma was suggested to be a potential clue to the proposed process of a burned-out tumor due to the chemotherapy, as was also suggested by the presence of microfocal embryonal carcinoma in other cases.[14]

Sonneveld *et al*[15] reported their experience with 51 patients with mature teratoma in resected retroperitoneal residual tumor masses after chemotherapy, showing a 17.6% relapse rate, with more than half of the relapsed tumors growing from mature teratoma. The possibility of viable malignant cells remaining within a mature metastatic teratoma has led many to suggest further resection of these lesions immediately after chemotherapy, in order to determine the presence of residual viable tumor cells and to remove mature teratoma to prevent malignant transformation.[10]

Weisberger *et al*[13] reported their experience with limited neck dissection following chemotherapy in 45 patients with GCT back in 1999. In most of the cases benign metastasis—either mature teratoma or necrotic changes—was identified, and only in 7 cases were viable malignant cells found in the neck specimen. The latter also explains the logic of doing a neck dissection for the treatment of malignant disseminated disease that has metastasized from below the diaphragm. Testicular carcinoma represents an entity where dissection of postchemotherapy residual neck disease is indicated, and it results in a very favorable prognosis. If residual viable tumor cells are found in a resected lesion, additional chemotherapy should be considered.[16]

Conclusions

Benign metastasis of testicular GCT to the neck is rare. All patients in our series had salvage surgical therapy, including a neck dissection following chemotherapy, with benign features found in the neck specimen, even though malignancy was proven histologically in other areas. One patient had a postoperative chyle leak, which resolved spontaneously after several days, whereas the others had an uneventful recovery from the neck dissection. We join the recommendation to proceed to neck dissection in those patients with a persistent neck lump after chemotherapy, because malignancy cannot be excluded, nor can subsequent malignant transformation.

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