Case Report

Cystic trophoblastic tumor – The effect of chemotherapy in metastatic testicular germ cell tumor to retroperitoneal lymph nodes

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Abstract

Cystic trophoblastic tumor is an uncommon lesion which is occasionally seen after chemotherapy in metastatic retroperitoneal lymph nodes in patients with testicular germ cell tumor. The tumor cell clusters show cystic change lined by single to multiple layers of cells with abundant dense eosinophilic vacuolated cytoplasm, large pleomorphic vesicular nuclei with smudged chromatin, and prominent nucleoli. It is important to identify this lesion as its prognosis is similar to a teratoma and does not require any additional chemotherapy.

Keywords: Chemotherapy, cystic trophoblastic tumor, germ cell tumor, retroperitoneum, testicular

INTRODUCTION

Testicular germ cell tumors (GCTs) are uncommon and are seen predominantly in the age group of 25–45 years.¹ These tend to metastasize more commonly to retroperitoneal lymph nodes (RPLNs). Retroperitoneal lymph node dissection (RPLND) is performed as a part of the treatment of residual disease for patients with metastases. Cystic trophoblastic tumor (CTT) is an uncommon lesion which is occasionally seen after chemotherapy in metastatic RPLND in patients with testicular GCT.²

CASE REPORT

A 17-year-old male was referred to our unit after undergoing low orchidectomy for a malignant yolk sac tumor of the right testis followed by six cycles of chemotherapy. A year ago, he had developed a testicular swelling. Contrast-enhanced computed tomography (CECT) showed a testicular mass measuring 12 cm × 10 cm along with retroperitoneal lymphadenopathy. On further investigations, serum alpha-fetoprotein (AFP) level was 1660 ng/mL and beta-human chorionic gonadotropin (hCG) was 15000 mIU/mL. Right low orchidectomy was performed which showed a malignant yolk sac tumor. This was performed by a general surgeon at an overseas facility. On follow-up, he presented with vomiting and abdominal distension. CT scan showed a 15 cm × 12 cm × 8 cm heterogeneous hypodense mass in the retroperitoneum causing considerable mass effect for which he underwent a gastrojejunostomy. It was followed by four cycles of bleomycin, etoposide, and cisplatin and two cycles of etoposide and cisplatin. CT scan abdomen showed a residual conglomerate nodal mass in the retroperitoneum

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measuring 8.8 cm × 7.7 cm × 5 cm, which was unresectable. Two cycles of salvage chemotherapy with TIP (paclitaxel, ifosfamide, and carboplatin) were administered, and he was referred to us for further management. After chemotherapy, serum AFP dropped to 1.7 ng/ml and beta-hCG dropped to 1.2 mIU/ml. He was counseled and consented for a RPLND. Intraoperatively, there were multiple large retroperitoneal lymph nodal masses which were cleared to constitute a R1 resection. Microscopic examination showed multiple small foci of metastatic viable tumor which constituted 8%–10% seen as scattered nests and islands in close proximity to teratomatous component. Some of these tumor cell clusters had cystic change lined by single to multiple layers of cells with abundant dense eosinophilic vacuolated cytoplasm, large pleomorphic vesicular nuclei with smudged chromatin, and prominent nucleoli [Figure 1]. The central portions of the cystic structures were either empty or contained eosinophilic and fibrinoid material. These morphological features were suggestive of CTT. Areas of mature teratoma represented 50%–60% with differentiated somatic-type epithelium. The stroma showed smooth muscle bundle fibers, adipose tissue, and areas of calcification. There was a moderate degree of fibrosis, foamy histiocytic aggregates, inflammatory cells, hemorrhage, hemosiderophages, and focal necrosis which constituted 20–30%. With a provisional diagnosis of CTT, immunohistochemistry was performed. The CTT cells on immunostaining showed positivity for Pan cytokeratin, Cytokeratin 7, Cytokeratin (HMW), CD10, and GATA3, focal and weak positivity for beta-Human chorionic gonadotropin, and negativity for Alpha fetoprotein, inhibit, Carcinoembryonic antigen, S100, CD30, p63, PLAP, SALL4, and C-KIT [Figure 2]. Ki-67 proliferation index was 2%–3%. Immunohistochemical stains confirmed the diagnosis of CTT excluding the other differential diagnosis summarized in Table 1. Postoperative CECT abdomen report showed a residual retroperitoneal nodal mass for which he received two cycles of chemotherapy with paclitaxel, carboplatin, ifosfamide, and mesna. The patient is disease free 8 months postsurgery.

DISCUSSION

After the introduction of cisplatin-based multidrug chemotherapy followed by surgery, there has been a marked increase in the cure rates in patients with testicular GCT who had metastases. The findings in RPLND masses are categorized as follows:

1. Absent viable tumor
2. Residual teratoma
3. Residual malignant GCT
4. Secondary malignancy
5. CTT.

Microscopic examination of these lymph nodes removed by RPLND after chemotherapy showed no viable tumor in 67% of patients in a study by Donohue et al. Viable tumor after chemotherapy should be categorized. The most favorable persistent tumor is teratoma. Residual GCT after chemotherapy has a guarded prognosis. RPLND specimen showing only necrosis and fibrosis has a very good prognosis. In a study by Svatek et al., 24 patients relapsed after a 37-month follow-up; 10 patients had teratoma, 12 had other GCTs, and 2 had non-GCT. Persistent

![Figure 1](image1.png)

**Figure 1:** (a) Nests and islands of cystic trophoblastic tumor on a background of hyalinization and inflammation (H and E, ×40). (b) Cyst lined by stratified cells with abundant cytoplasm and smudged nuclei (H and E, ×100). (c and d) Lining epithelial cells with a squamoid appearance and lumen of the cystic space filled with fibrinoid material (H and E, ×400)

![Figure 2](image2.png)

**Figure 2:** (a) Immunohistochemistry of cystic trophoblastic tumor staining positive with CD10 (×100). (b) Positive with GATA3 (×100). (c) Weak and focal positive with beta-human chorionic gonadotropin (×400). (d) Ki-67 2%–3% (×100)
nonteratomatous GCT is an indication for chemotherapy, sometimes with intensive regimens including bone marrow transplantation. CTT is an uncommon benign tumor in RPLND which consists of varying sized cysts lined by mononucleated trophoblastic cells. Occasionally, the cyst may have papillary infoldings. These cysts are usually <3 mm in size. Multilayering up to 4 and solid foci of pleomorphic trophoblastic cells may be seen. Ulbright et al.[5] have extensively studied testicular CTTs. Patients’ age ranged from 15 to 43 years at the time of surgery. CTT was a minor component in all the cases which range from <1% to 10%. They have noted that serum beta-hCG levels were either normal or mildly elevated in these patients. In a study by Gondim et al.,[8] they have demonstrated immunostaining for beta-hCG and inhibin in a patchy manner in six of six cases, p63 (focal nuclear staining) in two of six cases, and focal Human placental lactogen (HPL) immunostaining in one of six cases. CTT can be diagnosed based on the histomorphological features and confirmed by immunohistochemistry. The list of differential diagnoses is summarized in Table 1.

It is important to identify this lesion as its prognosis is similar to a teratoma and does not require any additional chemotherapy in the absence of nonteratomatous GCT component. CTT was earlier called as choriocarcinoma-like lesion; however, with increasing data, this term is disregarded, and they are now termed as CTT.[6,7] Seventy-two percent of CTTs are seen as a part of metastatic disease and 83% are seen in the setting of chemotherapy.[8] Only a few reports have been identified of CTT developing in testicular primaries without a history of prior chemotherapy.[8] It was thought by Gondim et al.[8] that CTT may arise from choriocarcinoma where more aggressive cells were destroyed either after chemotherapy or by spontaneous resolution and less aggressive component of intermediate type of trophoblast-like cells remained which transformed to CTT. They also proposed that CTT may represent an intermediate stage in the transformation of choriocarcinoma to teratoma which is supported by the morphologic and immunohistochemical profile as both the entities are positive for beta-hCG and inhibin.

CONCLUSION

CTT represents a distinctive trophoblastic lesion seen secondary to either chemotherapy or spontaneous regression of choriocarcinoma. It has a good prognosis and behaves similar to a teratoma, and further, additional adjuvant chemotherapy is not required.

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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Conflicts of interest

There are no conflicts of interest.

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