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Case Report

Enlarging Retroperitoneal Mass after Chemotherapy in Mixed Germ Cell Tumor of Testis: Growing Teratoma Syndrome

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Abstract

Back ground: Growing teratoma syndrome is a rare entity characterized by growing tumor mass in different locations (like retroperitoneum, abdomen, pelvis, liver, chest, bone, or lymph nodes) in patients with non-seminomatous germ cell tumors of ovary or testis, during or after chemotherapy. Tumor markers will be normal. Histopathological examination confirms the diagnosis. ***Case report:*** We report a case of 29 years old male presenting with slow growing retroperitoneal mass after complete treatment for non-seminomatous germ cell tumor of testis. ***Conclusion:*** Growing teratoma syndrome occurs in patients with non-seminomatous germ cell tumors and have serum tumor markers with in normal limits. Early diagnosis of this condition helps for complete curative resection of the tumor for better prognosis.

Key words: Growing teratoma syndrome, Non-seminomatous germ cell tumor, Testis, Tumor markers.

INTRODUCTION

Non-seminomatous germ cell tumors comprise 1% of malignancies in men. These tumors occur in young adults with peak incidence in 20 and 35 years of age. Prognosis of these tumors depend upon the staging of tumor, histology, and serum tumor marker levels [1]. Growing metastatic masses developing in patients with non-seminomatous germ cell tumors during or after chemotherapy, with normalized serum markers are termed as "Growing teratoma syndrome"(GTS). This entity was first described in 1987 by Logothetis et al. [2]. Histopathological examination of these metastatic masses reveal elements of benign mature teratoma without viable germ cell components. The incidence of GTS is 1.9 to7.6 % [3]. Awareness of this condition and role of chemotherapeutic agents in the etiology of this condition is important as early diagnosis and treatment with appropriate radical surgery will yield excellent prognosis [4].

CASE HISTORY

A 29 years old man presented with left scrotal swelling. Tumors markers Alpha Feto Protein (AFP), Human chorionic gonadotropin (HCG) and Lactate Dehydrogenase (LDH) were elevated. Left high inguinal radical orchidectomy was performed in November 2018 and specimen was sent for histopathological examination. We received left orchidectomy specimen measuring 9X6X6cms with attached cord measuring 6cms in length. Cut section revealed circumscribed grey-brown lesion measuring7.5X5.5X6cms which had cystic spaces and hemorrhagic areas. Microscopy revealed mixed germ cell tumor [yolk sac tumor (80%) and mature teratoma (20%)] involving rete testis and hilar soft tissue (Figure 1, 2).

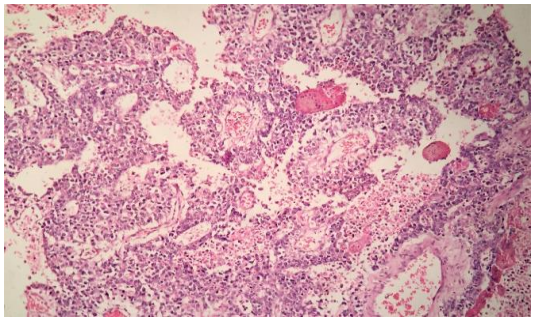

Fig-1: Mixed germ cell tumor with yolk sac component showing Schiller-duval bodies with perivascular tumor cell collection (H&E, X100)

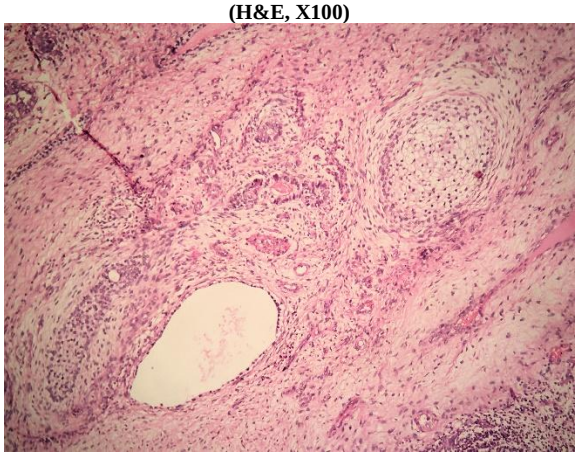

Fig-2: Mixed germ cell tumor with dermoid component showing few ducts and epithelial cell islands (H&E, X100)

The pathological staging was pT2N0Mx

Post operatively patient received 3 cycles of chemotherapy (Bleomycin, Etoposide, Cisplatin) in February 2019. Again in March 2021 patient presented with complaints of abdomen distension for 1 week, pain abdomen for 4 days, vomiting and altered sensorium since 2 days. On general examination pulse was – 72/min, BP - 140/90mm hg and respiratory rate measured – 16/min. Patient had grossly distended non-tender abdomen. Fluid thrill was present and shifting dullness was absent. Tumor markers like serum Human chorionic gonadotropin (<0.1IU/ml), AFP (2.62 ng/ml) and LDH (192IU/ml, were with in normal limits. Hematological investigations were normal. Ultrasound abdomen revealed large cystic lesion with thin internal septations arising from left renal area. CT abdomen – non-ionic contrast revealed non-enhancing large well defined cystic lesion measuring 16X25X30cms with multiple thin enhancing internal septations noted in upper and lower abdomen. Superiorly lesion is extending up to retro gastric region. Left lobe of liver was compressed and displaced superiorly by the lesion. Lesion was displacing fundus of stomach superiorly, displacing head, body tail of pancreas posteriorly, displacing aorta posteriorly, and compressing inferior vena cavae. Bilateral adrenals were normal. Lesion was displacing left kidney posteriorly, superiorly and laterally. Lesion was compressing left pelvi-ureteral junction and proximal left ureter.

Surgical retroperitoneal resection was performed and sent for histopathological examination. We received cystic mass measuring 18X15X5cms (Figure 3). Cut section showed multiple locules filled with serous fluid, mucinous and pultaceous material. Histopathological examination revealed mature teratoma having cyst lined by stratified squamous epithelium with lumen showing lamellated keratin material (Figure 4). Few cysts were filled with mucinous material and were lined by columnar epithelium (Figure 5, 6).

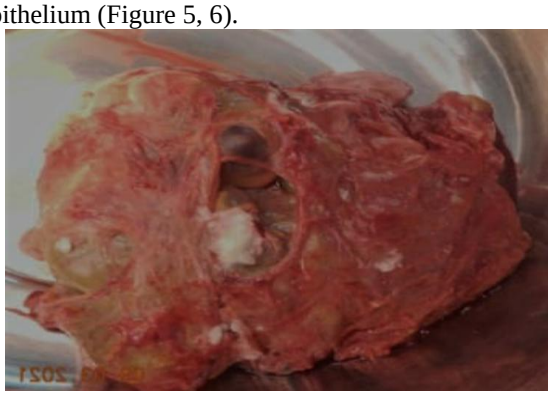

Fig-3: Large multiloculated cystic lesion

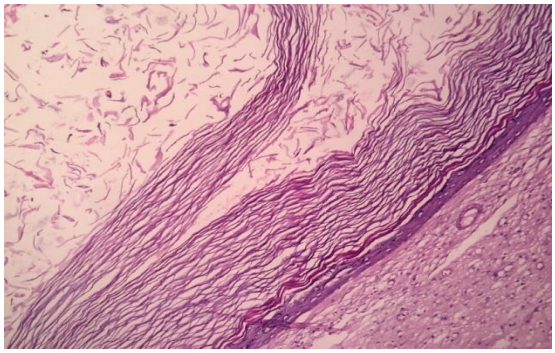

Fig-4: Cyst wall lined by stratified squamous epithelium. Lumen of the cyst showing laminated keratinous material (H&E, X200)

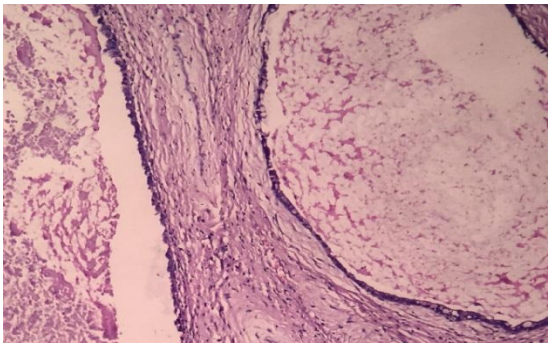

Fig-5: Section shows adjacent foci with cysts lined by columnar epithelium having supra nuclear mucinous vacuole (H&E, X100)

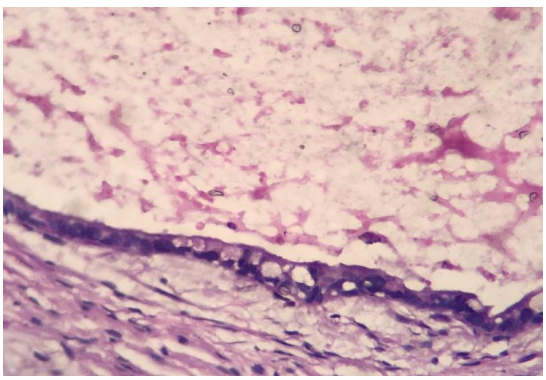

Fig-6: Section shows adjacent foci with cysts lined by columnar epithelium having supra nuclear mucinous vacuole (H&E, X400)

DISCUSSION

Enlarging metastatic masses and their benign transformation in non-seminomatous germ cell tumor of testis was first observed in 1970, and were reported in 1982 by Logesthetis et al. who coined the term "Growing teratoma syndrome" [1]. He described this entity in 6 patients who had primary mixed non-seminomatous germ-cell tumor of testis. Later they developed enlarging metastatic masses during systemic chemotherapy. They had normal serum markers. Histopathology of these growing masses showed benign mature teratoma components without viable germ cell elements. Disaia et al. named similar entity in the ovarian germ cell tumor as "Chemotherapeutic retroconversion" and described it as transformation of metastatic immature teratoma to mature teratoma due to chemotherapy. Amsalem et al found that both "growing teratoma syndrome" in testicular germ cell tumor and "chemotherapeutic retroconversion" in ovarian germ cell tumors were synonymous [5].

Prevalence of GTS is 1.9 to 7.6%. Most common site is retroperitoneum, but can also occur in mediastinum, lung, supraclavicular and inguinal lymph nodes, mesentery, liver, and forearm [6]. In India, Tongaonkar et al. from Tata Memorial Hospital, Mumbai and Ravi R from Cancer Institute of Adyar, Chennai reported 4 and 3 cases respectively of growing teratoma syndrome presenting as enlarging retroperitoneal masses [7, 8].

Growing teratoma syndrome in patients with testicular carcinoma should be suspected when the patients had 1. History of non-seminomatous germ cell tumor 2. Metastatic lesions increasing in size during or after systemic chemotherapy for testicular cancer 3. Serum tumor markers are normalized 4. Histopathology shows mature teratoma component without any malignant germ cell tumor.

Etiopathogenesis of GTS is unclear. The most accepted hypothesis regarding GTS are a) Chemotherapy changes the cell kinetics from a totipotential malignant germ cell to benign mature teratoma b) Chemotherapy destroys all the immature malignant cells, leaving only the mature teratomatous component [9] c) Inherent and spontaneous differentiation of malignant tumor cells into benign tissue, which is due to prolonged life due to chemotherapy which permits the spontaneous evolution to occur in disease [1].

Proposed predisposing factors for the development of GTS are- presence of mature teratoma in primary tumor, no reduction in size of metastatic tumor on chemotherapy, presence of mature teratoma tissue in post chemotherapy residual masses and incomplete resection of tumor after chemotherapy [10].

Jones et al., described correlation between non- teratomatous germ cell tumor components and metastatic mature teratoma. Both tumors revealed identical genetic alterations on several chromosomes (1p36, 9q21, 9p21, 13q22-q311, 8q21, 18q22) [11].

Germ cell tumors originate from primordial germ cells which on genetic divergence (either genetic instability, or abnormal division or retention of embryonic features) leads to formation of germ cell neoplasia in situ (GCNIs). This on further continuous genetic alterations (e.g. amplification of chromosome 12 and CCND2/KRAS/MDM2 mutations) yield germ cell tumors [12].

Patterns of cell differentiation explains that probably mature teratomas resides with in additional germ cell components simultaneously in a patient diagnosed with Non-seminomatous germ cell tumor. On chemotherapy, germ cell components are destroyed but teratomatous components continues to differentiate leading to growth of metastatic masses.

Though no specific growth rate has been described for GTS masses, some studies have shown that growth of median volume of 12.9ml/month (95% confidence interval (CI), 0.85-4.5) and increase in median circumferential diameter of 0.7/month (95% CI, 0.1-2.4) [13].

Characteristic feature of GTS is that serum tumor markers like α-fetoprotein (AFP), Lactate dehydrogenase and β- human chorionic gonadotropin are normalized. If the serum tumor markers are not in normal range then the non-malignant causes (like Liver dysfunction leading to elevated AFP, or elevated Luteinizing hormone or use of marijuana can elevate HCG) should be excluded [14].

On computed tomography scan, GTS masses have circumscribed margin, an increased cystic changes with punctuate, curvilinear calcifications, elements of fat, or an increased density of masses [15].

GTS tumors can be identified by using 18F-Fluorodeoxyglucose (FDG) positron emission tomography. Positive uptake on FDG imaging suggests viable tumor whereas negative uptake on imaging suggest either mature teratoma or likely necrosis [17].

Although histology of GTS masses appears benign, their aggressive expanding and enveloping growth pattern can cause morbidity and mortality. GTS masses are resistant to radiotherapy and chemotherapy. Total surgical resection is the treatment of choice. Surgical treatment should be adequate and complete as

it determines the prognosis. Recurrence in these tumors has been observed in 0 – 4% of patients with complete resection and in 75% - 83% of patients with incomplete resection [15]. Medical therapy with interferon has been suggested for inoperable abdominal GTS masses [18].

In rare cases, malignant teratoma transformation has also been reported (3% approximately) [19].

CONCLUSION

GTS should be considered in patients with history of non seminomatous germ cell tumors presenting with enlarging metastatic tumor mass during or after chemotherapy and having serum tumor markers with in normal limits. Regular follow-up of patients with imaging is essential for the patients with non-seminomatous germ cell tumor, as they may develop GTS after several years of chemotherapy. Early diagnosis of this condition helps for complete curative resection of the tumor for better prognosis

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