Original Research Paper

Volume - 13 | Issue - 06 | June - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Oncopathology

"METASTATIC MATURE TERATOMAS IN TESTICULAR CANCER- A RARE CASE HIGHLIGHTING GROWING TERATOMA SYNDROME".

Dr. Lalhmingmawii Renthlei	Junior Consultant Pathologist, Plus Care International Private Limited, Sewri, Mumbai
Dr. Abhijit Bhanji	Consultant Pathologist Plus Care International Private Limited, Sewri, Mumbai
Dr. Amrita Neelakantan	Consultant Pathologist Plus Care International Private Limited, Sewri, Mumbai

ABSTRACT Testicular cancer comprises 1-2% of male solid malignancies and is most common in males aged 20-34 years. Non-Seminomatous Germ Cell Tumours(NSGCTs) are less common but more aggressive than Seminomas. Approximately 50% of NSGCTs have teratomas, and Metastatic Mature Teratoma(MMT) patients often show teratoma in their primary tumour(1). We present a rare case: a 26-year-old with a history of inguinal orchidectomy 8 months ago, diagnosed with Malignant Mixed Germ Cell Tumour. He received 2 cycles of chemotherapy, the last one 4 months ago, and now presents with enlarging left-sided neck and retroperitoneal swellings. Two specimens are received: Retroperitoneal and left Supraclavicular masses. Both are nodular, bosselated multiloculated cystic tumours with cysts ranging from 0.2-4 cm. Histopathological findings are similar in both, consistent with Metastatic Mature Teratoma. Testicular neoplasms have excellent 5-year survival with complete excision(64%) and chemotherapy(96%)(2). However, MMT often persist despite chemotherapy, necessitating regular follow-up with serum markers and imaging.

KEYWORDS : Testicular Cancers, Non-Seminatous Germ Cell Tumour, Metastatic Mature Teratoma, Malignant Mixed Germ Cell Tumour, Chemotherapy, Retroperitoneal mass.

INTRODUCTION:

Testicular cancer is common among males aged 20-34. Most cases are Germ Cell Tumours (GCTs), divided into Seminomas or NSGCTs. NSGCTs are less common but more aggressive. Teratomas (NSGCTs) contain fully developed tissues and organs from all three germinal layers. They are found in about 50% of NSGCTs, and most patients with MMT have teratoma in their primary tumour(1). Excision and chemotherapy yield excellent 5-year survival rates (64% and 96% respectively) (2). Around one-third of NSGCT patients have metastatic disease at initial diagnosis. Metastatic spread typically follows primary lymphatic drainage.

The Growing Teratoma Syndrome (GTS) is an extremely rare metastatic complication of a Malignant GCT described for the first time by Logothetis et al. (3).The syndrome appears in 1.9– 7.6% of the patients after treatment for testicular NSGCT (4). The syndrome is defined as a detection of an enlarged mass during or after chemotherapy treatment for GCT. The histology of the metastasis is of Mature Teratoma with no malignant elements. Theoretically, chemotherapy treatment can eliminate the malignant element allowing the benign mature elements to flourished.

According to Logothetis's original description, three criterias are required for the definition of the GTS. First, normalisation of previously elevated tumour markers [alpha-fetoprotein(AFP) or beta-human Chorionic Gonadotropin (β-HCG)]. Second, enlargement of the primary tumour or finding a new tumour mass. Third, only Mature Teratoma elements in pathologic examination. All these criteria should be met after or during chemotherapy treatment of NSGCT.

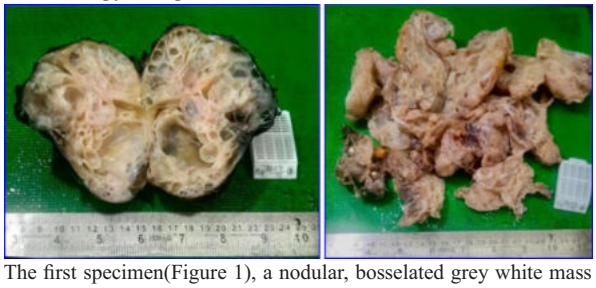
Case Report:

This case report describes the presentation, diagnosis, and histopathological findings of a 26-year-old male with scrotal and left-sided neck swelling. The patient exhibits elevated serum levels of Lactate Dehydrogenase (LDH), AFP, and β-hCG. After undergoing inguinal orchidectomy, the histopathology report revealed Malignant Mixed Non-seminomatous Germ Cell Tumour. Subsequently, the patient received two cycles of chemotherapy(Bleomycin, Etoposide, Cisplatin). However, within three months the neck swelling increased in size, and the patient complained of gradually increasing retroperitoneal swelling.

Radiology investigations reveal a conglomerated nodal mass measuring 9.4x13x10 cm in the retroperitoneum and a large left supraclavicular nodal mass. The laboratory investigations are as follows:

Serum parameters	Before orchidectomy	1 week post orchidectomy	2 months post orchidectomy	8 months post orchidectomy
LDH (<=250U/L)	259	226	208	149
AFP (0.89-8.78 ng/mL)	320	332	160	3.70
Beta - hCG (<=2.0mIU/mL)	287.6	406.9	63.7	1.03

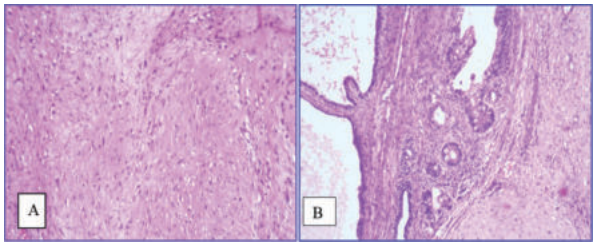
Eight months post-orchidectomy and three months post-2 cycles of chemotherapy, two specimens are received for examination:

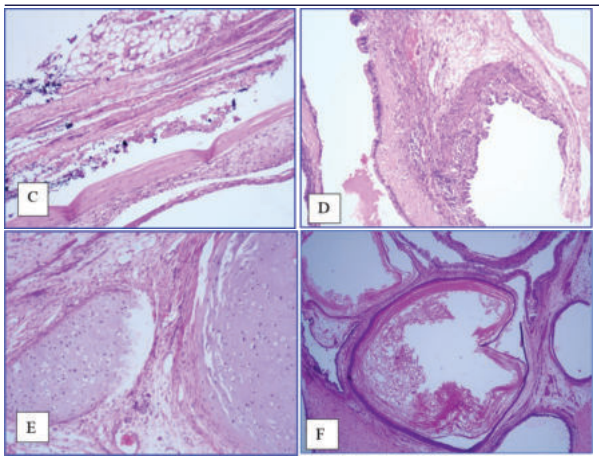


The first specimen(Figure 1), a nodular, bosselated grey white mass measuring 12x10x7 cm, is obtained from the left supraclavicular region. The mass has an intact capsule and appears congested. Upon sectioning, a multiloculated cystic tumour is observed, with cysts ranging from 0.2 to 4 centimetres in diameter. The cysts are separated by thin fibrous septae and filled with clear fluid.

The second specimen(Figure 2), fragments of a retroperitoneal mass, measure 26x24x8 cm in aggregate. The cut sections of all pieces show multicystic features with few whitish and yellow areas. No solid areas are identified. Extensive sampling is performed.

Histopathological Findings:





A) Mature neural tissue ; H&E,100 x B) Colonic mucosa; H&E 100x C) Inked margin with adipose tissue; H&E 40 x D) Cysts with columnar lining ; H&E 100 x E) Mature hyaline cartilage ; H&E 100x F) Cysts with squamous lining and filled with keratin ; H&E 100 x

Sections from both specimens exhibit similar findings. The tumours are well-circumscribed and multiloculated, with cystic spaces lined by columnar to pseudo-stratified cubo-columnar epithelium. These cysts are filled with dense eosinophilic secretions and foamy macrophages. Additionally, some cysts are lined by stratified squamous columnar epithelium and filled with lamellated keratin flakes. The intervening stroma consists of fibrocollagenous tissue, neural tissue, and mature cartilage. Dense mixed inflammatory infiltrates, including neutrophils, lymphocytes, plasma cells, histiocytes, and multinucleated giant cells,are also present. With above findings, we have given a diagnosis of Metastatic Mature Teratoma.

DISCUSSION:

In the case presented, a rare occurrence of Metastatic Mature Teratoma was observed in a 26-year-old male with a history of inguinal orchidectomy and 2 cycles of Chemotherapy for Malignant Mixed Germ Cell Tumours. While this case primarily focuses on Metastatic Mature Teratoma, it is crucial to discuss Growing Teratoma Syndrome (GTS) as it relates to the behaviour of teratomas in testicular cancer patients. Growing teratoma syndrome is characterized by the growth of mature teratomas despite chemotherapy treatment (Kollmannsberger et al., 2014)(5). It is important to differentiate GTS from chemoresistant or refractory disease, as the latter refers to the persistence or progression of viable malignant elements in the tumour (Kollmannsberger et al., 2014). GTS typically presents as an enlarging mass during or after chemotherapy, often associated with normalisation of previously elevated serum markers(Kollmannsberger et al., 2014).

In the presented case, the patient underwent 2 cycles of chemotherapy (Bleomycin, Etoposide, Cisplatin) following inguinal orchidectomy for Malignant Mixed GCTs. However, metastatic mature teratoma was observed in the retroperitoneal and left supraclavicular regions. This raises the possibility of GTS, as mature teratomas are known to have the potential for continued growth even after chemotherapy treatment. This highlights the challenges in managing teratomas within the context of NSGCTs, as these tumours can exhibit different behaviours compared to other malignant elements.

The exact mechanisms underlying GTS are not yet fully understood. One proposed hypothesis is the resistance of Mature Teratoma components to chemotherapy agents compared to malignant elements present in the tumour (Kollmannsberger et al., 2014)(5),concept of chemotherapeutic “retroconversion or insitu destruction” of immature tissue may be the mechanism for conversion of malignant to mature tumours(6). Additionally, the presence of chemotherapy-resistant cancer stem cells within teratomas has been suggested as a contributing factor to GTS (Pectasides et al., 2015)(7).

Regular follow-up with serum tumour markers and radiological imaging is critical in monitoring for the development of GTS, as observed in present case, or the persistence of viable malignant elements. The early detection of GTS can prompt appropriate intervention, such as salvage surgery or alternative treatment approaches.

In conclusion, while the presented case highlights the occurrence of Metastatic Mature Teratoma, it is important to consider the possibility of Growing Teratoma Syndrome. GTS represents a unique challenge in the management of testicular cancer, where mature teratomas can exhibit continued growth despite chemotherapy treatment. Further research is needed to elucidate the underlying mechanisms of GTS and explore novel treatment strategies to improve patient outcomes.

Abbreviations:

- NSGCTs: Non-Seminomatous Germ Cell Tumours
- MMT: Metastatic Mature Teratoma
- GCT: Germ Cell Tumour
- GTS: Growing Teratoma Syndrome
- β-HCG: Beta Human Chorionic Gonadotropin
- LDH: Lactate Dehydrogenase
- AFP: Alpha Fetoprotein

REFERENCES:

(1) Bahrami A, Ro JY, Ayala AG. An overview of testicular germ cell tumors. Arch Pathol Lab Med. 2007;131:1267–1280.
(2) Borni M, Kolsi F, Kammoun B, Kallel R, Souissi G, Boudawara MZ. Testicular non-seminomatous germ cell tumors (NSGCT) and brain metastases: About a rare location of the posterior fossa. Urol Case Rep. 2018 Nov;21:61-63.
(3) Logothetis CJ, Samuels ML, Trindade A, Johnson DE. The growing teratoma syndrome. Cancer 1982 (Oct. 15);50(8):1629 – 35.
(4) Jeffery GM, Theaker JM, Lee AH, Blaquiere RM, Smart CJ,Mead GM. The growing teratoma syndrome. Br J Urol 1991(Feb.);67(2):195 – 202.
(5) Kollmannsberger, C., Hartmann, J. T., Kanz, L., Bokemeyer, C. (2014). "Chemotherapy in adult testicular cancer." Seminars in Oncology, 41(3), 328-342. doi: 10.1053/j.seminoncol.2014.03.008
(6) André F, Fizazi K, Culine S, Droz J, Taupin P, Lhommé C, et al. The growing teratoma syndrome: results of therapy and long-term follow-up of 33 patients. Eur J Cancer. 2000;36:1389–1394.
(7) Pectasides, D., Pectasides, M., Kostopoulou, M., Farmakis, D., Ardavanis, A., Koumpouros, N., ... & Economopoulos, T. (2015). "Testicular cancer: sperm cryopreservation and cancer treatment." Cancer Treatment Reviews, 41(7), 811-816. doi: 10.1016/j.ctrv.2015.05.004