Case Report

Malignant Teratoma Arising From Mediastinal Non-Seminomatous Germ Cell Tumor: A Rare Case Report

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DOI: 10.21276/APALM.3181

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Submitted: 11-Apr-2022
Final Revision: 29-Jul-2022
Acceptance: 13-Aug-2022
Publication: 03-July-2023

Abstract

Introduction: Primary mediastinal non-seminomatous germ cell tumors (NSGCT) have a worse prognosis than gonadal germ cell tumors (GCTs). Malignant transformation of teratomatous components of GCT to a somatic malignancy is rare.

Materials and methods: A case of primary mediastinal NSGCT with malignant transformation of a teratoma was seen in a 23 years old male. Resected tumor specimen was received. Tissue processing was done and sections were prepared for Histo Pathological Examination.

Results: Histopathology confirmed NSGCT with yolk sac and teratomatous components. Chemotherapy for GCT transiently normalized serum tumor markers with little effect on the mediastinal mass. Incomplete resection of the residual tumor revealed intermediate grade chondosarcoma. Here we discuss this rare case.

Conclusion: malignant transformation to chondrosarcoma is a rare possibility which needs to be considered while managing the patient of Primary Mediastinal Germ Cell Tumors (PMGCT)

Keywords:

Mediastinum, Non-seminomatous germ cell tumor, Chondrosarcoma

Introduction

Primary Mediastinal Germ Cell Tumors (PMGCTs) account for 15% of adult anterior mediastinal tumors, and between 5% and 10% of all GCTs[1]. These tumors are histologically and serologically identical to gonadal GCTs but have a worse prognosis. The non-seminomatous components may comprise of embryonal, extra-embryonal or somatic-type histology (teratoma). Extent of disease and pathology of the resected tumor are the most important prognostic indicators. Malignant transformation of the teratomatous component of GCT to a histologically identical somatic malignancy is a rare but well-described feature of NSGCT[2].

Case presentation

A 23-year-old male had presented with history of gradually progressing fatigue, cough, and breathlessness on exertion since last two years. A chest radiograph revealed an 8 cm anterior mediastinal mass. CT scan of the chest, abdomen, and pelvis showed a 8 x 1 x 12.5 cm heterogeneous right anterior mediastinal mass with right hilar lymph node enlargement. Initial laboratory workup revealed normal haematological and biochemical parameters. The serum levels for germ cell tumor markers were deranged with elevated lactate dehydrogenase (LDH) 497 IU/L, alpha fetoprotein (AFP) 7450 ng/mL, and beta- human chorionic gonadotropin (b-HCG) 687.52mIU/mL. Resting pulmonary function tests showed a mild restrictive defect (forced expiratory volume in 1 second: 71% predicted, forced expiratory volume in 1 second/forced vital capacity 72%). Testicular ultrasound was normal. A core-needle biopsy was performed which showed features of mixed germ cell tumor with the following components: seminoma (15-20%), embryonal carcinoma (50-55%) and yolk sac tumor (30-35%).

The patient was subjected to four cycles of adjuvant chemotherapy with VIP regimen (Cisplatin, ifosfamide and etoposide) from November 2019 to January 2020. Patient showed a biochemical response with normalization of b-HCG (0.539 mIU/ml) and serum AFP levels (44.26 IU/ml) on completion of chemotherapy. The tumor markers repeated after a two month follow up period showed rising levels of all three serum markers. A repeat contrast enhanced CT scan showed no significant change in size of the lesion with additional findings of central necrosis and bilateral pleural effusion. The patient underwent incomplete surgical resection of the tumor.

Materials and methods

A written informed consent was taken from the patient for conduct of the study. On histopathological examination, the mass showed residual tumor with predominance of teratomatous component forming approximately 90% of the tumor mass along with focal areas of non- seminomatous GCT (10%). The teratomatous areas comprised of predominantly lobules and islands of atypical chondrocytes with increased cellularity, moderate nuclear pleomorphism and occasional mitotic activity. There were other foci comprising of glial tissue, mature adipose tissue, and an epidermal inclusion cyst. The section shows foci of tumor arranged in sheet with glial tissue comprising of small tumor cells with scant cytoplasm, hyperchromatic nuclei and nuclear pleomorphism as shown in Figure 1. Mature adipose tissue is also seen in this section. The sections show lobules of atypical chondrocytes with increased cellularity, moderate nuclear pleomorphism, irregular nuclear contour and mitosis as shown in Figure 2 (a to e). Therefore, a final diagnosis of PMGCT with somatic type malignancy (Chondrosarcoma - intermediate grade) was established. Patient was subjected to second round of chemotherapy, however, there was disease progression in the form of regrowth of tumor to the initial size and development of metastasis in the lung and liver.

Discussion

We present an unusual case of PMGCT presenting with transformation of teratomatous elements to intermediate grade chondrosarcoma. This case underscores the importance of keeping PMGCT in the differential diagnosis of a young, otherwise healthy, patient presenting with mediastinal mass [3].

Mixed GCTs contain 2 or more components of germ cells, which differ in their exact composition. Several distinct mixtures of these tumours have been identified but it has been shown that certain combinations, such as those comprising teratoma and embryonal carcinoma, are more likely to occur [4,5]. In a study of 2,589 primary testicular tumour patients, 1765 (68.2 %) of whom were diagnosed with mixed GCTs, the most common histologies comprised of embryonic carcinoma (84.4 % of cases),

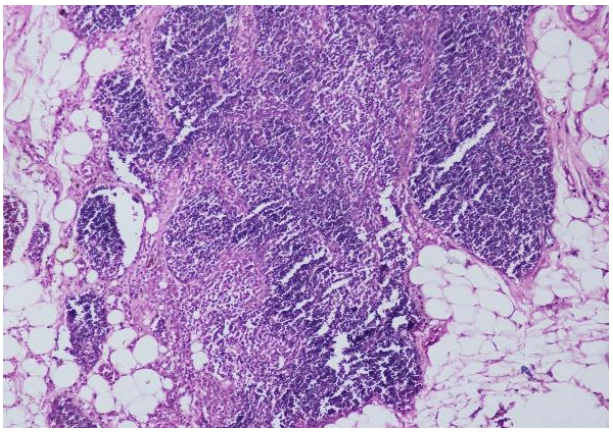

Figure 1 Histopathology of tumor depicting glial and adipose tissue

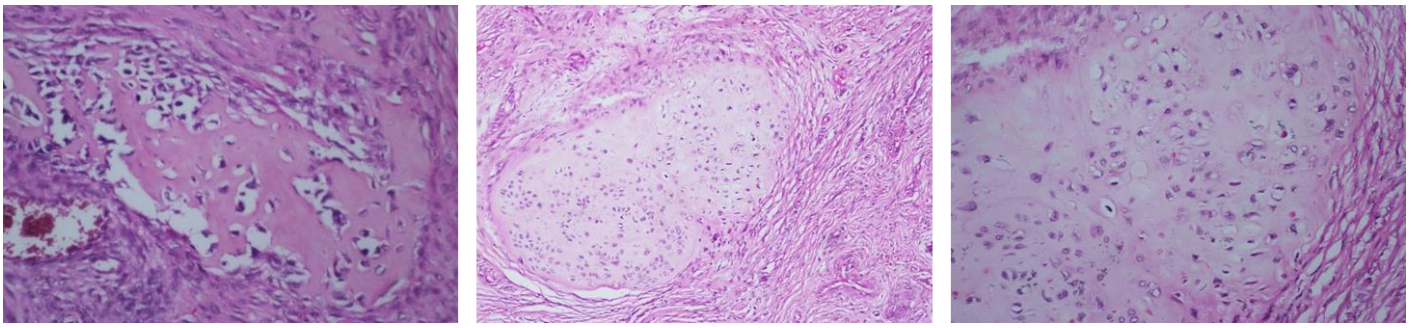

Figure 2 a to c Histopathology showing malignant transformation to intermediate grade chondrosarcoma

teratoma (69.7 %) and yolk sac tumour (60.1 %). Somatic type malignant transformations (SMTs) is a well-known phenomenon in mixed GCTs but very rare. It occurs in about 3-6% of these tumours and is thought to develop as a result of malignant transformation of teratomatous components, although there may be other mechanisms, such as abnormal differentiation of primordial germ cells [6–8]. Tumors accompanied by malignant transformation are more likely to metastasize and have an increased propensity for aggression than those without this phenomenon. Sarcomas, especially rhabdomyosarcomas, and carcinomas are among the most commonly delineated histological transformations [9].

However, as seen in this article, malignant transformation to chondrosarcoma is considered rare, and has seldom been documented in the English literature. Even after the extensive literature search, we came across only a single case report illustrating chondrosarcoma as mixed sarcoma arising from PMGCT[10] as shown in Table 1e.

PMNSGCT has a poorer prognosis than its gonadal equivalents due to the risk of residual unresectable disease after chemotherapy and an unusual transformation of GCT to somatic malignancy in 3% to 6% of cases[1]. The cause of malignant transformation in GCT is based on chromosomal study of the resected specimen, with chromosome 12 abnormalities (isochromosome 12, i12p, or excess 12p copy number via insertion)[3].

Conclusion

The most important indicator of survival is the pathology of the resected specimen after chemotherapy[1]. Patients undergoing chemotherapy that achieve normalisation of tumour markers and have necrotic tissue in the resected residual mass have an

Table 1 Summary of cases of chondrosarcoma arising in gonadal and extragonadal GCTs

S.No.	Reference	Age /sex	Site of primary	Malignant component	Treatment	Final outcome
a	Tulek F et al, 2014 [11]	64/F	Ovary	Rhabdomyosarcoma+ Chondrosarcoma	Adriamycin and Vincristine	Died within 2 months of completion of chemo
b	Wang J et al, 2011 [12]	44/M	Testis	Rhabdomyosarcoma+ Chondrosarcoma	Vincristine, Dactinomycin and Cyclophosphamide with alternating Irinotecan	Disease free
c	Yasunaga M et al, 2011 [13]	69/F	Ovary	Chondrosarcoma	Docetaxel and Gemcitabine	Disease free survival
d	Alrehaili M et al, 2020 [14]	34/M	Testis	Chondrosarcoma	Etoposide and Cisplatin	Died within 15 days of completion of chemo
e	Collen J et al, 2008 [10]	23/M	Mediastinum	Mixed Sarcoma	Doxorubicin, Ifosfamide and Mesna	Died within 06 months due to secondary Acute Myeloid Leukemia
f	Present case	23/M	Mediastinum	Chondrosarcoma	Cisplatin Ifosfamide and Etoposide	Under follow up

outstanding result. On the other hand, following chemotherapy the residual carcinoma in the resected specimen has a high risk of relapse. PMNSGCT is graded as a low-risk GCT and transition to a high-grade mixed sarcoma is a severe prognosis [3]. Thus, we can conclude, PMGCT can be present without primary in testes. Mediastinal, extrapulmonary and elevated serum tumour markers show worse prognosis.

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