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Granulocytic Sarcoma occurring in association with Mediastinal Germ cell tumor– report of a case and literature review

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Abstract: Mediastinal nonseminomatous germ cell tumors have a high incidence of hematologic disorders which include acute megakaryocytic leukemia, acute myeloid leukemia, myelodysplasia, malignant mastocytosis and histiocytosis. Most often, these hematologic abmormalities follow the diagnosis of germ cell tumor. We report the case of a 33 year old man with mediastinal germ cell tumor who had associated isolated granulocytic sarcoma also along with the germ cell components. The rarity of this case is the concurrent occurrence of germ cell tumor and granulocytic sarcoma without bone marrow involvement which has been reported only twice before in world literature.
Keywords: Germ cell tumor, Mediastinal, Granulocytic sarcoma.

INTRODUCTION

Hematological malignancies associated with germ cell tumors (GCT) represent one of the most intriguing diseases in oncology. Patients with mediastinal nonseminomatous GCTs have a high incidence of hematologic disorders which include acute megakaryocytic leukemia, acute myeloid leukemia, myelodysplasia, malignant mastocytosis and histiocytosis. Most of these hematologic abmormalities had followed the diagnosis of GCT. We report the case of a 33 year old man with mediastinal GCT who had associated granulocytic sarcoma also along with the germ cell components. The rarity in this case is the concurrent occurrence of germ cell tumor and granulocytic sarcoma without bone marrow involvement which has been reported only twice before in world literature [1,2].

CASE REPORT

A 36 year old man presented with swelling of the neck since 2 months. A computed tomogram (CT) of the thorax showed a soft tissue mass 19x7.2x13 cm with smooth margins in neck and anterior mediastinum on left showing mild enhancement on post contrast study, with no evidence of calcification or cystic areas (Figure 1).

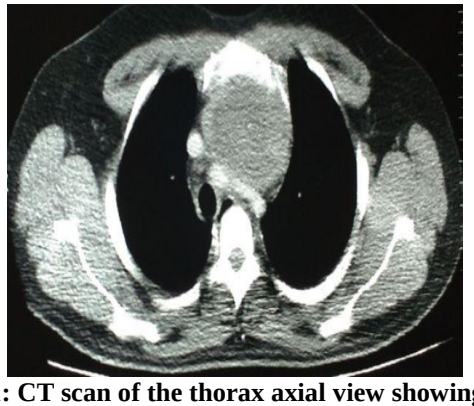

Fig-1: CT scan of the thorax axial view showing the soft tissue density mass in the anterior mediastinum.

He underwent resection of the mass at the local hospital and intraoperatively, there was a large tumor of size 20x18x16 cm involving entire anterior mediastinum with extension into lower neck and infiltrating the anterior pericardium, left phrenic nerve, hilar surface of left lung and brachiocephalic vein. The histopathology was malignant mixed germ cell tumor, predominant component was immature teratoma, with yolk sac tumor and seminomatous areas.He presented to us subsequently. On examination, his performance status was 1 and he had hoarseness of voice. A repeat CT scan of the thorax showed residual soft tissue mass in the anterior mediastinum, enlarged mediastinal lymph nodes, pleural deposit, pleural effusion and mild pericardial effusion (Figure 2).

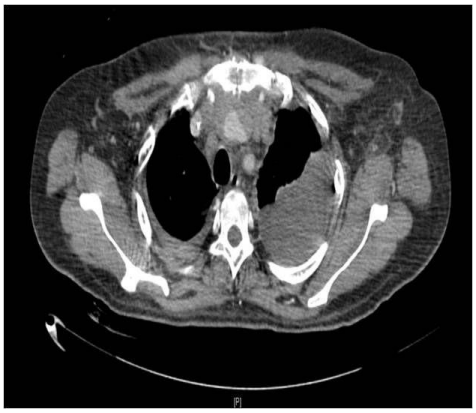

Fig-2: CT scan of the thorax axial view showing soft tissue mass in the anterior mediastinum, pleural deposit and effusion.

His haemogram, liver function and renal functions were normal. The serum tumor markers alfa fetoprotein was 398 ng/ml, β HCG was 0.3mIU/ml, and lactate dehydrogenase was 772 u/L. CT scan of the abdomen, ultrasonogram of the testes and pleural fluid cytology were normal. He was started on combination chemotherapy with cisplatin, ifosfamide and VP16 (VIP) pending a histopathology review.

Histopathologic review showed malignant mixed germ cell tumor consisting of immature teratoma, yolk sac tumor, with foci of round to polygonal cells which were positive for CD43, MPO, CD68, CD15 and CD34 and negative for CD20 and CD30. The histomorphology and immunohistochemistry was suggestive of granulocytic sarcoma occurring along with the germ cell tumor. A bone marrow examination and cytogenetics were normal. He has completed 4 cycles of VIP chemotherapy, the markers have normalized, and the residual mediastinal mass is stable. He is continued on conventional AML induction chemotherapy with cytosine arabinoside and daunorubicin for the granulocytic sarcoma. He is planned for resection of the residual mediastinal mass after the completion of chemotherapy.

DISCUSSION

Malignant transformation of GCT can occur in any primary site, but they arise usually from mediastinal nonseminomatous GCT than from other sites [3]. Such malignant transformation lead to aggressive malignancies showing histologic differentiation along different lineages such as sarcomas, leukaemia, carcinomas and primitive neuroectodermal tumours[4].

The association between mediastinal GCT and haematological malignancies was first recognized in 1985[5]. Although mediastinal GCT accounts for only 2-5% of all GCTs, most of the hematological abnormalities associated with GCT occur with the mediastinal primary[5,6]. The incidence of leukemia in patients with mediastinal nonseminomatous GCT is estimated to be 5.9% and teratoma, which derives from embryonal carcinoma, has been associated with the hematologic malignancies[7,8].

In a series of 16 patients with GCT and hematologic malignancies, the median time interval from the diagnosis of mediastinal GCT to the occurrence of a hematologic disorder was 6 months[9]. Both disorders occurred simultaneously in one third of patients, and the megakaryocytic lineage was involved resulting in acute megakaryoblastic leukemia, myelodysplasia with abnormal megakaryocytes, or idiopathic essential thrombocytosis. The other hematological disorders were acute lymphoblastic leukemia, acute myeloid leukemia, malignant histiocytosis or systemic mastocytosis[9,10,11]. In another series of 287 patients with primary mediastinal nonseminomatous GCT, 6% developed a hematologic malignancy, the median time to onset was six months, the median survival following diagnosis was five months, and no patient survived more than two years [7]. John et al reviewed the data on 26 cases of mediastinal GCT with acute megakaryocytic leukemia, all patients received platinum based chemotherapy which was directed towards management of the GCT. The median time from diagnosis of GCT to development of leukemia was 4 months and the median time to death 6 months[12].

However, mediastinal GCT associated with granulocytic sarcoma without bone marrow disease was reported in only 2 instances before in world literature. A 29 year old man with mediastinal mature teratoma with coexistence of angiosarcoma and granulocytic sarcoma was reported[1]. Another 24 year old man with mediastinal GCT associated with granulocytic sarcoma was also reported[2]. Our patient also had a similar presentation of mediastinal GCT with granulocytic sarcoma without bone marrow involvement making this the third report in world literature.

The malignant cells in these hematologic disorders have isochromosome 12p as evidence of derivation from the GCT [7,9]. The finding of both isochromosome 12p and trisomy 21 in leukemic cells and GCT supports the theory that these malignant cells arose from a common precursor. In a series of six patients with mediastinal GCT and concurrent hematologic malignancy, the investigators were able to identify hematopoietic precursor cells within the yolk sac component of the GCT[13]. Thus, granulocytic sarcoma may originate from a yolk sac tumor-derived progenitor cell capable of undergoing hematopoietic differentiation, with subsequent homing to the bone marrow.

Hematologic disorders associated with primary mediastinal germ cell tumors have to be distinguished

from therapy-related secondary leukemia. Leukemias associated with the use of alkylating agents is preceded by a preleukemic period of myelodysplasia, occur after an interval of 5-7 years and are associated with abnormalities of chromosome 5 or 7. Topoisomerase II inhibitor-related secondary leukemias are diagnosed 2-3 years after chemotherapy, often are FAB M4 or M5 phenotype and associated with translocations of the long arm of chromosome 11 (11q23).

The clinical course of the hematologic malignancy in patients with GCT tend to be very aggressive, and a substantial proportion of these patients die before treatment. The approach to treatment of patients with granulocytic sarcoma without evidence of AML on bone marrow biopsy is similar to that of patients with overt AML. Allogenic bone marrow transplantation has been tried without much benefit [14,15]. Survival for such patients has been poor with a median survival of 5 months and no patients alive beyond 2 years.

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