A Rare Case of Mediastinal Non-seminomatous Germ Cell Tumour with Acute Megakaryocytic Leukaemia

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Abstract
The most common extragonadal site of Nonseminomatous Germ Cell Tumours is the mediastinum. These are similar to their gonadal counterparts in histology but have a poorer prognosis. The association of mediastinal germ cell tumours with blood borne malignancies has been established in many case reports. However, the association of concomitant mediastinal non seminomatous germ cell tumours with Acute Megakaryocytic Leukemia is very rare with only 26 cases reported in the last 07 Decades. These patients have a very poor prognosis with only one survivor being reported till present date. AML (M7), a rare variant of Primary AML, has been more commonly associated with non seminomatous germ cell tumours. Here, we report such a rare case of dual malignancy, Non Seminomatous Germ Cell Tumour with AML (M7) which was managed at our centre.

Introduction
The association between mediastinal germ cell tumors and hematological malignancies has been known to the medical community for more than 2 decades.1,2 This association was established as a clinical entity by Nichols et al. in 1990. Our extensive literature review has revealed that there are only 26 reported cases of such dual malignancies coexisting together since in 1946.

The etiology is different compared to treatment-related leukemia. Acute Megakaryoblastic leukemia, which is a rare form of primary AML, is found to be more commonly associated with primary mediastinal non seminomatous germ cell tumours. Here, we report a case of acute megakaryocytic leukemia associated with a nonseminomatous primary mediastinal germ cell tumor whose diagnosis was a challenge.

Case History
A 30 year old male, serving soldier, resident of Ahmedabad and hailing from Karnataka, presented with a 01 week history of retrosternal pin pricking type of chest pain radiating to the back with acute onset non progressive dyspnea on exertion (MMRC Class II) and episodic dry cough which would aggravate on supine position. There was no history of associated fever, hemoptysis, wheezing episodes, seasonal variation of symptoms. The patient denied history of any addictions, similar episodes in the past or any high risk behaviour. He had no history of associated comorbid illness. His initial general and systemic evaluation was normal with a normal testicular examination. During his initial workup, he was found to have polymorphonuclear leucocytosis (TLC-14,300/cmm) with thrombocytopenia (60,000/cmm) and marginally raised serum LDH levels (234 IU/L) with his Chest Radiograph showing a well defined Radio-opaque mass in the mediastinum to the left with a wavy outline. His contrast enhanced CT Thorax showed an Anterior mediastinal mass lesion (82 x 72 mm in axial plane with 84 mm craniocaudal extension) predominantly on the left side with lesion compressing the arch of aorta and left side main Pulmonary artery and Inf pulm vein while a Whole Body PET CT scan showed Large mass lesion with heterogenous FDG uptake measuring (82.3 x 110.0 x 92.9 mm) in the Anterior Mediastinum mainly on the left side with a diffusely increased FDG uptake in the bone marrow. His serum tumour markers were also elevated; AFP-641.23 ng/ml (normal-0-9) and BHCG-58.9 mIU/ml (non pregnant – 5). A ultrasound guided trucut biopsy of his mediastinal mass showed features of a mediastinal non seminomatous germ cell tumour, likely teratoma on histopathology (Figure 1).

In view of persistent thrombocytopenia and a peripheral blood smear showing leucocytosis with Blasts (High N/C ratio, sieve like Chromatin and 1-2 nucleoli) and thrombocytopenia (<10,000/cmm) (Figure 2), we performed a Bone Marrow Aspiration and Biopsy. Bone marrow studies showed Focal high cellularity of large bizarre cells with a high N: C ratio, moderate cytoplasm and convoluted to lobated nuclei with brisk mitotic activity with reduced normal hematopoietic marrow elements and no mature megakaryocytes or glands/mucin/ epithelial cells, MPO and PAS stain negative (Figure 3). The Bone marrow immunohistochemistry and Flow Cytometry showed CD 61 positive blasts suggestive of Megakaryocyte lineage with normal lymphoid and myeloid series. He was managed as a case of Mediastinal germ cell Tumour with Acute Megakaryoblastic Leukemia (AML M7) with 2 cycles of BEP regimen followed by Induction Chemotherapy with Daunorubicin and Cytosine-Arabinoside (7+3 regimen). However, he developed febrile neutropenia after induction chemotherapy with progressed to septic shock with multiorgan dysfunction. He subsequently succumbed to sepsis after 45 days of diagnosis.
Discussion

The mediastinum is the most common site of primary extragonadal germ cell tumours. One to six percent of all mediastinal tumours are primary malignant germ cell tumours. Extragonadal germ cell tumours generally occur in the midline of the body, like the pineal gland, mediastinum and retroperitoneum. The histological characteristics of extragonadal germ cell tumours are similar to their testicular counterparts, but have a poorer prognosis. These tumours are closely related to serum Alpha fetoprotein and Beta HCG levels, which aid in the diagnosis of the disease. Our case was a diagnostic challenge as the bone marrow studies revealed features of Acute Megakaryocytic Leukemia morphologically, but had inconclusive Immuno-Histochemistry and Flow Cytometry on two instances. It was only after a review of the slides was done with the intention to look specifically for Megakaryocytic precursors that the tissue diagnosis was achieved. It was a tricky task to manage this patient as he had persistent thrombocytopenia requiring frequent platelet component therapy in order to initiate chemotherapy. He eventually developed chemotherapy related febrile neutropenia which progressed to sepsis with septic shock and he succumbed to his illness after nearly 10 weeks from the time of first clinical suspicion diagnosis. Our extensive review of literature of the association between non seminomatous mediastinal germ cell tumours and Acute Myelocytic Leukemia revealed a total of 26 such cases reported since 1946. Out of these cases, 26 were males while the sex of 6 was not known. The median age of presentation with this malignancy has been found to be 23 years (15-46 years) with an average time to diagnosis being 09 weeks (2-39 mths) and a median time to death being 06 months. Out of these cases there has been only one survivor reported who underwent allogenic bone marrow transplant. The prognosis of these patients has been found to be poor even after timely diagnosis and initiation of treatment. The review of literature also revealed that most of the cases succumbed to chemotherapy related complications.

Conclusion

To conclude, Mediastinal Non Seminomatous Germ Cell Tumours with Acute Megakaryocytic Leukemia (AML M7) is a rare combination of dual malignancies which affects the young male population and has a poor prognosis.

References


Fig. 2: Peripheral blood smear showing a blast with peripheral blebbing of the cytoplasm suggestive of a megakaryocytic lineage

Fig. 3: Bone marrow biopsy showing proliferation of megakaryoblasts