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Case Report

A rare case report of 27-year-old young male with synchronous testicular non seminomatous germ cell tumour and acute myeloid leukemia

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Abstract

Non-seminomatous germ cell tumors have been not more frequently linked to Acute Myeloid Leukemia (AML) (M7), a rare form of primary AML. Review of literature regarding the case has shown that there were 26 case reports of concomitant mediastinal non seminomatous germ cell tumors in the last seven decades. However not a single case of testicular germ cell tumour with acute myeloid leukemia was reported making this case report rare of its kind. Here, we described a rare instance of dual malignancy that was treated at our center, synchronous testicular non- seminomatous germ cell tumour and acute myeloid leukemia (M7), which led to the patient's death as he was unable to tolerate chemotherapy.

Keywords: Synchronous testicular, Non-seminomatous germ cell tumour (NSGCT), Acute myeloid leukemia, Chemotherapy.

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1. Introduction

Testicular neoplasm is the most common solid malignancy in males between the ages of 15 to 35 years and the incidence has increased significantly over the last two decades. Germ cell tumors are the predominant primary category of testicular neoplasms. The non-seminomatous germ cell tumor (NSGCT) is the type of testicular cancer most commonly associated with metastasis, with the lungs, liver, central nervous system, and bones being the primary sites affected, listed in order of prevalence.[1] Hematological malignacies in germ cell tumours are extremely rare and are associated with poor prognosis.[2] In the existing literature germ cell tumours are frequently associated with AML with Megaloblastic differentiation. However case reports of germ cell tumours along with myelodysplastic syndromes, malignant histiocytosis, myeloproliferative neoplasms, and acute lymphoblastic leukemia are also reported.[3-9] The case reports documened about synchronous germ cell and hematological tumours indicate a poor prognosis, with only one survivor reported to date in the literature. But, there are no documented cases in the literature concerning the combination of synchronous testicular non-seminomatous germ cell tumour and acute myeloid leukemia.

We report a unique case involving a young male diagnosed with both synchronous testicular germ cell tumor (GCT) and acute myeloid leukemia (AML).

2. Case Presentation

A 27-year-old male had painless testicular swelling which was gradually increasing in size for 3 months. Ultrasound scrotum and CECT (Contrast-Enhanced Computed Tomography) were done which showed features suggestive of testicular tumour. Serum markers alpha feto protein (AFP), beta human chorionic gonadotropin and lactate dehydrogenase were elevated – confirming Non seminomatous germ cell tumour. He underwent left high inguinal orchiectomy (size of tumour 4 x 3 cms) at local hosptital. He was subsequently referred to our hospital for additional evaluation and treatment. Surgical pathology slides and blocks were reviewed which showed have mixed

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germ cell tumor (seminoma, yolk sac and mature teratoma). Serum tumour markers which were repeated showed high LDH 580 IU/ml, High AFP (alpha feto protein)-1160 ng/mL and high beta - hCG 1160 Miu/ml. In view of high tumour marker levels despite of surgical debulking we have done a complete staging work up again at our hospital which included a CECT Chest and CECT Abdomen. Histolpathological slides and their descriptions are mentioned in the figures (**Figure 1** A, B). CECT Chest showed mildly enhancing enlarged conglomerated left supraclavicular nodes measuring 3.6 cm and a conglomerated left anterior mediastinal mass with enhancing intra lesional neovascularity measuring 7.5 x 5.6 cm (**Figure 2** A). A multifocal hypodense lesion was detected in the spleen, with the largest measuring 4.5 x 4 cm, suggestive of metastasis. Peripheral subpleural enhancing hypodense lesion (5.8 x 4 cm) in segment VI / VII of liver (**Figure 2** B, C). Here primary tumour is testicular tumour.

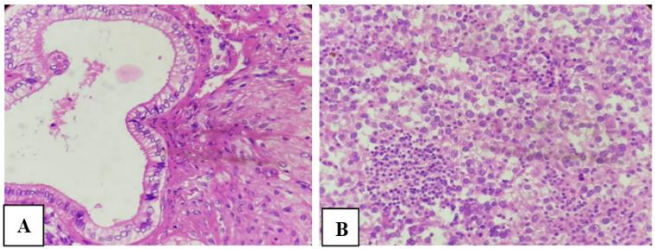

Figure 1: **A**) Teratoma component; **B**) Seminomatous component

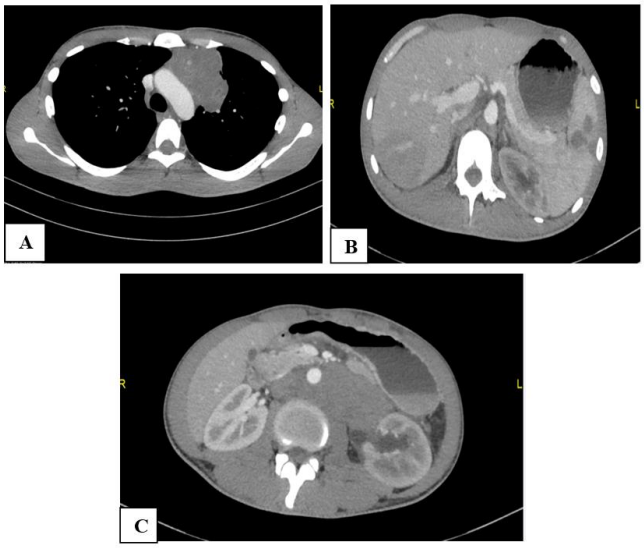

Figure 2: A): CECT Chest showed mildly enhancing enlarged conglomerated left supraclavicular nodes and conglomerated left anterior mediastinal mass with enhancing intra lesional neovascularity. **B, C):** Peripheral subpleural enhancing hypodense lesion in segment VI / VII of liver

3. Treatment Course

After reviewing previous reports he was diagnosed as Non seminomatous germ cell tumour-poor risk. Patient and his attenders were explained about disease its prognosis and complications associated with the treatment. He was planned for chemotherapy with 4 cycles of Bleomycin Etoposide and Cisplatin. Before 1st cycles of chemotherapy, he underwent complete blood picture, renal function tests, liver function tests and pulmonary function tests. He was also advised for semen preservation but patient did not undergo any fertility preservation procedure due to logistical reasons. Informed consent was taken and he underwent 4 cycles of BEP without any serious adverse events. CBP, RFT, LFT and Serum Tumour Biomarkers were repeated before each cycle-proceeded with next chemotherapy only if the values were normal for 4 chemo cycles, Beta hCG and AFP levels reduced but LDH increased to 14129 IU/ml. Line plots of serum tumour biomarkers are depicted (**Figure 3** A, B,C).

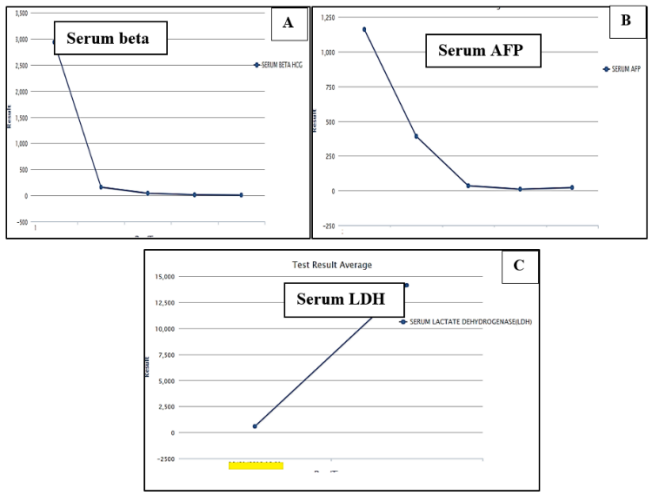

Figure 3: A): Beta hCG with each cycle of chemotherapy; **B**): Serum AFP with each cycle of chemotherapy; **C**): Serum LDH with each cycle of chemotherapy

4. Re-evaluation for Residual Disease

CECT CHEST and Abdomen done to assess residual disease status for further need of resection. On re-evaluation scan (6 weeks after last chemo) shown response in mediastinal mass.(3 x 3 cms) CBC has been repeated which was showing low hemoglobin, persistent thrombocytopenia. He underwent bone marrow aspiration in view of persistent pancytopenia and biopsy showing acute leukemia-Acute Myeloid leukemia (M7). Trephine section of bone marrow had megakaryoblasts are medium / large cells with blue vacuolated, agranular, basophilic cytoplasm containing free granules, cytoplasmic projections (blebs and pseudopods) (**Figure 4** A, B). Immunotyping showing dim 45 expression with presence of CD 34, CD 41 and CD61 in blast population (**Figure 5**). MPO and other myeloid markers were negative. Antigens associated with both B and T lineages were found to be absent. Diagnosis of Acute megakaryoblastic Leukemia (M 7) was rendered. His karyotyping has been done and which was complex karyotype (**Figure 6**).

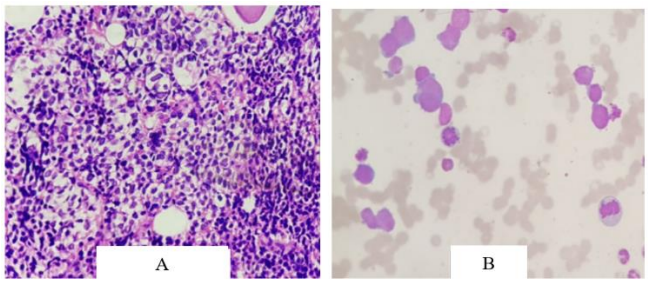

Figure 4: **A**) and **B)**: Trephine section of bone marrow showed megakaryoblasts are medium / large cells with blue vacuolated cytoplasm containing free granules, cytoplasmic projections (blebs and pseudopods)

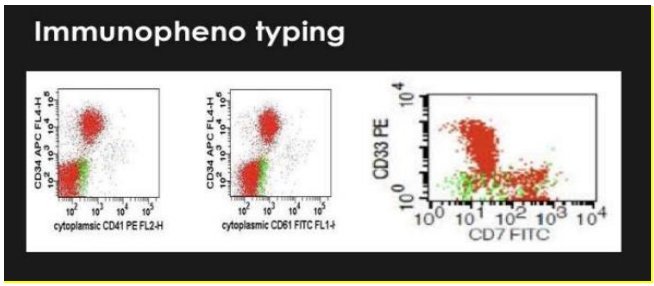

Figure 5: Immunophenotyping suggestive of AML –M7

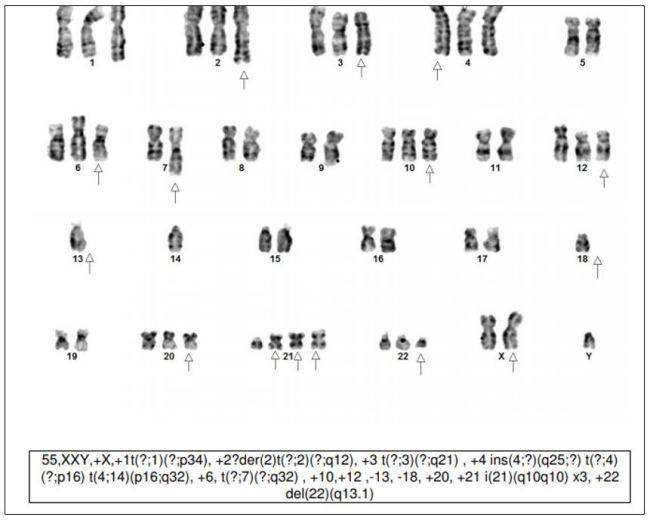

Figure 6: Karyotyping suggestive of complex type

5. Further Treatment

Patient has received multiple blood transfusions with packed red cell volume and platelets. He couldn't able to tolerate chemo (induction 7+3) and died after two weeks of supportive treatment.

6. Discussion

This case is testicular germ cell tumor which presented with anterior mediastinal mass. Here as tumor markers were raised at presentation so no biopsy has been done from mediastinal mass. In literature, testicular germ cell tumor post treatment developing AML in less than 6 months has not been described. This is unique presentation what was present in this case. There are no documented cases in the literature concerning the combination of synchronous testicular non-seminomatous germ cell tumour and acute myeloid leukemia. More commonly association is with Mediastinal GCT and moreover it is with metachronous association.

The prognosis for primary nonseminomatous mediastinal germ cell tumors (mGCTs) in the absence of hematogenous metastases (HMs) is unfavorable, with a 5-year overall survival rate of 45%. In contrast, pure seminomas exhibit a significantly higher survival rate of approximately 90%, irrespective of their primary site.[10,11] Furthermore, patients diagnosed with mGCT and associated HMs face a dire prognosis, with a median OS of merely 5 months.[12] The conventional chemotherapy for germ cell tumors (GCT) proved to be largely ineffective in this instance. Additionally, the induction therapy for acute myeloid leukemia (AML) did not enhance the mGCT, resulting in its further enlargement. The thrombocytopenia associated with acute myeloid leukemia (AML) complicated the administration of chemotherapy for the malignant germ cell tumor (mGCT).[13] In terms of the treatment strategy, a multimodal approach was employed, which included hematopoietic stem cell transplantation for AML and surgical resection for the germ cell tumor. In addition to multitargeted therapy, novel targeted therapies based on the molecular abnormalities may be required to improve the dismal prognosis.[14-18]

AML may well represent malignant transformation of hematopoietic tissues within GCT without any influence of chemotherapy. A common clonal origin was long hypothesized given the temporal relationship between the two malignancies, and recent research has effectively shown the presence of conserved isochromosome 12p rearrangements along with somatic point mutations.[19] This is because isochromosome 12p is the most common chromosomal abnormality in GCTs, but is exceptionally rare in AML without mGCT association.[20-21]

7. Conclusion

Individuals diagnosed with germ cell tumors face a significant risk of developing acute leukemia. The short interval between these two disease entities in relation to biological and molecular etiology remains unclear. Even treatment wise need for research and needs long term follow up and research on targeted therapy warranted.

8. Source of Funding

No funding sources.

9. Conflict of Interest

None declared.

10. Ethical Approval

Not required.

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