An exceptional case report on acute myeloid leukemia affecting four members of the same family

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Introduction

Familial leukemia is uncommon. A few genes transmitting lymphocytic leukemia both acute and chronic have still been reported however, descriptions of inherited myelogenous leukemia are still rarer.(1) It has been researched in many studies that some sort of inherent genetic mutations in a particular family may predispose it to develop hematopoietic malignancies specially leukemias. As also, in particular to acute leukemia, it has been proven that twins especially monozygotic thereby of same sex develop leukemia. This association gives clue to the investigators to study some inherent genetic link to acute leukemia in children. Similar associations have been studied for leukemia in complete & it has been observed that persons with family history of leukemia have two to three times higher risk of getting affected by it.(2)

We report one such rare case report of three members of the same family who were affected by acute myeloid leukemia (AML).

Case Report

A female patient aged 65 yrs (case 1) her two sons and, reported to the hospital with complaints of recurrent fevers and malaise with generalized fatigue. On examination, there was evidence of pallor, spleenomegaly, hepatomegaly &gum hypertrophy was evident. Investigations suggested were complete blood count (CBC), peripheral blood smear (PS). The results are shown in the following chart (Table 1). The patient was confirmed with acute myeloid leukemia (AML) & expired within 6 months with treatment. Two years later, her son aged 45 yrs (case 2) came to the hospital OPD with similar complaints and subsequently next year her second son 52 yrs (case 3) reported to us. Both were diagnosed with AML and did not survived for more than a year.

Following is the chart showing absolute blood counts of all the three patients-

Cases	**Blood** TLC, DLC, Plts	**Investigations** Peripheral blood smear	**Bone marrow aspirate**
Case 1	TLC- 1,52,000/cumm DLC-Myeloblasts ++ 52% Platelets- 1,10,000	R.B.C's –Normocytic, Normochromic W.B.C- Myeloblasts 52%	Myeloperoxide staining showed blast cells of Myelo monocytic lineage confirmes AML (M4 subtype)
Case 2	TLC- 1,28,000/cumm DLC-Myeloblasts ++ 45% Platelets- 1,25,000	Same as Case 1	Showed poorly differentiated Monoblasts confirmed AML (M5 subtype)
Case 3	TLC- 1,00,000/cumm DLC-Myeloblasts ++ 49% Platelets- 1,25,000	Same as case 1	M 4 subtype

Discussion

The above case report describes genetic predisposition for leukemia, which has thereby taken a familial form. Very recently, a study done by Ram J et al.(3) identified mutated CCAAT/enhancer-binding protein-a (CEBPA) resulting from germ line CEBPA mutations as a causative factor for familial acute myeloid leukemia (AML).

These mutations cause abnormal increase in the yield of a short protein isoform termed p30. The interference of this short protein with the normal full length protein synthesis leads to AML with near complete penetrance. His study concluded the importance of genetic analysis and germline testing in patients with family history of AML, as these mutations are not very rare and their prevalence according to latest researches is about 7% and 11%. Familial AML is an autosomal dominant type and occur at much younger age as compared to other forms of AMLs. Not much is known about the condition as very few cases are being documented.(3,4) The first family was reported by Smith et al.(5) with three members, in two generations of the family suffered with AML. The investigations showed a consistent mutant CEBPA protein in the germline of the

patients. Most of the patients had FAB M1 or M2 subtypes in contrast to our case where mostly the patients had M4 & M5 subtype.[3] One more finding in our case report was the poor prognosis of the patients with the disease. In the extensive review by Owen C et al, they stated that patients with familial AML were having good prognosis irrespective to relapse but unfortunately in our case, there was loss of all the three patients within six months under treatment.[4]

Conclusion

Familial AML or types of myeloid malignancies occurring in familial patterns should be reported as it can help in investigations regarding germline mutations or inherited mutations running in the families and thus new treatment targets can be designed. Moreover, the case also sheds light on the importance of family history taking and suggests preventive screening of complete family members for such gravid familial diseases.

References

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