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MYELOID BLAST CRISIS OF CHRONIC MYELOID LEUKAEMIA- A CASE STUDY

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ABSTRACT

Chronic Myeloid leukemia is a slowly progressive disease which affects Bone marrow, where multiple White blood cells are produced. Blast crisis (BC) is still the most difficult aspect of managing chronic myeloid leukemia (CML). In chronic phase survival rate in average is considered to be 25 to 30 years. The first line therapy in chronic myeloid leukemia is Imatinib which is also a standard therapy due to its exceptional effects and mild toxicity, however in some cases the therapy may be a failure due to poor hematological response, in that case second line TKI agents are administered also in certain cases Bone Marrow Transplantation are preferred. We present a case study of a patient with chronic myeloid leukemia – Blast crisis in a south Indian hospital.

KEYWORDS: Chronic myeloid leukemia (CML), Imatinib, Blast crisis(BC), TKI (Tyrokinase Inhibitors)

INTRODUCTION

Leukemia is considered to be cancer of White Blood Cells, which functions as necessary in fighting infection.[1] The chronicity of leukemia reflects the age of the abnormality in cells, which might be immature (similar like stem cells) or mature (resemble white blood cells). Chronic leukemia can be partly or completely mature.[2] These cells look comparatively normal, but they are not. Chronic Myeloproliferative neoplasm or Chronic Myeloid leukemia is a slowly progressive disease which affects Bone marrow, where

multiple White blood cells are produced.[1] In 2013 a data indicates that 6677 Indian patients were identified with CML and were reported to be under treatment at various cancer centers.[3] The major symptoms are weight loss, fatigue, sweating at night, Anemia and splenomegaly. If not properly treated it may lead to the following phases Biphasic/Triphasic Natural course. After the initial chronic indolent phase, then comes the accelerated phase which is the blast phase leading to genetic Instability, damage and repair of DNA. Multiple Mutations occurs during blast phase.[4] It is also represented by percentage of blasts in blood and bone marrow. ≥ 20% blast in blood defined as Blast crisis by World Health Organization. In chronic Myeloid leukemia blast crisis is detected rarely.[5] In chronic phase survival rate in average is considered to be 25 to 30 years. A Non Random pattern in blast crisis shows more chromosomal abberations where mutations are 80%.[6] The first line therapy considered in chronic myeloid leukemia is Imatinib which is also a standard therapy due to its exceptional effects and mild toxicity. Imatinib is a Tyrokinase Inhibitor (TKI) that can help patients with chronic myeloid leukemia achieve long-term cytogenic and hematological remissions. Unfortunately, functional resistance to TKI develops in a considerable proportion of individuals. In CML, recognizing this resistance is critical because the effect of some mutations can be mitigated by increasing Imatinib dosage. Tyrosinase kinase domain mutations include around a hundred distinct variations. The T3151 mutation, in which Threonine is changed to Isoleucine, is the most prevalent.[7] The quality of life and survival rate can be greatly improved if treated early in the chronic phase and chemotherapy is adhered by patients properly. We present a case study of a patient with chronic myeloid leukemia – Blast crisis in a south Indian hospital.

CASE PRESENTATION

We are presenting a case of 49 year old male, ex smoker and alcoholic evaluated for left hypochondrial pain and found to have spleenomegaly of 15cm. He was found to have a total count of 3.2 lakh, and also diagnosed with chronic myeloid leukemia-Chronic phase, Break point cluster Region, ABL positive, EUTOS (European Treatment and Outcome Study) score 92 (high risk).Patient was started on Imatinib 400mg OD in October 2020. At three month evaluation patient had attained complete hematological response but quantitative BCR (Breakpoint Cluster Region) ABL RTPCR showed 19.77%. He was continued on Imatinib and revaluated at 6 months, at which time he was found to have BCR ABL, RTPCR quantitative of 3.13%. He was planned for Bone marrow evaluation with cytogenetics and RTPCR but in view of COVID crisis, Imatinib was continued. At 12 months starting

treatment he presented with rising WBC Counts and was advised reevaluation and IRMA Study, Imatinib dose was hiked to 600mg OD. Patient responds with a poor compliance and non adherence to treatment. Within a month, patient developed symptoms like chronic cough followed by dysphagia, loss of sleep, loss of appetite, weight loss, fever, vomiting and abdominal swelling due to the lack of a complete hematologic response. At this last admission its is found that the Patient presented with Myeloid Blast crisis.

Table 1: Flow Cytometry Report of the patient.

MYELOID MATTER		**T AND NK CELL MARKERS**		**OTHER MARKERS**	
CD 13	**POSITIVE**	CD 2	NOT DONE	CD 23	NOT DONE
CD 14	**NEGATIVE**	CD 3	**NEGATIVE**	CD 25	NOT DONE
CD 33	**POSITIVE**	CD 4	**DIM POSITIVE (in subject)**	CD 34	**POSITVE**
CD 61	NOT DONE	CD 5	**NEGATIVE**	CD 41	NOT DONE
CD 64	**NEGATIVE**	CD 7	**NEGATIVE**	CD 36	**NEGATIVE**
CD 117	**DIM POSITIVE (in subject)**	CD 8	**NEGATIVE**	CD 200	NOT DONE
Anti MPO	**POSITIVE**	CD 56	NOT DONE	CD 138	NOT DONE
CD 11C	**POSITIVE**	CyCD3	**NEGATIVE**	CyCD41	NOT DONE
CD 11b	NOT DONE	AntiTdT	NOT DONE	FMC7	NOT DONE
B CELL MARKERS		TCrab	NOT DONE	HLA DR	**NEGATIVE**
CD 10	**NEGATIVE**	CD 1a	NOT DONE	Anti –Kappa	NOT DONE
CD 19	**NEGATIVE**			Anti lambda	NOT DONE
CD 20	**NEGATIVE**			GLY:PHO	NOT DONE
CyCD79a	**NEGATIVE**				

+ve/-ve Results were determined on 45% of the gated events on light scatter points. Picture is compatible with Myeloid Blast crisis of chronic myeloid leukemia. Patient shifted to another health care facility where on admission the Total leukocyte count was 104x 10^3/µl and Platelets were 26000/µl, CT chest shows fungal pneumonia, IV antibiotics were given to eliminate the infection. Imatinib Resistant Mutation Analysis (IRMA) studies were reconducted for this patient and the result is negative. Treatment recommendation as guided by oncologist according to NCCN guidelines version 4.2018 are as follows.

Table 2: Treatment recommendation as per NCCN guidelines.

MUTATION	**TREATMENT RECOMMENDATION**
Y2453H, E255K/V or F359V/C/I	**Dasatinib**
F317L/V/I/C, T315A or V299L	**Nilotinib**
E255K/V, F317L/V/I/C, F359V/C/I T315A or Y253H	**Bosutinib**
T315I	**Ponatinib**
T315I	**Omacetaxine**

DISCUSSION

After extensive counseling by the oncology professionals the compliance level is found to be far great also the patient is recovering well. Chemotherapy with second line TKI agents of one session is completed, blood transfusion is done for the patient during chemotherapy and the patient has better compliance for treatment and food. The doctors have planned for AML like induction with second line TKI (based on IRMA Results) and considered allogenic Bone marrow Transplantation if a matching sibling donor is available.

CONCLUSION

This case study emphasizes the importance of a medication adherence throughout the therapy; Poor compliance in therapy may lead to relapse of the leukemia which will be the more complicated for providing therapy.

ETHICS APPROVAL AND INFORMED CONSENT

The Mother and wife of the patient gave consent for publication of this case report, spoken and written.

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