Hydroxyurea refractory Chronic Myeloid Leukemia treated with Imatinib

Bishnu D. Paudel, MD
Fellowship in Hemato-Oncology, USA

ABSTRACT
Chronic Myeloid Leukemia (CML) is a form of leukemia. Historically, it has been treated with chemotherapy like hydroxyurea, interferon and bone marrow transplantation. But at present imatinib has emerged as front line drug for CML especially on chronic phase. A lady of 48 years with diagnosis of CML refractory to Hydroxyurea treatment presented with progression of disease. After confirming diagnosis by cytogenetic analysis she was treated with Imatinib therapy which has improved her clinically, hematologically and cytogenetically.

INTRODUCTION
Chronic myelogenous leukemia (CML) is an acquired abnormality that involves the hematopoietic stem cell. Chronic myeloid leukemia (CML) accounts for 20% of all leukemias affecting adults. It typically affects middle-aged individuals. It is characterized by a cytogenetic aberration consisting of a reciprocal translocation between the long arms of chromosomes 22 and 9; t(9;22).[1] Generally, 3 phases of chronic myeloid leukemia (CML) are recognizable. Most patients are diagnosed while still in the chronic phase. This phase varies in duration depending on therapy used. It usually lasts 2-3 years with hydroxyurea therapy, but the chronic phase has lasted for longer than 9.5 years in patients who respond well to interferon therapy. Furthermore, the addition of imatinib in recent years has dramatically improved the duration remissions.

CASE REPORT
A lady of 48 years who is school teacher by profession presented to emergency with breathlessness, abdominal pain and discomfort. On general examination she was conscious and oriented to time place and person. She was pale looking and had bilateral pedal edema. Her systemic examination revealed hepatosplenomegaly. History taking revealed that she was on Hydroxyurea since 2001 for CML. Blood and bone marrow report at that time was suggestive of CML on chronic phase(high wbc with features of left shift TLC 66,500; Polymorph 58%;Lymphocytes 13%; Myelocytes 15% and metamyelocytes 10%; Basophils 4% and Blast % was less than 1% in blood and bone marrow).

Her present blood (leukocytosis with left shift wbc 29,000; Hb 7%; Plateletes 79,000) and bone marrow report (6 % blast) was suggestive of CML in Accelerated Phase (Figure 1 & 2). Her blood sample was positive for Philadelphia Chromosome by FISH technique. USG abdomen recorded hepatosplenomegaly(liver 19.2cm; spleen 25.1cm).

Oral Imatinib was started as 400mg/day after supportive and symptomatic treatment. At present she is on 400mg /day which has already induced complete hematological, clinical remission and cytogenetic remission. Dose will be increased up to 600mg/day if she can tolerate but till now she is finding difficult to tolerate the 400mg/day dose. Sometimes we have to reduce the dose of imatinib and occasionally we have to stop the imatinib due to low neutrophil count. At this time, the duration of therapy is unclear. Few patients have discontinued the imatinib therapy, after they attained complete remission including the molecular
one. But this has usually resulted in relapse. Thus, until further evidence becomes available, she should continue imatinib therapy indefinitely.

In a randomized trial imatinib mesylate was compared with interferon plus cytarabine which was standard treatment of CML before imatinib. After 5 years' median follow-up, imatinib induced complete cytogenetic responses in more than 80% of newly diagnosed patients; in addition, the annual rate of progression to accelerated phase or blast crisis dropped from 2% to less than 1% in the fourth year on the imatinib arm.[3]

Even in patients who were previously treated with interferon and whose treatment failed or who were unable to tolerate therapy, a complete hematologic remission was achieved in 88% (532 patients), with a major cytogenetic response in 49% of patients.

Different studies have clearly shown that Imatinib has better response as first line and second line chemotherapy in CML. This hydroxyurea refractory case was also treated with imatinib after confirming the diagnosis by cytogenetic analysis. It is important to note that Glivec International Patient Assistance Program (GIPAP) provides Glivec (Imatinib) at no cost to poor patients in developing countries including Nepal. She is getting Glivec from Patan Hospital but patients can get Glivec from B.P. Koirala Memorial Cancer Hospital, Chitwan, also.

CONCLUSION

From this case study we can conclude that all suspected CML patients should undergo cytogenetic analysis to detect Philadelphia chromosome. If the diagnosis is confirmed as Philadelphia positive CML then we should recommend all patients for Imatinib therapy. This drug is the best option for a country like Nepal where stem cell transplant is not available.

REFERENCES: