Clinical Use Of Ponatinib In Mixed Lineage Acute Leukaemia Associated With T 8:22

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Letter to the Editor

The 8p11 myeloproliferative syndrome (EMS) is a rare and aggressive haematological neoplasm caused by rearrangements involving fibroblast growth factor receptor 1 (FGFR1) gene on chromosome 8p11. Involvement of t 8:22/ BCR-FGFR1 is extremely rare and presents as a chronic myeloid leukaemia – like disease rapidly evolving into acute leukaemia [1,2]. The cell origin of EMS is a very early progenitor cell retaining the potential for both myeloid and lymphoid differentiation. The prognosis is poor and there are no documented cases of complete remission after conventional chemotherapy. A number of FGFR1 inhibitors have shown promising in vitro activity in this condition but none have shown significant clinical responses [3,4]. Ponatinib, a potent pan – FGFR1 inhibitor has shown potent in vitro activity and is clinically available [5].

I present the case of a 48 year old lady who presented with an abnormal blood count WBC 75 × 10^9/l Hb 10.5 g/l Platelets 9 × 10^9/l. The blood film looked like blastic phase CML with 20% blasts, left shifted neutrophilia and basophilia. Examination of 16 metaphases revealed t 8:22. Flow cytometry showed two blast cell populations of myeloblasts (6.6%) and CD 20 negative lymphoblasts (13%). She was induced with hyperCVAD/MA resulting in clearance of blasts from the marrow aspirate. A second inductio with FLAG/Ida was carried out and she went on to receive two further cycles of FLAG. Immunologically, the lymphoblasts were cleared but the myeloblasts persisted at low but stable levels and she eventually developed overt acute myeloid leukaemia. It was at this stage that ponatinib was introduced with the aim of achieving a remission period long enough for her to undergo a sibling allogeneic transplant. However there was no response and she died of progressive disease.

This case demonstrates the biphenotypic nature of the leukaemia associated with t8:22. It also documents the failure of clinical activity of ponatinib. Although stem cell transplantation is the only curative option, in almost all cases there is a failure to attain a durable remission with both conventional chemotherapy, PDGF1 inhibitors and tyrosine kinase inhibitors even when these are used in combination.

References