Pediatric CML presenting in Mixed Phenotypic Blast Crisis: A Rare Occurrence

Pediatric CML comprises 3% of childhood leukemias. Similar to adults, most of the patients present in chronic phase but 5% may present in blast crisis (BC). Mixed phenotypic blast crisis has rarely been reported in children. A ten year male presented with fever, fatigue and dull abdominal pain and massive splenomegaly for two months. Complete Blood Count - Total leukocyte count (TLC) 544 x10^9/L, Hemoglobin 8 g/dl and platelet count 80 x10^9/L. Differential count on peripheral smear - blasts 25%, promyelocytes-03%, myelocytes-20%, metamyelocytes - 10%, eosinophils-05%, basophils- 04%, monocytes-02%, lymphocytes-16% and neutrophils-15%. No dysplasia was noted. The blasts had moderate cytoplasm and prominent nucleoli. On cytochemistry, these blasts were negative for Myeloperoxidase and Periodic acid Schiff’s. Bone marrow aspirate revealed a hypercellular marrow with myeloid predominance (M: E ratio-25:1) with 55% blasts. Megakaryocytes were adequate with some dwarf forms. Bone marrow biopsy was hypercellular with near total replacement of marrow spaces with sheets of blasts having vesicular nuclei and prominent nucleoli (Fig 1). Blasts were positive for CD34, anti-MPO, CD19 and CD20 (Fig 1) and negative for CD3. Considering the high TLC, peripheral blood and bone marrow picture, RT-PCR for \( M-BCR-ABL1 \) was done which confirmed presence of 210 kd transcript. Considering the clinical presentation, peripheral blood picture (basophilia, many myelocytes and metamyelocytes) and a 210kd \( BCR-ABL1 \) transcript, a diagnosis of mixed phenotypic blast crisis in CML was rendered and treatment initiated with Imatinib. Subsequently, the patient improved with lowering of TLC and disappearance of blasts from peripheral blood, however a molecular response on follow up could not be done due to economic constraints.

The incidence of progression to BC in adults is 10% but the same is not well known in children. Usually, blast crisis is myeloid and rarely mixed phenotypic. The biology of progression of pediatric CML to BC is supposed to be similar to that of adults.
of additional chromosomal anomalies in the proliferating clone especially deletions in CDKN2A/B gene, deletions in IKZF gene and chromosomal aberrations associated with myelodysplasia have been implicated with progression. \[5\] Mixed phenotypic BC in CML needs to be differentiated from de novo mixed phenotypic acute leukemia(MPAL). Differentiation may be difficult since MPAL can also show $M$-$BCR$-$ABL1$ translocation. \[6\] The points in favour of CML include high TLC at presentation, massive splenomegaly, peripheral blood basophilia and all myeloid precursors, absence of dysplasia, and p210kd transcript on PCR. In such cases if $M$-$BCR$-$ABL1$ fusion signals are detected by FISH/PCR in mature neutrophils as well as in blasts (present in our case) then CML-BC is the most likely diagnosis. \[3\] Moreover, in a case of MPAL, if post induction RT-PCR shows high number of abl-bcr transcript despite reduction in blast count, the diagnosis of BC in CML should be considered. The progression to blast phase warrants a poor prognosis in CML which is further worsened by the presence of mixed phenotypic type of blast crisis. \[3\] Such cases should be treated with Tyrosine kinase inhibitors plus chemotherapy based on the blast phenotype.\[4,7\]

References:

3. Woojin Choi, M.D., Myungshin Kim, M.D., Jihyang Lim, M.D., Kyungja Han, et al. 4 Cases of CML in MP BC at Initial Presentation Mimicking MPAL with t (9;22). Ann Lab Med 2014; 34:60-63
Figure Legends –

Figure 1A – BM biopsy showing hypercellular marrow; H & E; 100X
Figure 1B – BM biopsy showing blasts with prominent nucleoli; H & E; 400X
Figure 1C – BM biopsy showing CD34 positivity in blasts; 400X
Figure 1D – BM biopsy showing anti MPO positivity in blasts; 400X
Figure 1E – BM biopsy showing CD19 positivity in blasts; 400X
Figure 1F – BM biopsy showing CD20 positivity in blasts; 400X