CORRESPONDENCE

APL-The Age-Old Harlequin: Do We See it All?

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Dear Sir,

Acute promyelocytic leukemia (APL) is a unique type of acute myeloid leukemia characterized by distinct cytomorphological features, immunophenotype, molecular rearrangement t(15;17) involving the PML and RAR α genes and a very good response to all-trans retinoic acid (ATRA) [1]. However in rarity of cases, no evidence for rearrangement of RAR α is found indicating that alternative mechanisms could mediate the differentiation block that typifies this disease. Here we describe a case of APL, with classical morphological and immunophenotypic features, which was of interest because of presence of isochromosome(17) along with the absence of rearrangement of RAR α . APL hence always proves to be a harlequin that takes various molecular and morphological masquerades.

An 11-year-old male child presented at our centre with high grade fever and cervical lymphadenopathy for 2 months duration. Baseline laboratory investigations showed TLC of 14,800/ μ L with 85 % abnormal promyelocytes with hemoglobin of 7.7 gm% and platelet count of 20,000/ μ L (Fig. 1). On flow cytometry, abnormal promyelocytes were positive for cMPO, CD117, CD13, CD33, CD9, CD64 and CD65. These cells were negative for CD34, CD2, cCD79a, CD3, CD11b, CD18, CD14, CD38, CD56, CD4 and HLA-DR. A diagnosis of APL was made and genetic studies performed. RT-PCR was negative for PML–RAR α fusion transcript. Metaphase karyotyping

revealed 45–48,XY,i(17)(q10), –6, +8, –14, –21, +21[cp10] (Fig. 2). ATRA based combination chemotherapy with Daunomycin was given. Patient was in morphological remission at day 28 of induction and at the end of first consolidation cycle. After completion of consolidation phase, patient received maintenance therapy and is doing well at a follow up of 4 months.

APL can have varied clinical and morphogenetic presentation. Besides the conventional reciprocal translocation t(15;17)(q22;q21) disrupting the PML and RAR α genes, other chromosomal abnormalities such as t(11;17)(q23;q21), t(5;17)(q35;q12–21), t(11;17)(q13;q21) and der(17) are also observed in APL whereby RAR α is fused to the PLZF, NPM, NuMA, and STAT5b genes, respectively. An isochromosome of the long arm of the derivative chromosome 17 is rarely observed in APL patients. However our case is further rare as no evidence for rearrangement of RAR α was found. Only 3 such cases have been reported previously in literature [2–4]. Two of these three patients responded poorly to therapy and died within a year [2, 4]. The prognosis of third cases is not known [3]. Our case responded to standard doses of ATRA and BM was in morphological remission at day 45. Consolidation and maintenance was uneventful and is doing well on maintenance. The present case hence highlights the importance of immune-morphological and genetic basis of APL. These cases can still be managed by ATRA which shows that differentiation block by any molecular mechanism in APL can still be overcome by its therapeutic doses as in our case. Management and prognosis of such patients remains unknown as there is not much literature on management of such patients. The lack of independent prognostic value of additional chromosomal abnormalities in APL does not support the use of alternative therapeutic strategies when such abnormalities are found [5]. ATRA however remains

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Fig. 1 Metaphase karyotyping showing 45–48,XY,i(17)(q10), –6, +8, –14, –21, +21[cp10]

Fig. 2 Abnormal promyelocytes on peripheral smear of the patient

the mainstay drug as in our case. These cases help our understanding of pathogenesis APL better. Absence of $RAR\alpha$ transcript does not necessarily mean absence of

APL. It definitely signifies an alternate mechanism of pathogenesis unknown still to us.

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