A rare case of B-cell chronic lymphocytic leukemia with t(2;14)(p13;q32), +X, +11, +12, +13,+der(1p) karyotype

Sir,

Many B-cell lymphomas are characterized by chromosomal translocations most commonly involving the immunoglobulin heavy chain (IgH) locus at chromosome 14q32.[1] The t(2;14) is a rare recurrent chromosomal abnormality that has been identified predominantly in B-cell malignancies, including chronic lymphocytic leukemia (CLL) , acute lymphoblastic leukemia (ALL) and non-Hodgkin's lymphoma.[2-4] To date, only 12 cases of CLL with t(2;14)(p13;q32) have been reported.[5] We describe a case of CLL with a rare karyotype involving t(2;14) and hyperdiploidy. A 65-year-old female presented with fever, fatigue, night sweats and weight loss. Physical examination revealed generalized lymphadenopathy. A complete hemogram showed hemoglobin (Hb) level of 6.3 g/dl with mean corpuscular volume (MCV) 109 fl, reticulocytes 3%, white blood cell (WBC) count 39.5 $\times 10^{[9]}$/l and platelet count 152X10^9. Peripheral blood showed normochromic, normocytic anemia with differential count of neutrophils (61%), lymphocytes (33%), eosinophils (4%) and myelocytes (2%). The lymphocytes were small with scanty cytoplasm. Nucleus of some of these cells appeared cleaved with occasional basket cells. Serum lactate dehydrogenase (LDH) (418 IU/l; normal range: 105–333 IU/l) and b2-microglobulin (2.8 mg/l; normal range: 1.4–1.8 mg/l) levels were elevated. Serum electrophoresis showed a normal pattern with reduced g-globulin fraction. Bone marrow (BM) aspirate was hypercellular marrow with replacement of marrow cells by small lymphocytes and diffuse pattern of BM involvement. Immunohistochemistry showed cells positive for CD20, negative for CD23 and cyclin D1. The standard staging system was followed for clinical staging of the patient.

Immunophenotype of the patient showed expression of CD5, CD19, CD23, dim (weak) intensity of surface immunoglobulin and CD20. The expression was negative for CD3, CD10, CD79b/CD22 and absence of FMC7. The patient was diagnosed as having B-cell CLL. Chromosomal analysis from GTG-banded metaphases revealed hyperdiploidy with 51 chromosomal complements in 80% of the total metaphases scored. The patient's karyotype was 51, XX,+X, +11, +12,

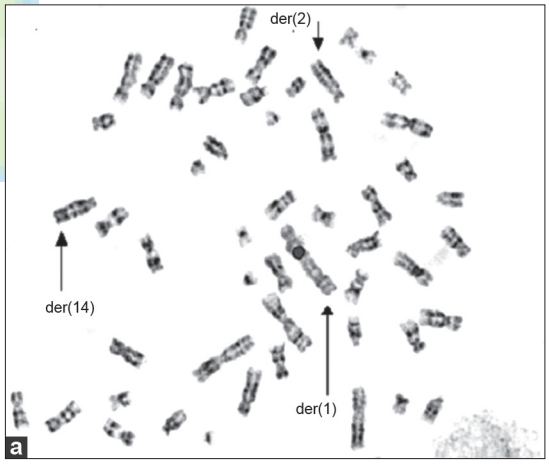

Figure 1a: Metaphase plate showing der(2), der(14) and der(1)

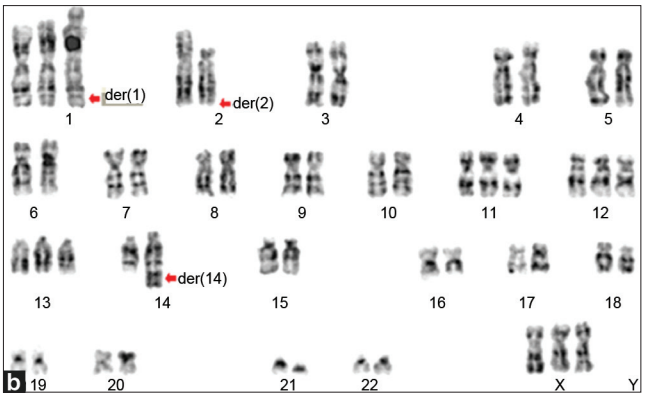

Figure 1b: Karyotype showing t(2;14)(p13;q32)

+13, t(2;14)(p13;q32),+der(1p) [43]/46, XX, t(2;14)(p13;q32) [6]/46, XX [6] [Figures 1a and b]. The patient was started on fludarabine, cyclophosphamide, rituximab (FCR) therapy. After 2, 4 and 5 cycles of FCR therapy, the clinical and hematological pattern did not change and the patient's BM aspiration showed B-cell CLL. Patient was died after 140 days with the disease.

Immunophenotype of the present case was suggestive of atypical B-cell CLL and associated with t(2;14)(p13;q32). This is the first case of chromosomal abnormality t(2;14)(p13;q32),+X, +11, +12, +13,+der(1p) with a rare karyotype in CLL patients, to the best of our knowledge. Though hyperdiploidy with t(2;14)(p13;q32) was observed in majority (80%) of cells in our case, t(2;14) alone was detected in a considerable number of metaphases (10%), which indicates that t(2;14) is a primary chromosomal abnormality, and as the disease progressed, the additional chromosomal abnormalities might have originated as a secondary genetic event. Though trisomy 12 has been frequently reported in CLL patients, the trisomies 11, 13 and X have not been reported in CLL patients. The karyotypic changes in the present case are considered as poor prognostic feature as the patient did not respond to the treatment after 2nd and 4th cycles of therapy, and the abnormal karyotype persisted and she died after 140 days of initial diagnosis. Hence, the additional chromosomal anomalies are poor prognostic indicators in CLL patients and more intensive therapy is required for the prolonged remission. Recently, Yin *et al.*[5] identified break point at 2p16 using FISH probe in six CLL patients and BCL11A/IgH rearrangement is characterized by atypical morphologic features and unmutated IgVH genes. The accurate analysis of break point regions is important in these patients to know the involvement of IgH genes.

Vundinti BR, Korgaonkar S, Kerketta L, Ghosh K

Department of Cytogenetics, National Institute of Immunohaematology, 13th floor, New Multistoried Building, KEM Hospital Campus, Parel, Mumbai - 400 012, India

Correspondence to: Dr. Babu Rao Vundinti, E-mail: vbaburao@hotmail.com

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