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CASE REPORT

Unusual cytogenetic abnormalities associated with Philadelphia chromosome

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Author contributions: Sharma SK designed and wrote the paper; Handoo A provided the laboratory data; Choudhary D and Gupta N provided the clinical data.

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Abstract

Cytogenetic abnormalities are the hallmark of leukemias. We report here two cases of unusual cytogenetic abnormalities associated with Philadelphia chromosome, one with mixed phenotypic acute leukemia showing monosomy 7 and t(9;22) (q34;q11.2) and the other with chronic myeloid leukemia and additional translocation involving chromosomes 10 and 13. Both patients achieved complete remission following imatinib based treatment.

Key words: Philadelphia chromosome; Cytogenetic abnormalities

Core tip: Cytogenetic abnormalities are the hallmark of leukemias. We report here two cases of unusual cytogenetic abnormalities associated with Philadelphia chromosome, one with mixed phenotypic acute leukemia showing monosomy 7 and t(9;22) (q34;q11.2) and the other with chronic myeloid leukemia and additional translocation involving chromosomes 10 and 13. Both patients achieved complete remission following imatinib based treatment.These two cases highlight the novel additional cytogenetic abnormalities associated with Ph chromosome.

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INTRODUCTION

Cytogenetic abnormalities are the hallmark of leukemias. Translocation (9;22) is the characteristic feature of chronic myeloid leukemia and is also seen in variable number of patients with acute lymphoblastic leukemia. Monosomy 7 is seen in patients with myelodysplastic syndrome, acute myeloid leukemia and few cases of acute lymphoblastic leukemia. Mixed phenotypic acute leukemia (MPAL) is commonly associated with t(9;22) and sometimes with monosomy or deletion 7, but combined cytogenetic abnormality involving t(9;22) and monosomy 7 has rarely been reported in MPAL. We report here two cases, one of MPAL showing monosomy 7 and t(9;22) (q34;q11.2) and the other with chronic myeloid leukemia and additional translocation involving chromosomes 10 and 13. Both patients achieved complete remission following imatinib based treatment.

CASE REPORT

Case 1

A 27 years old man was admitted with weakness and low grade fever for 20 d. On examination he was found to have pallor without lymphadenopathy or hepato-splenomegaly. Hemogram showed hemoglobin 5.8 g/dL, total leukocyte count 62 × 10^9/L with 60% blasts and platelet count 170 × 10^9/L. Flowcytometry revealed two distinct

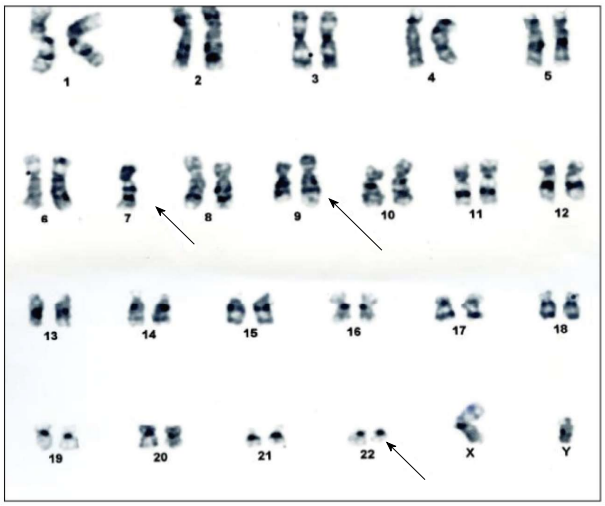

Figure 1 Karyotyping of the patient with mixed phenotype acute leukemia showing (arrows) 45, XY, monosomy 7, t(9;22) (q34;q11.2)[18]/46,XY[2].

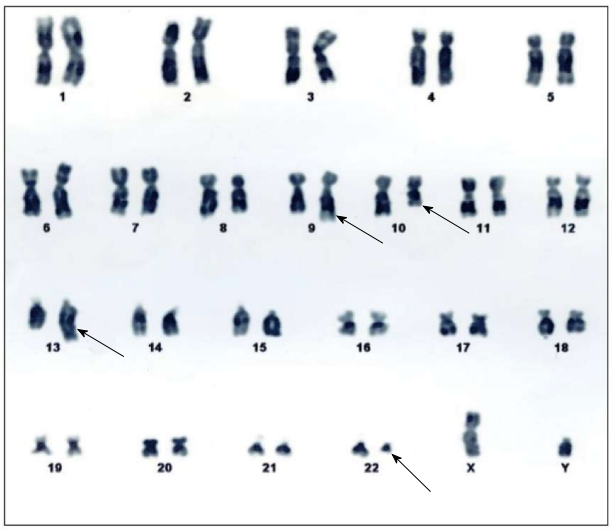

Figure 2 Karyotyping of the patient with chronic myeloid leukemia showing (arrows) 46 XY, t(9;22)(q34;11.2), t(10;13)(q23;q34)[20].

clusters of cells, one expressing CD34, HLD-DR, MPO, CD117, CD13 and CD33. The other cluster of blasts expressed cytoplasmic CD79a, CD19 and CD10. The blasts were negative for surface and cytoplasmic CD3, CD5, CD20 and CD16. The patient was diagnosed as a case of MPAL (Blymphoid/myeloid). Karyotyping revealed 45,XY, monosomy7, t(9;22)(q34;q11.2)[18]/46,XY[2] (Figure 1). RT-PCR for BCR-ABL detected genomic breakpoint at e13a2 corresponding to p210. Patient was treated with hyper-CVAD chemotherapy along with imatinib, which resulted in complete remission.

Case 2

A 50 years old man presented with complaints of mild weakness for 3 wk. His hemoglobin was 10.5 g/dL, total leukocyte count 46.7 × 10^9/L and platelet count 3.6 × 10^9/L, differential count showed neutrophils 62%, myelocytes 10%, metamyelocytes 8%, lymphocytes 12%, monocytes 3%, eosinophils 2% and basophils 3%. Leukocyte alkaline phosphatase was low. Karyotyping revealed 46 XY, t(9;22)(q34;11.2), t(10;13)(q23;q34)[20] (Figure 2). Real-time polymerase chain reaction for BCR-ABL was positive for p210. He was diagnosed as chronic myeloid leukemia-chronic phase and treated with imatinib. He achieved complete hematological remission in 2 mo.

DISCUSSION

Philadelphia (Ph) chromosome results from reciprocal translocation of chromosome 9 and 22. This translocation leads to the generation of a chimeric gene that results from the fusion of the *ABL* gene on chromosome 9 with the BCR gene on chromosome 22. MPAL is a rare leukemia arising from a hematopoietic pluripotent stem cell with a frequency of 0.5%-1%[1,2]. In a study by Matutes *et al*[2], comprising 100 patients of MPAL, cytogenetics revealed t(9;22) in 20%, 11q23/MLL-rearrangements in 8%, complex in 32%, aberrant in 27% and normal in 13% karyotypes. Three cases of CML[3,4] and one case of T-cell/myeloid MPAL[5] associated with del 7, t(9;22)(q34;q11) have been reported. Deletion/monosomy 7 is associated with poor prognosis in AML and t(9;22) confers a bad prognosis in ALL. Additional chromosomal abnormalities in CML may appear in about 5% of cases[6-8]. In a study by Luatti *et al*[9], 21 patients (5.6%) had additional chromosomal abnormalities; the overall cytogenetic and molecular response rates in these patients were significantly lower. None of these patients had translocations involving chromosome 10 and 13. Our patient with MPAL demonstrated characteristic bilineage leukemia and showed complete remission following hyper-CVAD plus imatinib therapy. The patient with CML also responded to imatinib. These two cases highlight the novel additional cytogenetic abnormalities associated with Ph chromosome. Whether this association of Philadelphia chromosome with these additional cytogenetic abnormalities adversely affect the prognosis needs to be evaluated. Though some studies have shown poor outcome with additional chromosomal abnormalities[9], our patients showed good initial response to imatinib based therapy.

COMMENTS

Case characteristics

A 27 years old man was admitted with weakness and low grade fever for 20 d. A 50 years old man presented with complaints of mild weakness for 3 wk.

Clinical diagnosis

Case 1: Hemogram showed hemoglobin 5.8 g/dL, total leukocyte count 62 × 10^9/L with 60% blasts and platelet count 170 × 10^9/L. Case 2: His hemoglobin was 10.5 g/dL, total leukocyte count 46.7 × 10^9/L and platelet count 3.6 × 10^9/L, differential count showed neutrophils 62%, myelocytes 10%, metamyelocytes 8%, lymphocytes 12%, monocytes 3%, eosinophils 2% and basophils 3%.

Laboratory diagnosis

Real-time polymerase chain reaction for BCR-ABL was positive for p210.

Treatment

Patient was treated with hyper-CVAD chemotherapy along with imatinib, which

resulted in complete remission.

Peer review

The manuscript demonstrates good initial response to imatinib based therapy of two rare cases of leukemia patients one with mixed phenotypic acute leukemia bilineage (B-lymphoid/myeloid) and the second with CML bearing an additional to t(9;22) chromosomal abnormality.

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