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Case Report Section

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A case of chronic lymphocytic leukemia (CLL) with a rare chromosome abnormality: t(1;14;6)(q21;q32;p21), a variant of t(6;14)(p21;q32)

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Clinics

Age and sex: 57 years old female patient.
Previous History :
- no preleukemia;
- no previous malignant disease;
- no inborn condition of note.

Organomegaly :
- no hepatomegaly;
- no splenomegaly;
- no central nervous system involvement.

Blood

WBC: 34.1 x 10^9/l; Absolute lymphocyte count = 28,244 x 10^9/l. The lymphocytes were small and mature in appearance. Rare (less than 1%) prolymphocytes were present. Hb: 13.2 g/dl; platelets: 187x 10^9/l; blasts: 0%.
Bone marrow: Variably cellular, areas of aplasia alternating with areas of residual hematopoiesis with 40% cellularity. The cellular areas show an interstitial lymphoid infiltrate comprised of small mature appearing lymphocytes with rare prolymphocytes. No clusters of large lymphocytes are present. No evidence of large cell or prolymphocytic transformation.

Cytopathology classification

Cytology: Chronic lymphocytic leukemia/Small lymphocytic lymphoma.
Immunophenotype: Peripheral blood 06/30/05: CD5+, CD19+, CD20+(dim), CD22+, CD23+, CD38+(dim), HLA-DR+, surface lambda+(dim), CD10- (ZAP-70 not performed). Matutes score = 4 of 5. Bone marrow 05/09/07: CD5+, CD19+, CD20+(dim), CD22+(very dim), CD23+, CD38+, HLA-DR+, surface lambda+(dim), ZAP-70+, CD10-. Matutes score = 4 of 5.
Pathology: See bone marrow above.
Electron microscopy: Not performed.
Precise diagnosis: Chronic lymphocytic leukemia/Small lymphocytic lymphoma.

Survival

Date of diagnosis: 06-2005; Original diagnosis made by flow cytometric analysis of peripheral blood on 06/2005. First bone marrow with cytogenetic analysis performed on 05/2007.
Treatment: None to date.
Complete remission: N/A.
Treatment related death: -
Relapse: N/A.
Status: Alive 04-2007.

Karyotype

Sample: Bone marrow; Culture time: 24, 48 and 72 hours; Banding: GTW (G-banding by Trypsin treatment followed by Wright stain).
Results: 46,XX,t(8;10)(p21;q22)c[16]/46, idem,t(1;14;6)(q21;q32;p21),-6,-12,+1-2mar [4]
Karyotype at relapse: N/A.
Other molecular cytogenetic technics: Fluorescence In Situ Hybridization (FISH) using Vysis LSI IGH break apart (Cat # 32-191019) on the mataphases, CLL I probe set (LSI ATM/p53) and CLL II probe sets (CEP

12/CEP13q14.3/CEP13q34 probes) (Cat # 32-191025) on interphase nuclei.
Other molecular cytogenetics results: 2. FISH analysis (Fig. 4) of IGH break-apart probe on G-banded metaphases (Fig. 1) showed the complex translocation, t(1;14;6)(q21;q32;p21). The LSI IgH 3' flanking region (250 kb) is labeled with Spectrum Orange and LSI IgH V 5' region (900 kb) is labeled with Spectrum Green. A normal fusion signal is seen on chromosome 14. A translocation between 14q32 and 6p21 led to the IgH signal being split with der(14) retaining the IgH 3' flanking region (red) and translocation of 5' IgH V region (green) to der(6). Subsequent complex translocations involving chromosomes 1, 14 and 6 are evident by der(14) and der(1) harboring the 1q and 6p regions, respectively.

Other molecular studies

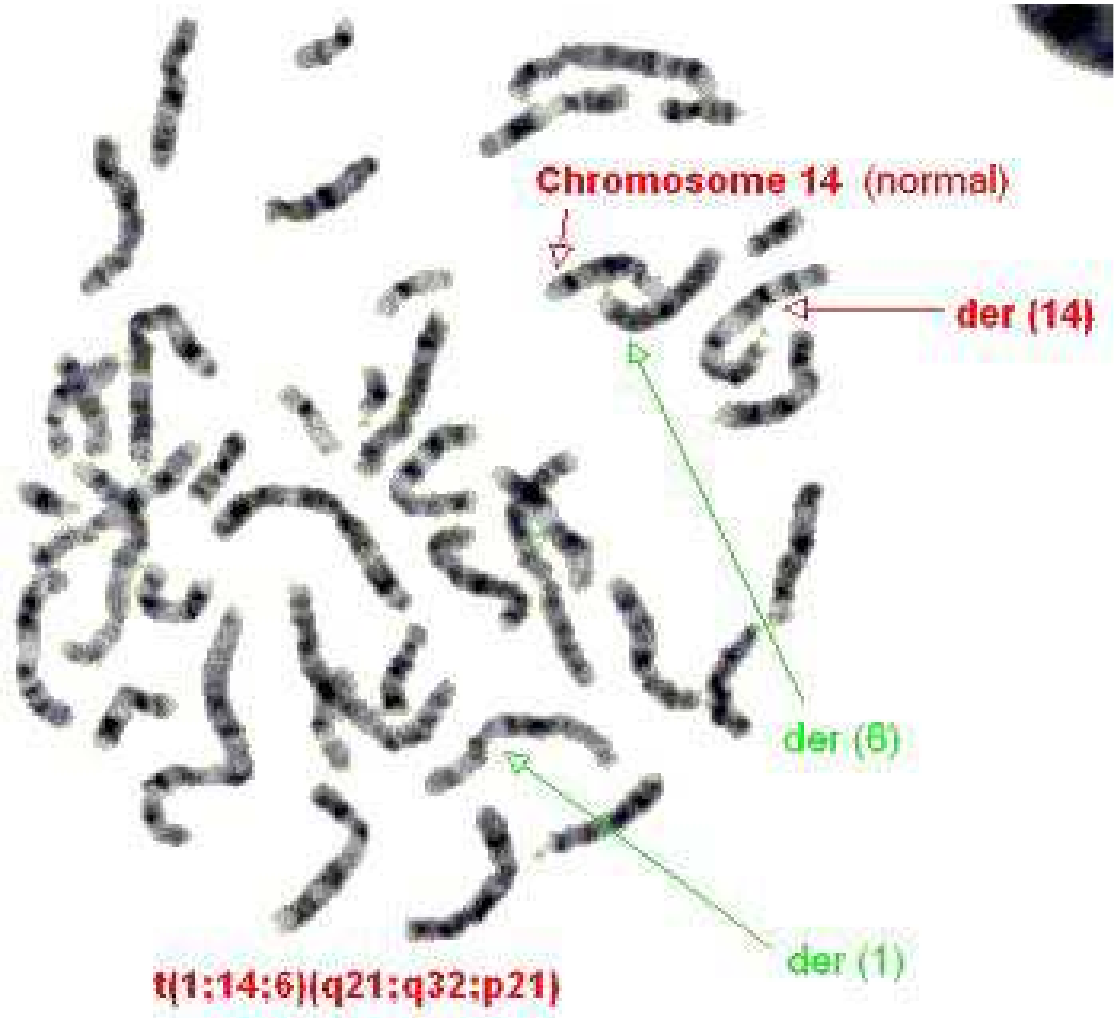
Technics: FISH studies on metaphases using LSI IGH break apart probes. Results: FISH analysis confirmed the t(1;14;6)(q21;q32;p21).

Other findings

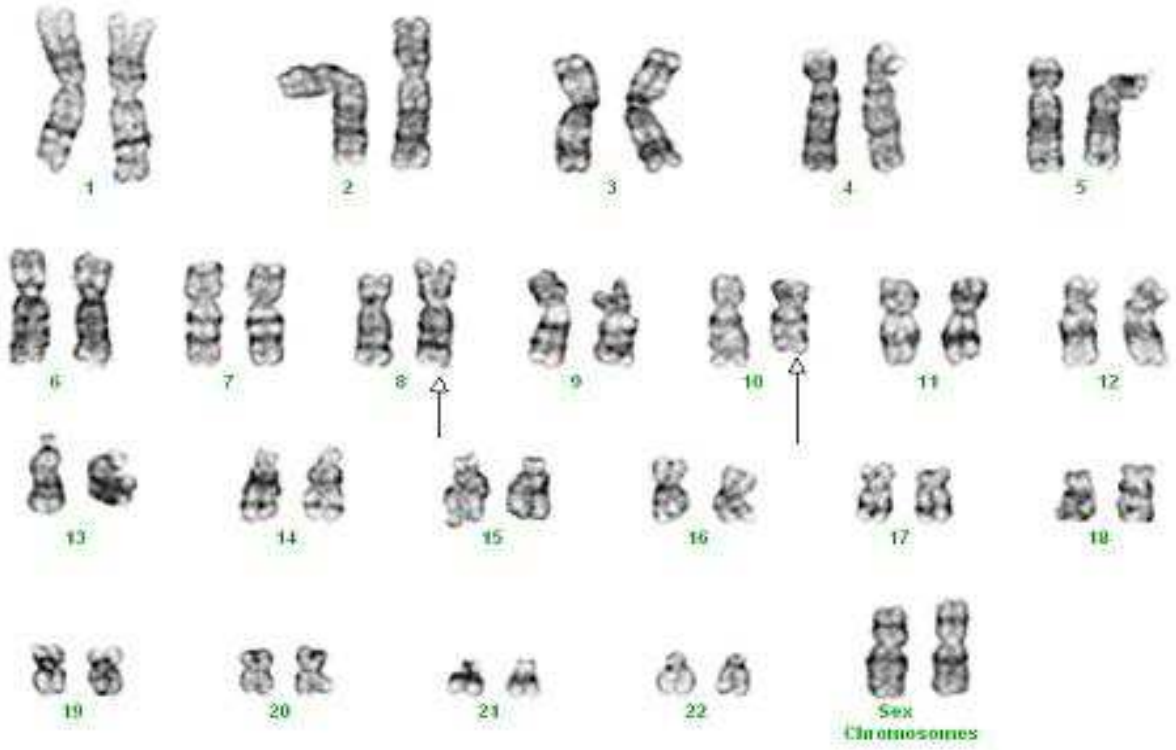
results : N/A

Comments

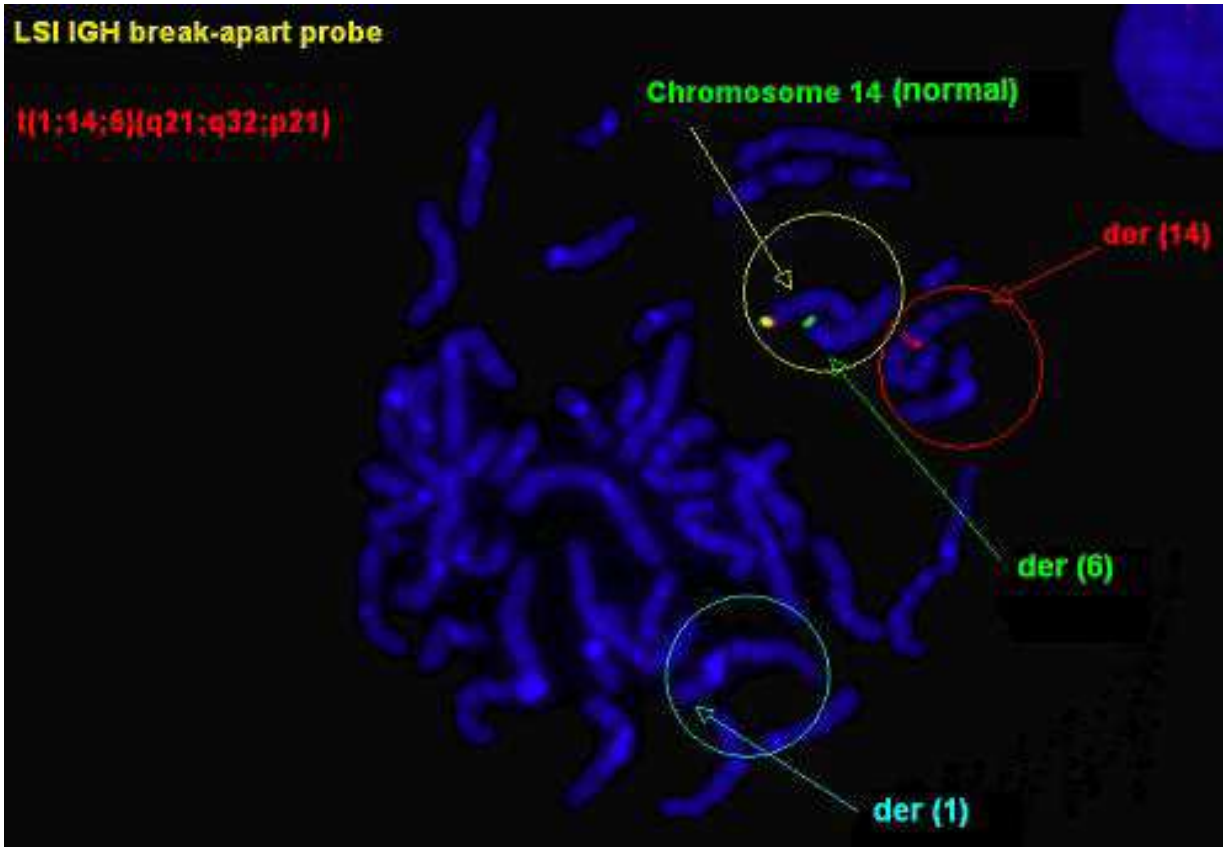
CLL is primarily a B-cell disease represented with the following anomalies; +12, del(11q) and del(17p). Cases of CLL with 14q32 (IGH) rearrangements have been reported. We present here a unique case of CLL showing a variant CCND3:IGH rearrangement in the form of t(1;14;6)(q21;q32;p21). The loss of 6q (indicated by -6) has been reported in CLL. Exact significance of monosomy 12 is not known. Interphase FISH showed del(13)(q34) in 10% cells, the significance of which is not known (Fig. 3). Metaphase FISH performed with the LSI IGH break apart probe confirmed the t(1;14;6) (Fig. 4).This case does not show the common deletions (6q, 13q14.3, 11q22-23 or 17p13) or amplification (trisomy 12).



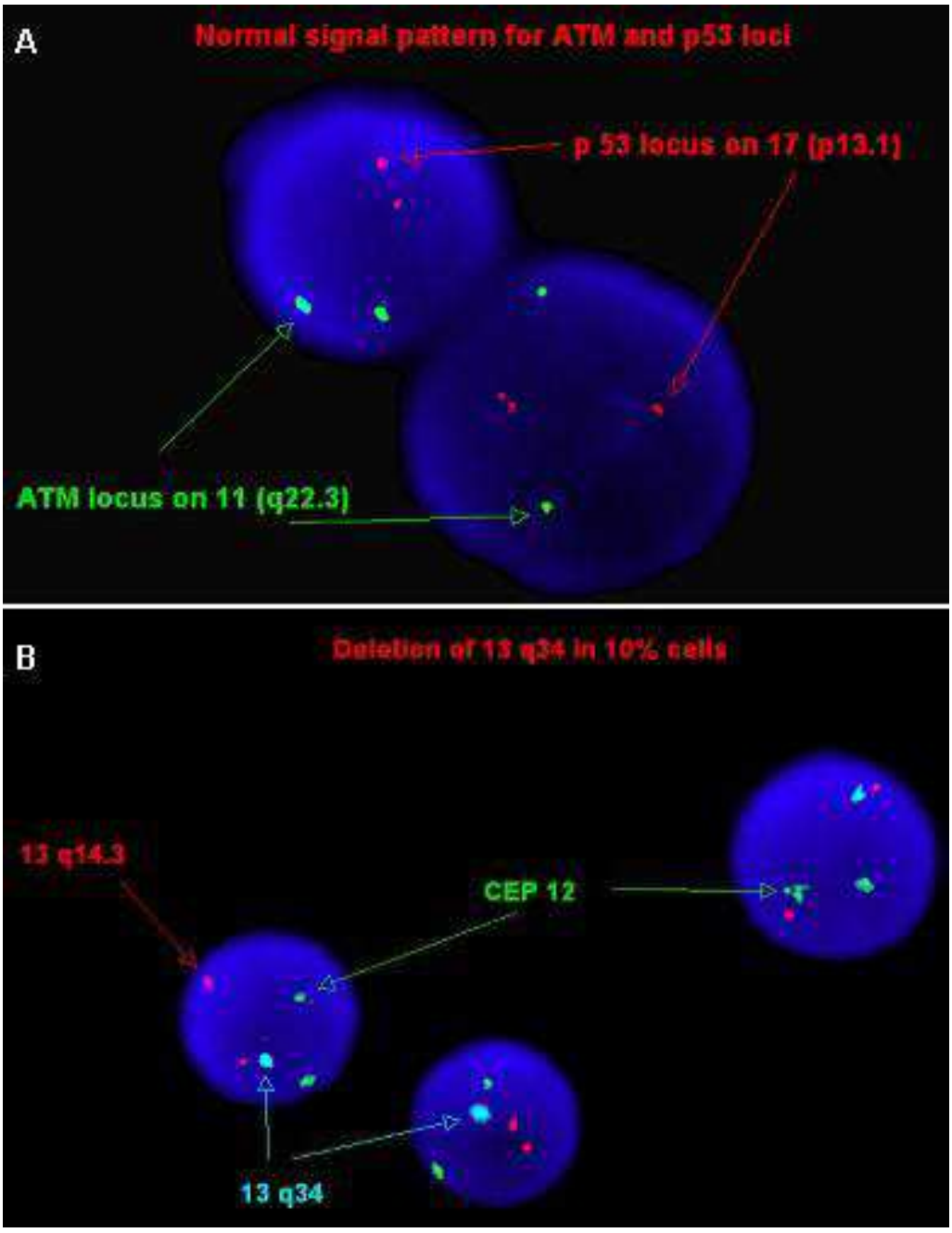
A representative metaphase showing t(1;14;6)(q21;q32;p21) and other anomalies.



A representative metaphase of PHA stimulated blood culture showing t(8;10)(p12;q22) as the constitutional abnormality.



A representative FISH result confirming the variant t(1;14;6)(q21;q32;p21) using the IGH break apart probe (entire IGH variable region (900 kb) labeled with Spectrum Green and IGH 3' flanking region (250 kb) labeled with Spectrum Orange). A normal fusion signal (yellow) is seen on chromosome 14. Abnormal signal pattern for this probe is seen on der (14) retaining the 3'IgH flanking region and translocation of 5'IGH V region to der (6).



A: A representative FISH result showing a normal signal pattern of ATM and p53 loci (ATM loci labeled with Spectrum Green and p53 loci labeled with Spectrum Orange).
B: A representative FISH result showing a deletion of 13(q34) (CEP 12, 13(q14.3) and 13(q34) labeled with Spectrums Orange, Green and Aqua, respectively).

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