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Case Report Section

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A case of sole i(4)(p10) in myelodysplastic syndrome

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Abstract

Case report on a case of sole i(4)(p10) in myelodysplastic syndrome.

Clinics

Age and sex
79 years old male patient.

Previous history
No preleukemia, previous malignancy (the patient had an acute myeloid leukemia (AML) of unknown type, 20 years ago), no inborn condition of note.

Organomegaly
No hepatomegaly, no splenomegaly, no enlarged lymph nodes, no central nervous system involvement.

Blood

WBC: 2.7 X 10^9/l
HB: 9.7g/dl
Platelets: 73 X 10^9/l
Blasts: 0%
Bone marrow: Hypercellular, multilineage dysplasia: 13% blasts, no Auer rods, 12% ring sideroblasts, 4% basophils.

Cyto-Pathology Classification

Cytology
Refractory anemia with excess blasts (RAEB)

Diagnosis
RAEB2 (WHO 2008)

Survival

Date of diagnosis: 01-2013

Treatment: Azacytidine. Blood transfusions were no more needed since.
Complete remission: no
Treatment related death: no
Relapse: no

Status: Alive

Survival: 4 months

Karyotype

Sample: Bone marrow

Culture time: 24h

Banding: BHG

Results
47,XY,+i(4)(p10).ish i(4)(p10)(FRGFR3++, wcp4+)[12] / 47,XY,+8[1]

Other molecular cytogenetics technics
FISH. probe cytocell: FGFR3/IGH; ERG1; RELN/TES; ETO/AML1 (RUNX1T1/RUNX1). probe Q-Biogene: wcp4.

Other molecular cytogenetics results
nuc ish 5p15(D5S721,D5S23x2)5q31(ERG1x2)[100] ; nuc ish 7q22(RELNx2)7q31(TESx2)[100] ; nuc ish 8q22(RUNX1T1x2),21q22(RUNX1x2)[100] ; nuc ish 4p16(FGFR3x4),14q32(IGHx2)[40/50] ; ish +i(4)4p16(wcp4+,FGFR3++)[3/3]

Comments

We present a new case of isochromosome 4p in a myeloid proliferation. The patient, a 79 years old man developed an MDS (RAEB2), occurring 20 years after an acute myeloid leukemia not otherwise documented. Cytogenetics on bone marrow aspirate revealed a unique abnormality in the karyotype, an additional isochromosome 4p. FISH with wpc4 and FGFR3 probes confirmed the i(4p) as an extra chromosome. The most frequent molecular/cytogenetic abnormalities in myeloid proliferations were absent: 5q31, 7q22-q31 probes (for del 5q or del 7q) and ETO + AML1 probes (for +8 or +21) showed no abnormality.

To our knowledge, this is the sixth reported case of myeloid proliferation with an isochromosome 4p as the sole karyotype abnormality. The previous published cases were M4-AML (3 cases), M2-AML (1 case) and RAEB-T (1 case) (Hagemeijer et al., 1981; Hoo et al., 1995; Chen et al., 1999; Soriani et al., 2010). In this short series, only one relapse is recorded after 9 months, it is the unique case of double i(4p); two cases are noted as being in complete remission and two are not documented. The present case is not relevant to the prognosis value of this karyotype anomaly: first, to date the duration of treatment is only three months, but also the age of the patient, and a previous history of AML are factors which impact the prognosis too greatly by themselves. Isochromosome 4p currently does not have a specific prognostic value in myeloid proliferations.

At the present time, what interpretation of i(4)(p10) can be proposed? "Considering that trisomy 4 as the sole abnormality of karyotype is common anomalies in AML and MDS", Chen et al. (1999) suppose that "amplification of genes on 4p but not on 4q may play a crucial role in the pathogenesis of MDS and AML". Recently, two genes located on chromosome 4 were identified as playing a role in myeloid proliferations. In 2003, Dvorak et al. have described the increased expression of FGFR3 (4p16), a member of the family of tyrosine kinase genes, in myeloid proliferating cells of CML and AML. Furthermore TET2 in 4q24 is a putative tumor suppressor in myeloid proliferations (Delhommeau et al., 2009; Jankowska et al., 2009, Vainchenker et al., 2011). Thus it can be assumed that the presence of a supernumerary isochromosome 4p can increase the expression of FGFR3 in 4p16 without increasing the copy number of the tumor suppressor gene TET2 in 4q24.

Call for Collaborations

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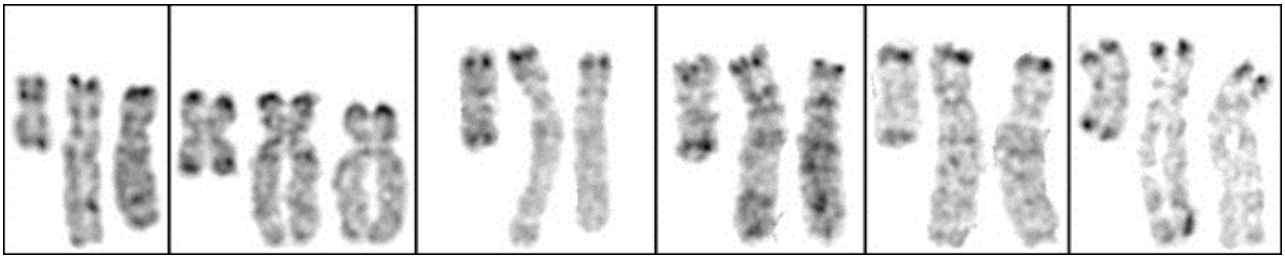

Figure 1: RHG; partial panel of chromosomes 4 and i(4)(p10).

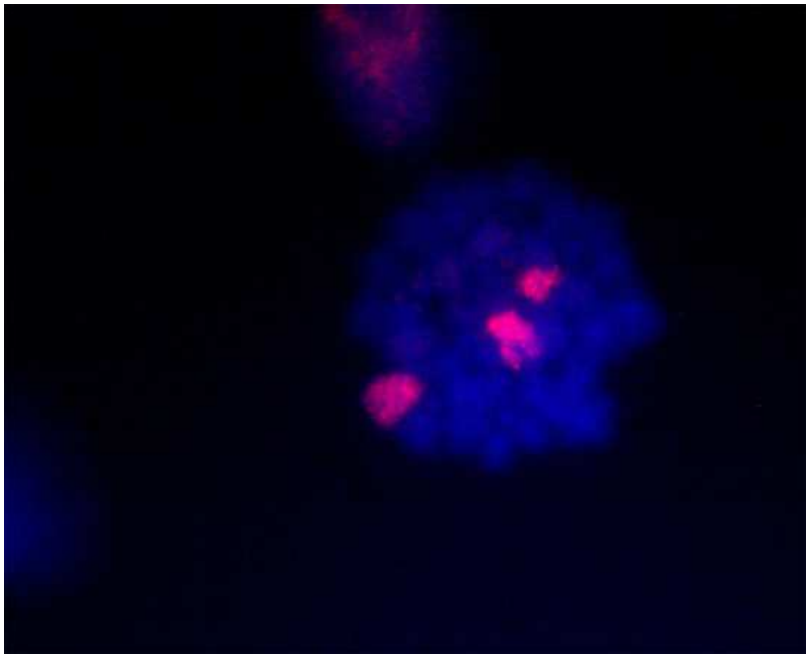

Figure 2: one metaphase labelled by wcp4: two normal chromosomes 4 and one extra derived chromosome 4.

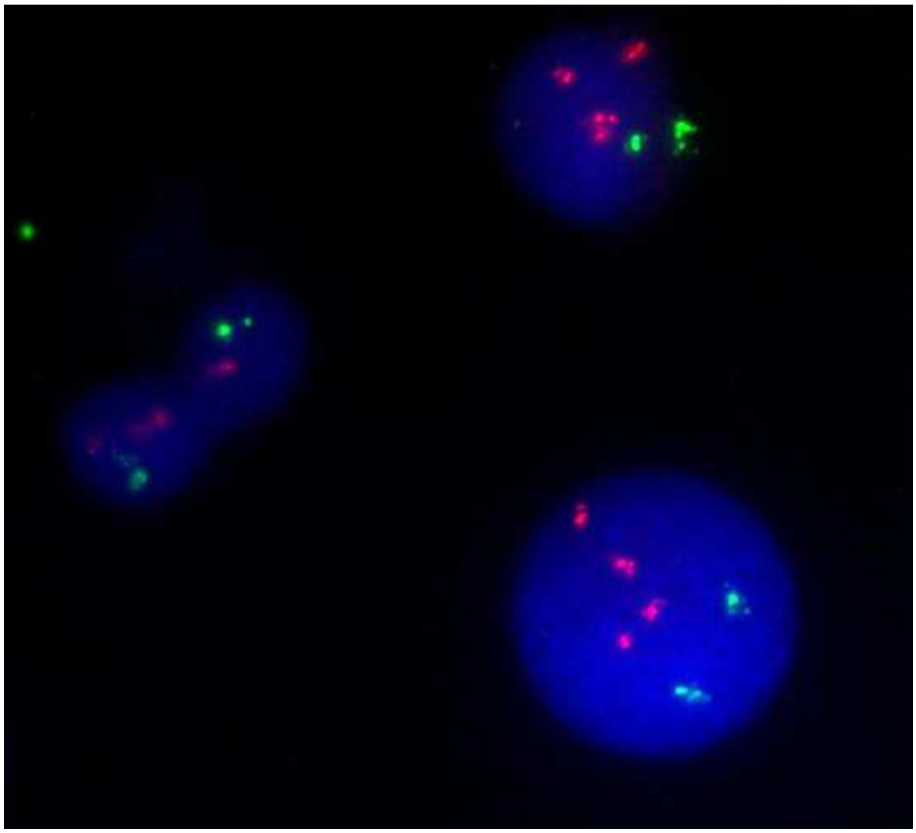

Figure 3: nuc ish(FGFR3x4,IGHx2); FGFR3 red and IGH green.

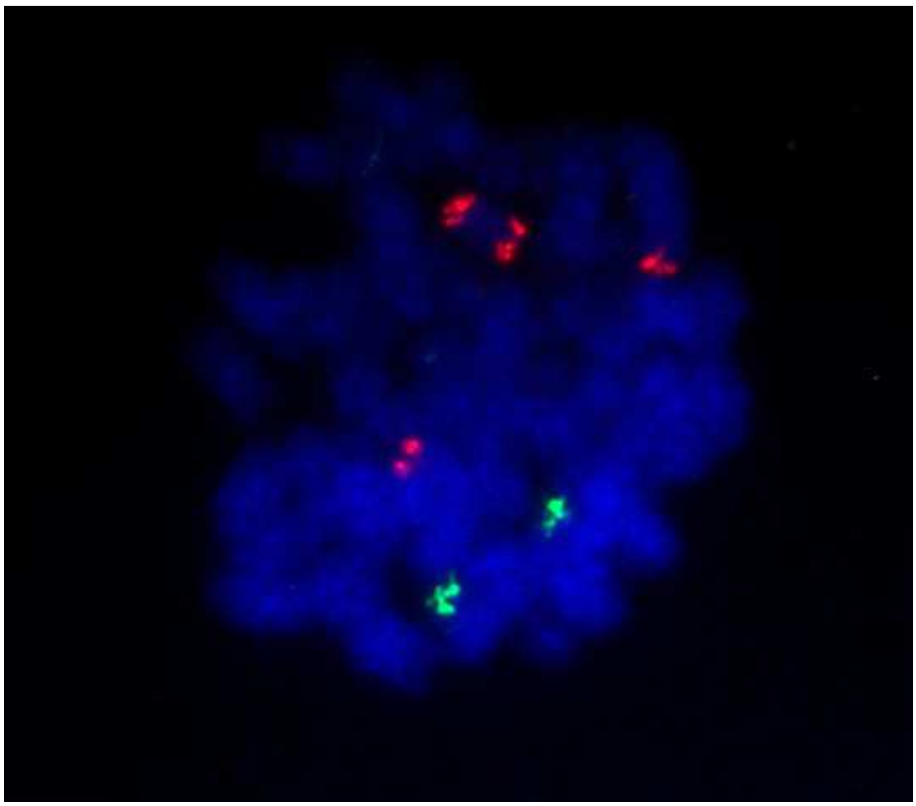

Figure 4: two normal chromosomes 4 labelled by an FGFR3 red probe, one extra chromosome labelled by an FGFR3 red probes and two normal chromosomes 14 labelled by an IGH green probe.

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