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Case Report Section

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Unbalanced rearrangement der(9;18)(p10;q10) and JAK2 V617F mutation in a patient with AML following post-polycythemic myelofibrosis

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Clinics

Age and sex
66 years old male patient.

Previous history
No preleukemia. No previous malignancy. No inborn condition of note.

Organomegaly
Hepatomegaly (enlarged liver (+ 20 cm)), splenomegaly, no enlarged lymph nodes , no central nervous system involvement.

Blood

WBC : 46 X 10^9/l
HB : 8.5 g/dl
Platelets : 239 X 10^9/l
Blasts : 15%
Bone marrow : 25%

Cyto-Pathology Classification

Cytology: NA

Immunophenotype: NA

Rearranged Ig Tcr: NA

Pathology: NA

Electron microscopy: NA

Diagnosis
Polycythemia vera. Myelofibrosis: hypocellular bone marrow with marked increase in reticulin fibres. AML M2.

Survival

Date of diagnosis: 01-1980

Treatment
Bleeding therapy and acethylsalicylic acid. 2005 - 2008: Etanercept (anti-TNF alpha). 2007: Hydroxyurea. Sept. 2008: Splenectomy. Feb. 2008: Pomalidomide, suspended after 1 month because of a severe neutropeny. Feb 2009: Bone Marrow allograft.
Complete remission : no (March-November 2009: complete hematological remission; molecular remission not reached (JAK-2 positivity in June 2009))
Treatment related death : no
Relapse : no

Status: Death. Last follow up: 11-2010 (due to gastrointestinal hemorrhage).

Survival: nearly 30 years.

Karyotype

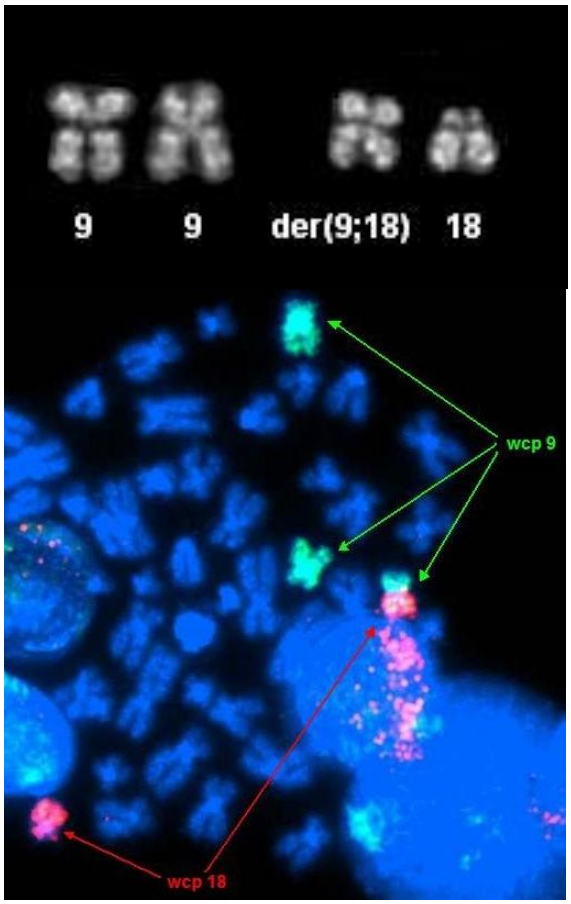
Sample: Bone marrow biopsy in Dec. 2008

Culture time: 24 and 48 h.

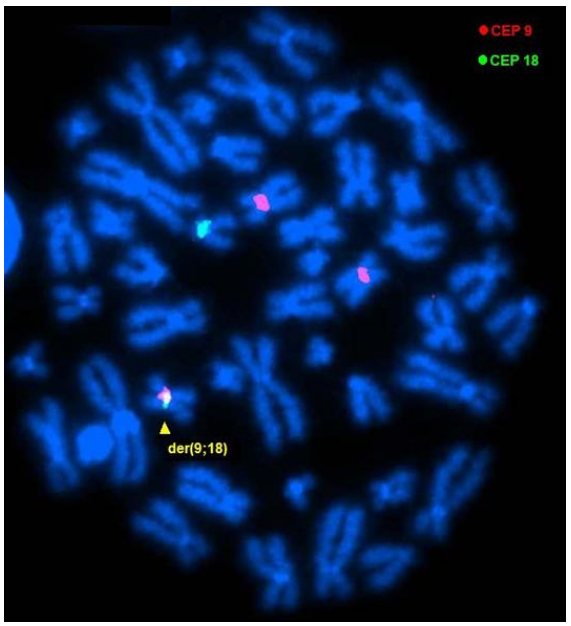
Banding: Cytogenetic analysis performed in QFQ banding; band level: 400.

Results

46,XY, +9,der(9;18)(p10;q10) in 25/25 cells scored.



Probes: whole-chromosome painting probes (wcp) and centromeric (CEP) probes of chromosomes 9 (9p11-q11 alpha satellite DNA) and 18 (D18Z1) (Abbott Molecular/Vysis).



Comments

Polycythemia Vera (PV) is a clonal myeloproliferative disorder characterized by excessive erythrocyte production, which may evolve into myelofibrosis and acute myeloid leukemia. Transformation to myelofibrosis occurs in 15-20% of cases and leukemic transformation in 5-10% of patients. The median survival time is 8-11 years and the median age at diagnosis is over 60 years. Normal karyotype is present at diagnosis in the majority of patients, while during transformation several acquired chromosome anomalies are present as trisomy 9 and gains in 9p.

The activating JAK2 V617F mutation, present in the majority of patients with PV, seems to have a primary role in the pathogenesis of myeloproliferative neoplasms. The JAK2 gene maps to 9p24, so patients carrying gains of 9p have an extra copy of the gene, in its normal or mutated form, leading to a gain of function.

The rearrangement here reported, der(9;18)(p10;q10), is rarely detected in patients with PV, myelofibrosis, essential thrombocythemia and therapy-related AML. Some authors suggest that the simultaneous presence of both JAK2 V617F mutation and this rearrangement could define a subgroup of PV patients with the proliferative phenotype of the disease, at high risk of transformation into postpolycythemic myelofibrosis and potentially acute myeloid leukemia.

We describe a new case of der(9;18)(p10;q10) detected in a patient with AML evolved from post-polycythemic myelofibrosis. The patient was diagnosed with PV in 1980 and died in 2010. He was in good health for several years after diagnosis with bleeding treatment and low dose aspirin, then he showed a progressive worsening of anemia with liver enlargement and splenomegaly. In February 2008 the diagnosis was of myelofibrosis post PV in progression. In December 2008, when the leukemic transformation was evident, the cytogenetic analysis on bone marrow aspirate found the unbalanced translocation leading to der(9;18)(p10;q10), with trisomy of the short arms of chromosome 9 and monosomy of the short arms of chromosome 18. FISH experiments with specific alphoid centromeric probes for chromosome 9 and 18 showed both positive signals on the der(9). Subsequent molecular analysis detected the presence of the JAK2 V617F mutation.

The patient here reported had a classical evolution of the disease, after a very long polycythemic phase with a noteworthy survival time likely correlated to the young age of the patient when PV occurred. Because of the absence of cytogenetic results at diagnosis and during the polycythemic phase, we cannot fully evaluate the significance of der(9;18)(p10;q10) in the natural history of the

disease before its evolution. Future reports could make clear this not negligible aspect.

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