

## Case Report Section

Paper co-edited with the European LeukemiaNet

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

Francesca Cambosu, Giuseppina Fogu, Paola Maria Campus, Claudio Fozza, Luigi Podda, Andrea Montella, Maurizio Longinotti

Clinical Genetics, Department of Biomedical Sciences, University of Sassari, Viale San Pietro 43/B 07100 Sassari, Italy (FC, GF, AM); Azienda Ospedaliero-Universitaria Sassari, Italy (PMC, CF, LP, AM, ML); Institute of Hematology, University of Sassari, Italy (CF, LP, ML)

Published in Atlas Database: September 2011

Online updated version : <http://AtlasGeneticsOncology.org/Reports/der918p10q10CambosuID100057.html>  
DOI: 10.4267/2042/47273

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.  
© 2012 Atlas of Genetics and Cytogenetics in Oncology and Haematology

### 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<sup>9</sup>/l

HB : 8.5 g/dl

Platelets : 239 X 10<sup>9</sup>/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 acetylsalicylic 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

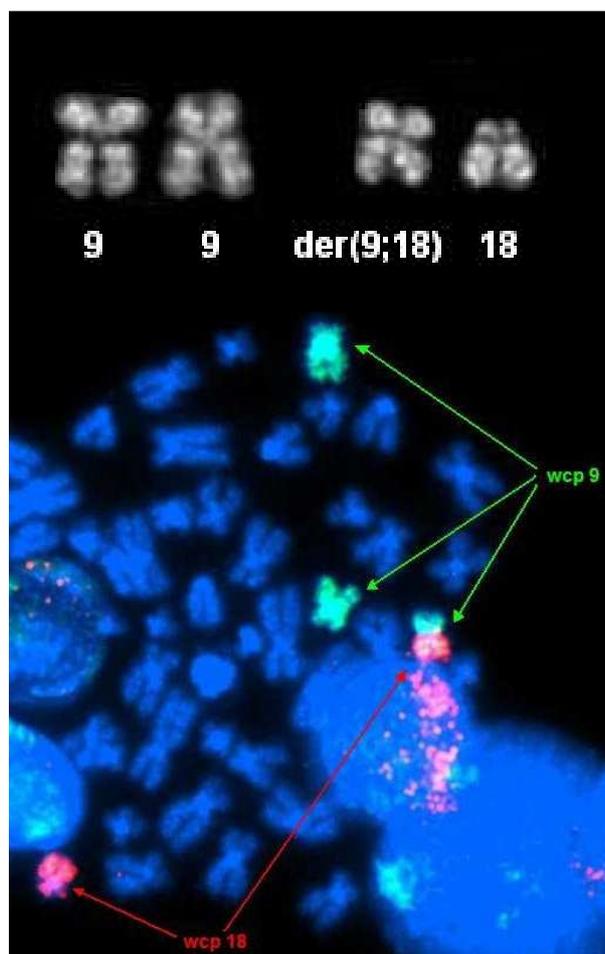
**Sample:** Bone marrow biopsy in Dec. 2008

**Culture time:** 24 and 48 h.

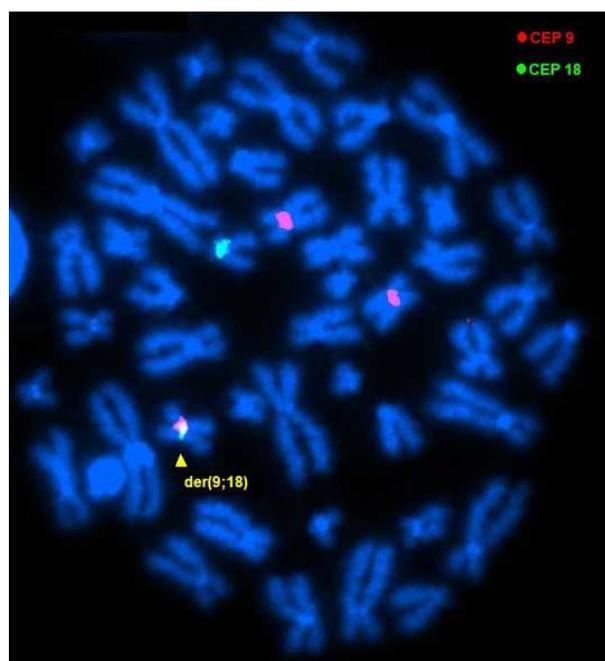
**Banding:** Cytogenetic analysis performed in QFQ banding; band level: 400.

#### 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.

## References

Chen Z, Notohamiprodjo M, Guan XY, Paietta E, Blackwell S, Stout K, Turner A, Richkind K, Trent JM, Lamb A, Sandberg AA. Gain of 9p in the pathogenesis of polycythemia vera. *Genes Chromosomes Cancer*. 1998 Aug;22(4):321-4

Andrieux J, Demory JL, Caulier MT, Agape P, Wetterwald M, Bauters F, Lai JL. Karyotypic abnormalities in myelofibrosis following polycythemia vera. *Cancer Genet Cytogenet*. 2003 Jan 15;140(2):118-23

Bacher U, Haferlach T, Schoch C. Gain of 9p due to an unbalanced rearrangement der(9;18): a recurrent clonal abnormality in chronic myeloproliferative disorders. *Cancer Genet Cytogenet*. 2005 Jul 15;160(2):179-83

Larsen TS, Hasselbalch HC, Pallisgaard N, Kerndrup GB. A der(18)t(9;18)(p13;p11) and a der(9;18)(p10;q10) in polycythemia vera associated with a hyperproliferative phenotype in transformation to postpolycythemic myelofibrosis. *Cancer Genet Cytogenet*. 2007 Jan 15;172(2):107-12

Ohyashiki K, Kodama A, Ohyashiki JH. Recurrent der(9;18) in essential thrombocythemia with JAK2 V617F is highly linked to myelofibrosis development. *Cancer Genet Cytogenet*. 2008 Oct;186(1):6-11

Xu X, Chen X, Rauch EA, Johnson EB, Thompson KJ, Laffin JJS, Raca G, Kurtycz DF. Unbalanced rearrangement der(9;18)(p10;q10) in a patient with polycythemia vera. *Atlas Genet Cytogenet Oncol Haematol*. April 2010. URL: <http://AtlasGeneticsOncology.org/Genes/der0918XuiD100044.html> .

---

*This article should be referenced as such:*

Cambosu F, Fogu G, Campus PM, Fozza C, Podda L, Montella A, Longinotti M. Unbalanced rearrangement der(9;18)(p10;q10) and JAK2 V617F mutation in a patient with AML following post-polycythemic myelofibrosis. *Atlas Genet Cytogenet Oncol Haematol*. 2012; 16(1):70-72.

---