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# Partial Trisomy 9 in a Patient with Polycythemia Vera

Trisomy 9 as sole abnormality has been described in several hematologic disorders, with acute non lymphocytic leukemia (ANLL) and polycythemia vera (PV) having the largest number of cases [1]. Trisomy 9 in PV can be complete or partial and is often associated with trisomy 1q [2, 3]. Other abnormalities in PV include trisomies for 8 and 1q, 13q- and 20q- [2-6].

We wish to present a patient with polycythemia vera, who had an abnormal clone in her bone marrow with a partial trisomy 9p, as a result of an unbalanced translocation, t(2;9). The patient, an 82-year old Caucasian female, presented with a two-month history of paresthesia of the left side of the body, without pruritus or increased bleeding tendency. At physical examination the spleen was not enlarged.

Laboratory findings included ESR 1 mm (normal <10), hemoglobin 11 mmol/L (normal 7.8 to 10.2), hematocrit 0.54 L/L (normal 0.37 to 0.48), mean corpuscular volume (MCV) 75.2 fl (normal 82 to 98), erythrocytes  $7.2 \times 10^6/\mu\text{l}$  (normal 4 to 5.5), leukocytes  $15.0 \times 10^6/\text{ml}$  (normal 4.0 to 10.0), and thrombocytes  $766 \times 10^6/\text{ml}$  (normal 150 to 350). The differential showed 79% neutrophils, 18% lymphocytes, and 3% monocytes.

A biochemical profile revealed a lactic dehydrogenase of 366 U/L (normal <290), uric acid 0.32 (normal <0.36), and was otherwise normal. Arterial O<sub>2</sub> saturation was 95% (normal 95 to 98).

Serum level of iron was 2.5  $\mu\text{mol/L}$  (normal 14 to 32), ferritin 12.2  $\mu\text{g/L}$  (7 to 283), and vitamin B<sub>12</sub> 812 pmol/L (normal 130 to 550). Leukocyte alkaline phosphatase activity was 159 (normal 20 to 90). On ultrasound the spleen was not enlarged. Bone marrow examination revealed active normoblastic and megaloblastic erythropoiesis, active myelopoiesis, and increased megakaryopoiesis with hypergranularity of the megakaryocytes. On histology numerous enlarged and hyperlobulated megakaryocytes were present without evident fibrosis. A myeloproliferative syndrome was diagnosed, compatible with polycythemia vera. The symptoms subsided after treatment with a low dose of acetylsalicylic acid (80 mg per day) and repeated phlebotomies.

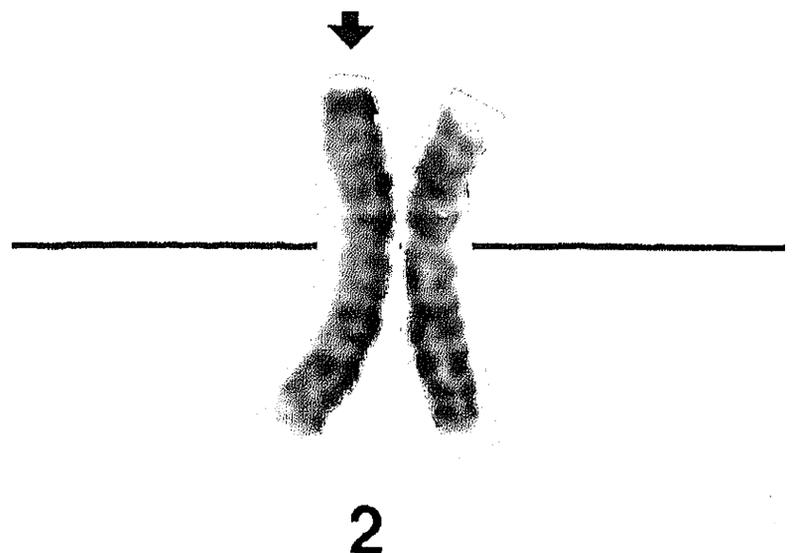
Cytogenetic analysis was performed on 24 hours cultured bone marrow without mitogen. The karyotype, based on conventional cytogenetics, was 46,XX,add(2)(p25)[24]/46,XX[9]. The abnormal chromosome 2 is shown in Figure 1.

Fluorescence in situ hybridization (FISH), using ICRF YAC y900B0992 and CEPH YAC 937c8 (kindly provided by J. Wagstaff, Children's Hospital, Boston), demonstrated that the extra material on the tip of chromosome 2 was derived from the short arm of chromosome 9 (Fig. 2.) The karyotype of the abnormal cell clone therefore is 46,XX,add(2)(p25).ish der(2)t(2;9)(p25;p?).

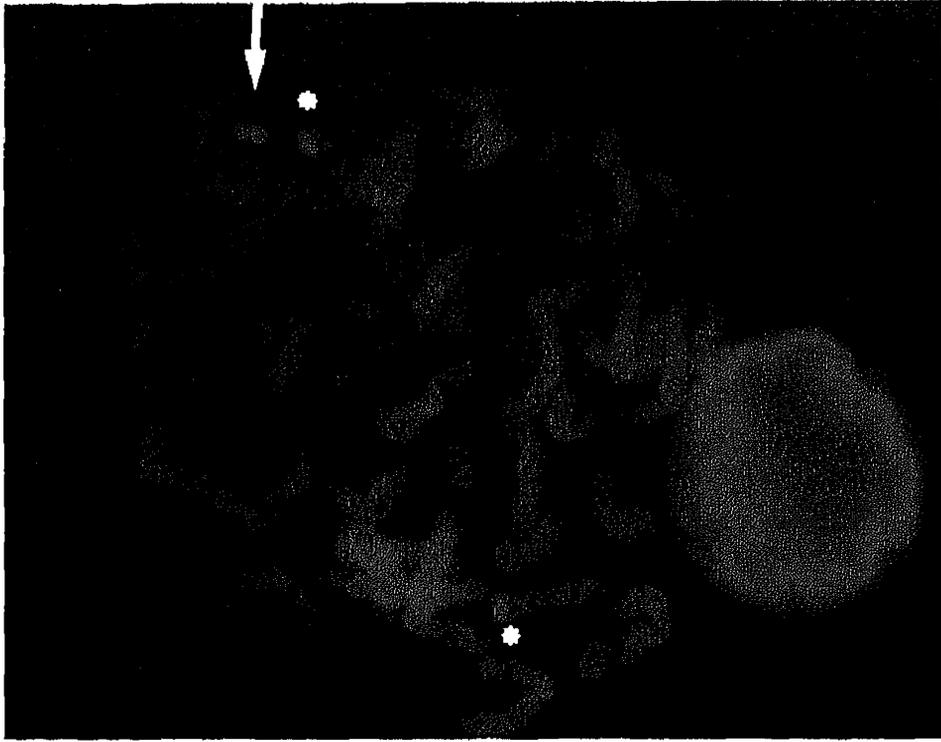
During the course of PV the percentage of patients with chromosomal abnormalities in the bone marrow increases, partly as a result of myelosuppressive cytostatic treatment [2]. Although patients with chromosomally abnormal clones at the time of diagnosis of PV may have a poor prognosis [4], the significance of trisomy 9 is not clear. Mostly no consistent relationship between the presence of trisomy 9 and the course of PV has been established [2, 4, 5]; in one report the presence of trisomy 9 was even associated with a long duration of the disease [6].

Recently, Amiel et al. [6] demonstrated that FISH is a more sensitive method for detecting trisomy 9 than conventional cytogenetics, offering the possibility to examine a large number of cells and thus detecting cells with trisomy 9 that would otherwise not have been found. Our patient had a structural abnormality resulting in a partial trisomy 9p, possibly in combination with a small monosomy 2p, that could only be identified by FISH.

**Figure 1** Partial G-banded karyotype, showing both chromosomes 2. The abnormal chromosome is indicated by an arrow.



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**Figure 2** Metaphase after fluorescence in situ hybridization with YACS located on the short arm of chromosome 9, showing signals on both normal chromosomes 9, indicated by asterisks, and on the der(2), indicated by an arrow.

The detection of more patients with partial trisomy 9, made possible by FISH, might help to delineate the critical region on 9p that contains the gene(s) involved in myeloproliferative diseases.

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