

An unusual clonal cytogenetic abnormality with t(15;17)(p11;q21) in a patient with severe aplastic anemia

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Sir,

Aplastic anemia is a rare, serious disease characterized by pancytopenia and hypocellular bone marrow. We present a case of severe aplastic anemia with a novel cytogenetic abnormality involving a balanced translocation between chromosomes 15p11 and 17q21. The breakpoint in chromosome 17q21 was similar to that involved in acute promyelocytic leukemia. A 68-year-old male presented with complaints of progressively increasing weakness and low-grade fever for 30 days. There was no bleeding from any site. Past medical history and family history were non-contributory. Clinical evaluation revealed palor with no lymphadenopathy or organomegaly. Hematological workup revealed pancytopenia with hemoglobin 6.8 g/dl, total leukocyte count $1.2 \times 10^9/l$, absolute neutrophil count $0.24 \times 10^9/l$, platelet count $26 \times 10^9/l$, and peripheral blood differential count with neutrophils 20% and lymphocytes 80%. Bone marrow biopsy revealed hypocellular marrow with overall cellularity less than 5%. There was no marrow dysplasia, tumor infiltration, or myelofibrosis. Investigations for viral infections like hepatitis B virus, hepatitis C virus, human immunodeficiency virus, and parvovirus B19 were negative. Chromosomal analysis revealed a male karyotype with the presence of translocation between chromosome 15 and 17 [46 XY, t(15;17)(p11;q21)] in all metaphases, detectable at the level of banding resolution (ISCN) 400. Paroxysmal nocturnal hemoglobinuria clone

was ruled out by flowcytometry on peripheral blood granulocytes. Prothrombin time and activated partial thromboplastin time were normal with no evidence of coagulopathy. He was given supportive treatment with packed red blood cell transfusion and started on oral cyclosporine 100 mg twice daily.

Most cases of aplastic anemia are acquired and do not have any cytogenetic abnormalities though few patients have been described with these abnormalities at presentation ranging from 4% to 12%.^[1-4] The relevance of cytogenetic abnormalities to the pathophysiology of AA is unknown in contrast to diseases like myelodysplastic syndrome and acute leukemias where diagnosis and treatment rests heavily on cytogenetic abnormalities. Both numerical and structural abnormalities have been reported in aplastic anemia. Numerical abnormalities include trisomies of chromosome 6, 7, 8, 13, 14 and 15 and monosomy 7 and 9 and structural abnormalities include t(3;11) and t(4;6).^[1,2,4] Overall, the most common chromosomal abnormalities reported are trisomies of 6 and 8 and loss of chromosome 7.^[1,4] Although unusual cytogenetics have been reported in patients with AA^[5,6] including t(9;22) but t(15;17) has not been reported. The response to immunosuppressive therapy, durability of response, and progression to later clonal disorders in these patients did not appear to be different from patients with a normal karyotype though they might be at higher risk of progressing to myelodysplastic syndrome or acute myeloid leukemia.^[2,4]

Reciprocal translocation t(15;17)(q22;q21) is the characteristic abnormality found in 95% of patients with acute promyelocytic leukemia (APL) and most of them present with cytopenias.^[7] Though our patient had chromosomal breakpoint 17q21 similar to that in APL, the breakpoint on chromosome 15 was different (i.e. at 15p11). The significance of this translocation in

the pathogenesis of aplastic anemia is unknown as is true for other cytogenetic abnormalities reported, but we conclude that this novel cytogenetic translocation involving 17q21 may be involved in pathogenesis of cytopenias seen in this patient and probably in some patients with APL presenting with cytopenias.

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References

1. Appelbaum FR, Barrall J, Storb R, Ramberg R, Doney K, Sale GE, *et al.* Clonal cytogenetic abnormalities in patients with otherwise typical aplastic anemia. *Exp Hematol* 1987;15:1134-9.
2. Maciejewski JP, Risitano A, Sloand EM, Nunez O, Young NS. Distinct clinical outcomes for cytogenetic abnormalities evolving from aplastic anemia. *Blood* 2002;99:3129-35.
3. Ohga S, Ohara A, Hibi S, Kojima S, Bessho F, Tsuchiya S, *et al.*: Aplastic Anaemia Committee of the Japanese Society of Paediatric Haematology. Treatment responses of childhood aplastic anaemia with chromosomal aberrations at diagnosis. *Br J Haematol* 2002;118:313-9.
4. Gupta V, Brooker C, Tooze JA, Yi Q, Sage D, Turner D, *et al.* Clinical relevance of cytogenetic abnormalities at diagnosis of acquired aplastic anaemia in adults. *Br J Haematol* 2006;134:95-9.
5. Suzan F, Terre C, Garcia I, Bastie J, Baumelou E, Gluckman E, *et al.* Three cases of typical aplastic anaemia associated with a Philadelphia chromosome. *Br J Haematol* 2001;112:385-7.
6. Varma N, Varma S, Movafagh A, Garewal G. Unusual clonal cytogenetic abnormalities in aplastic anemia. *Am J Hematol* 1995;49:256-7.
7. De Botton S, Dombret H, Saanz M, Miguel JS, Caillot D, Zittoun R, *et al.* Incidence, clinical features, and outcome of all transretinoic acid syndrome in 413 cases of newly diagnosed acute promyelocytic leukemia: The European APL group. *Blood* 1998;92:2712-8.

1. Appelbaum FR, Barrall J, Storb R, Ramberg R, Doney K, Sale GE, *et al.* Clonal cytogenetic abnormalities in patients