RARα fusion gene in acute promyelocytic leukemia. Leukemia. 1996;10:1214-1216.

3. Marasca R, Zucchini P, Galimberti S, et al. Missense mutation in the PML/RARα ligand binding domain in ATRA-resistant $A_{s2}O_3$ sensitive relapsed acute promyelocytic leukemia. Haematologica. 1999;84:963-968.
4. Hughes TP, Morgan HGJ, Martiat P, Goldman JM. Detection of residual leukemia after bone marrow transplant for chronic myeloid leukemia: role of polymerase chain reaction in predicting relapse. Blood. 1991;77:874-878.
5. Maurer J, Janssen JWG, Thiel E et al. Detection of chimeric BCR-ABL genes in acute lymphoblastic leukaemia by the polymerase chain reaction. Lancet. 1991;337:1055-1058.
6. Morris CM, Fitzgerald PH, Hollings PE, Archer SA, Rosman I, Beard MJ. Essential thrombocythemia and the Philadelphia chromosome. Br J Haematol. 1988;70:13-19.
7. Cervantes F, Urbano-Ispizua A, Villamor N, et al. Ph-positive chronic myeloid leukemia mimicking essential thrombocythemia and terminating into megakaryoblastic crisis: report of two cases with molecular studies. Leukemia. 1993;2:327-330.
8. Kwong YL, Chiu EKW, Liang RHS, Chan V, Chan TK. Essential thrombocythemia with BCR/ABL rearrangement. Cancer Genet Cytogenet. 1996;89:74-76.
9. Singer IO, Sproul A, Tait RC, Soutar R, Gibson B. BCR-ABL transcripts detectable in all myeloproliferative states [abstract].Blood.1998;92:427a.
10. Marasca R, Luppi M, Zucchini P, Longo G, Torelli G, Emilia G. Might essential thrombocythemia carry Ph anomaly? Blood. 1998;91:3084-3085.
11. Solé F, Florensa L, Espinet B, Besses C, Lloveras E, Woessner S. Absence of bcr/abl rearrangement in 41 patients with essential thrombocythemia. Haematologica. 2000;85:214-221.

To the editor:

Increase in platelet count in response to rHuEpo in a patient with thrombocytopenia and absent radii syndrome

The thrombocytopenia and absent radii (TAR) syndrome is a rare congenital defect characterized by the association of skeletal malformations with hematologic disturbances.[1] Additional manifestations are absence or hypoplasia of other bones of the extremities, short stature, dislocation of hip, and various other abnormalities. In an investigation on 5 unrelated children with TAR syndrome, Ballmaier et al found that the thrombocytopenia was caused by a defective megakaryopoiesis and thrombocytopoiesis, which was due to a lack of response to thrombopoietin, despite normal expression of the thrombopoietin receptor on the megakaryocytes.[2] Letestu et al showed evidence of dysmegakaryopoiesis, with a blockage of cellular differentiation at an early stage.[3] In these experiments, megakaryopoiesis in cell culture was not responsive to stimulation with mixtures of cytokines, including erythropoietin.

We now report the case of a 49-year-old female with TAR syndrome who was referred to our clinic for investigation of bleeding risk for elective hip surgery. The patient had suffered from severe coxarthrosis for several years. Absence of radii was confirmed by roentgenograms. The patient is of short stature, with a body height of 148 cm. Platelet count was in the range of 50×10^9/L to 60×10^9/L both in ethylenediaminetetraacetic acid (EDTA) anticoagulated blood, as well as in citrated whole blood. Red blood cells were within the normal range, whereas the patient showed elevated leukocyte counts throughout the observation period. Expression of platelet receptors CD41, CD61, CD42a, and CD42b was found to be normal in flow cytometric analysis. Erythropoietin levels were within the normal range.

Erythropoietin has been shown to induce an increase in platelet count[4] and has been employed in the preparation of anaemic patients for hip surgery[5] and for prevention of anaemia and thrombocytopenia in cancer patients receiving radiotherapy.[6] Treatment with rHuEpo leads to elevated numbers of megakaryocytes in the bone marrow of patients with renal anemia[7] and an increase in platelet counts in animal experiments.[8,9]

We treated the patient with 2 courses of erythropoietin. Upon the first instance, she received 1000 IU/d of recombinant erythropoietin (rHuEpo) (Neo-Recormon; Roche, Mannheim, Germany) (16 IU/kg body weight) for 3 days. The second time, we administered 2000 IU/d (32 IU/kg body weight) for 4 days. During the first series, platelet counts increased from 48×10^9/L to 84×10^9/L on day 5. In the second series, platelet count increased from 50×10^9/L to 80×10^9/L on day 6. Erythrocyte count, as well as leukocyte counts, remained unchanged during rHuEpo treatment. (See Table 1 for a summary.) The results indicate that the thrombocytopenia of patients with TAR syndrome may be responsive to rHuEpo treatment, resulting in a therapeutically relevant increase in platelet count. Treatment with rHuEpo may be useful in patients scheduled for surgical procedures, in order to reduce the amount of heterologous platelet concentrates needed for maintaining a sufficient hemostatic capacity. Additional experiences are needed in order to determine the required dosage of rHuEpo. In animal experiments, large chronic doses of rHuEpo have been shown to cause thrombocytopenia, caused by competition between precursor cells of the erythrocytic and megakaryocytic cell lines.[10] In view of these limitations, treatment with rHuEpo in patients with TAR syndrome should presumably be limited to short-term applications.

Table 1. Platelet count, erythrocyte count, leukocyte count, and rHuEpo dosage administered

Date	Platelets ($\times 10^9$/L)	Erythrocytes ($\times 10^{12}$/L)	Leukocytes ($\times 10^9$/L)	rHuEpo dose
7/24/99	57	5.20	15.1	NA
11/29/99	56	4.14	13.1	NA
12/1/99	49	4.43	14.5	NA
12/10/99	48	4.10	14.7	1000
12/11/99	ND	ND	ND	1000
12/12/99	ND	ND	ND	1000
12/14/99	84	4.64	13.2	NA
4/27/00	49	4.80	12.0	NA
5/4/00	50	4.97	16.4	2000
5/5/00	50	4.76	15.4	2000
5/6/00	51	4.63	13.2	2000
5/7/00	56	4.53	14.6	2000
5/8/00	68	4.31	12.5	NA
5/9/00	80	4.60	15.3	NA
5/21/00	54	5.20	12.9	NA

ND, not determined; NA, not applicable.

Carl-Erik Dempfle, Christine Burck, Tina Grützmacher, Jan Wizenmann, and Dieter L. Heene
Mannheim University Hospital
I Department of Medicine
Mannheim, Germany

References

1. Hedberg VA, Lipton JM. Thrombocytopenia with absent radii. A review of 100 cases. Am J Pediatr Hematol Oncol.1988;10:51-64.

2. Ballmaier M, Schulze H, Strauβ G, et al. Thrombopoietin in patients with congenital thrombocytopenia and absent radii: elevated serum levels, normal receptor expression, but defective reactivity to thrombopoietin. Blood.1997;90: 612-619.
3. Letestu R, Vitrat N, Massé A, et al. Existence of a differentiantion blockage at the stage of a megakaryocyte precursor in the thrombocytopenia and absent radii (TAR) syndrome. Blood.2000;95:1633-1641.
4. McDonald TP, Cottrell MB, Clift RE, Cullen WC, Lin FK. High doses of recombinant erythropoietin stimulate platelet production in mice. Exp Hematol.1987;15: 719-721.
5. Hasegawa Y, Takamatsu J, Iwase T, Iwasada S, Kitamura S, Iwata H. Effects of recombinant human erythropoietin in thrombosis and fibrinolysis in autologous transfusion for hip surgery. Arch Orthop Trauma Surg.1999;119:384-387.
6. Sweeney PJ, Nicolae D, Ignacio L, et al. Effect of subcutaneous recombinant human erythropoietin in cancer patients receiving radiotherapy: final report of a randomized, open-labelled, phase II trial. Br J Cancer.1998;77:1996-2002.
7. Horina JH, Schmid CR, Roob JM, et al. Bone marrow changes following treatment or renal anemia with erythropoietin. Kidney Int.1991;40:917-922.
8. Wolf RF, Peng J, Friese P, Gilmore LS, Burstein SA, Dale GL. Erythropoietin administration increases production and reactivity of platelets in dogs. Thromb Haemost.1997;78:1505-1509.
9. Shikama Y, Ishibashi T, Kimura H, Kawaguchi M, Uchida T, Maruyama Y. Transient effect of erythropoietin on thrombocytopoiesis in vivo in mice. Exp Hematol.1992;20:216-222.
10. McDonald TP, Clift RE, Cottrell MB. Large, chronic doses of erythropoietin cause thrombocytopenia in mice. Blood.1992;80:352-358.