Anti-Cancer Drugs 1997, **8**, pp. 466–467

Case report

Effect of low-dose 1-hydroxyvitamin D_3 in a patient with myelodysplasia after induction therapy for acute myelocytic leukemia

Shin Fujisawa, Shigeki Motomura, Rika Sakai, Naoto Tomita, Katsumichi Fujimaki, Hiroshi Mohri[1] and Takao Okubo[1]

First Department of Internal Medicine, Urafune Hospital, and [1]First Department of Internal Medicine, Yokohama City University School of Medicine, Urafune-cho, 3-46, Minami-ku, Yokohama 232, Japan. Tel: (+81) 045 261-5656; Fax: (+81) 045 241-2812.

Key words: Hematopoiesis, low dose 1-hydroxyvitamin D_3, M6.

Several clinical trials in patients with myelodysplastic syndrome (MDS) have indicated that 1,25-dihydroxyvitamin D_3 acts to induce differentiation of blast cells in MDS, but a high dose of 1,25-dihydroxyvitamin D_3 produces hypercalcemia.[1–3] We present a patient with acute non-lymphoblastic leukemia (ANLL; FAB classification M6) whose marrow transformed to MDS after induction chemotherapy. Administration of a low dose of 1-hydroxyvitamin D_3 produced elevation of a previoulsy low platelet count and hemoglobin level.

A 69-year-old man was admitted to our hospital with pancytopenia on 10 July 1995. Hemoglobin was 6.1 g/dl, white blood cell count (WBC) 1900/μl with 87% lymphocytes and platelet count 33 000/μl. Nucleated cells on bone marrow examination included 60.8% erythroblasts and 27.6% myeloblasts. The blasts were negative to periodic acid–Schiff stain and positive to peroxidase. Morphologic study showed megaloblastoid changes in many erythroblasts and many granulocytes were degranulated or showed a pseudo-Pelger–Hüet abnormality. Immunophenotypic analysis of the blasts revealed positive reactions for CD33 and HLA-DR. On the basis of these results, we diagnosed ANLL (M6) according to the FAB classification[4] and treated the patient with ICP therapy consisting of idarubicin (IDR), cytosine arabinoside (Ara-C) and prednisolone (PSL). Two months later, hemoglobin and WBC had improved, but thrombocytopenia had worsened, hemoglobin 11.8 g/dl, WBC 8000/μl, platelets 59 000/μl and reticulocytes 54 000/μl. Bone marrow examination revealed normocellular marrow with morphologic dysplasia. Myeloblasts constituted 2.4%, erythroblasts 25.2% and monocytes 3.6% of all nucleated marrow cells (87 200/μl). Biochemical evaluation showed normal serum levels of LDH (332 mU/ml), haptoglobin (319 mg/dl) and total bilirubin (1.1 mg/dl). We concluded that the marrow had transformed to refractory anemia (RA) after induction chemotherapy. Because of the patient's age and the occurrence of heart failure after induction chemotherapy, he was administered only 1 μg of 1-hydroxyvitamin D_3 per day. Without side effects hemoglobin gradually rose to 16.0 g/dl over 12 weeks and the platelet count to 96 000/μl over 22 weeks (Figure 1). With continued treatment for 10

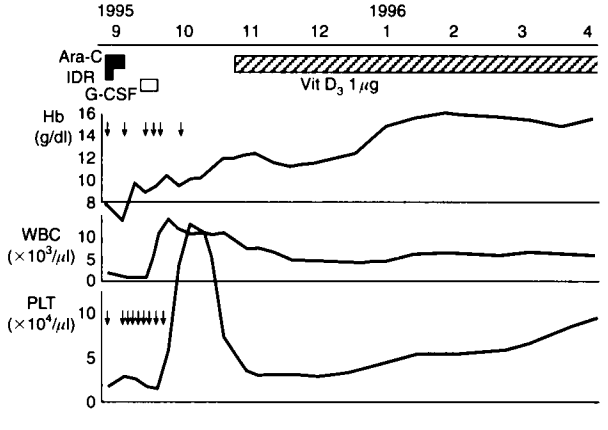

Figure 1. Clinical course of a patient with marrow transformation to MDS after induction therapy for acute myelocytic leukemia.

Correspondence to S Fujisawa

months, hemoglobin was maintained at about 14 g/dl with reticulocyte counts over 50 000/μl and the platelet count at about 80 000/μl. Bone marrow aspirates were performed after 3 and 10 months. Total nucleated cell counts were 180 000 and 97 000/μl, respectively with myeloblasts constituting 2.0 and 3.6% and erythroblasts constituting 41.2 and 36.0% of nucleated cells. Monocytes represented 1.2 and 4.8% of all nucleated cells, respectively.

In the present case, the drug may have accelerated hematopoiesis rather than inducing differentiation of blasts. Since, despite increased total nucleated cell counts and proportions of erythroblasts, monocytes in the bone marrow did not increase and the occurrence of myeloblasts did not change.

The mechanism of 1-hydroxyvitamin D_3 effects on hematopoiesis is unknown. Motomura *et al.* have reported success elevating hemoglobin concentrations accompanied by reticulocytosis with administration of a low dose of 1-hydroxyvitamin D_3 in a case of RA.[5] We suggest that low doses of 1-hydroxyvitamin D_3 may be beneficial in treating patients with M6 who transform to MDS after induction chemotherapy.

References

1. Koeffler HP, Hirji K, Itri L, The Southern California Leukemia Group. 1,25-dihydroxyvitamin D_3: *in vivo* and *in vitro* effects on human preleukemic and leukemic cells. *Cancer Treat Rep* 1985; **69**: 1399–407.
2. Tricot G, Boogaerts MA, Verwilghen RL. Treatment of patients with myelodysplastic syndromes: a review. *Scand J Haematol* 1986; **36**: 121–7.
3. Cheson BD. The myelodysplastic syndromes: approaches to therapy. *Ann Intern Med* 1990; **112**: 932–41.
4. Bennett JM, Catovsky D, Daniel MT, *et al.* Proposals for classificaton of the myelodysplastic syndrome. *Br J Haematol* 1982; **51**: 189–99.
5. Motomura S, Fujisawa S, Tsunooka S, Fujimaki K, Mohri H, Okubo T. Haematologic benefits of 1-hydroxyvitamin D_3 in an elderly patient with chronic myelodysplastic syndrome. *Am J Hematol* 1996; **53**: 143–4.