

LETTER TO THE EDITOR

Bone Marrow Damage during Treatment of Psoriasis with Busulphan

In recent years a number of publications have appeared regarding the favourable effects of cytostatic drug treatment on psoriasis. We have earlier published a paper (1) regarding the treatment of 9 patients who reacted well on busulphan (Myleran®). The complications seen in some of these patients during the last year have convinced us about our responsibility to publish a brief warning note regarding such possible dangers. Three patients of the original 9 were given a second course of busulphan and thereby all developed signs of bone marrow damage after such treatment during 6 weeks, 10 weeks and 8 months, resp. Therapy had to be stopped. In 2 patients the blood values increased again and these patients now seem to be in good shape. The third patient developed signs of acute leukemia 1 1/2 years after busulphan was stopped. The patient was admitted with an acute blast cell leukemia and died rapidly of an overwhelming infection. This case history seems to show that even in persons with no neoplastic disease of the blood-forming organs, acute leukemia might possibly be induced by treatment with alkylating agents. It is of course impossible to draw conclusions from just one case but we think that a warning should be issued not to treat psoriatics with alkylating agents. It seems quite possible that in the present case the treatment with methotrexate might also have been of importance from the point of view of leukemia.

Case history

Man born in 1906. Previous history, except for psoriasis, is of no special interest. Has never been treated with irradiation or had other exposure to carcinogens.

Since 1937 the patient has had severe psoriasis. In November 1969 he was treated for 2 months with busulphan 4 mg/day with a favourable effect on his skin disease and no signs of bone marrow damage in the peripheral blood. Because of relapsing psoriasis the treatment was reinstituted in August 1970 with a similar

effect on the skin. However, the treatment was discontinued after 10 weeks because of thrombocytopenia. This improved spontaneously, and in September 1971, for another bout of psoriasis, the patient was started on oral methotrexate 7.5 mg once a week. Again, the patient developed lowered thrombocyte counts and this treatment was therefore given for 1 month only. Thrombocytopenia was persistent during 1972, and with signs of pancytopenia the patient was admitted to the Department of Medicine, Malmö General Hospital, on February 20th 1973, i.e. 27 months after busulphan treatment was stopped and 16 months after methotrexate administration.

Findings

Several subcutaneous hematomata. Lgll. and spleen not palpable. Hb 8.2. RBC 2.3 mill. WBC 1 000. Reticulocytes 18 000. Platelets 14 000. IgA somewhat increased. Sternal puncture showed some increase in myeloblasts in a cellular marrow. His bleeding time was increased but no signs of fibrinolysis were present. Coagulation factors normal. Sent home after 3 days.

Readmitted on March 23rd. Very tired. RBC 1.5. Hb 5 (34%). WBC 2 200. Platelets 22 000. No sternal puncture. Treated with transfusions. Blood cultures were repeatedly positive for staph. and beta hemolytic streptococci. Treated with large doses of antibiotics but died febrile after 10 days in hospital in a septic condition. D. leukemia acuta?

The post mortem confirmed the clinical diagnosis. The bone marrow was hypercellular with abundant large atypical blast-like cells and numerous large megakaryocytes. The spleen showed massive proliferation of plasma cells. The testes showed bilateral atrophy. Diagnosis: acute blast cell leukemia.

It is evident that one case is not sufficient to prove that the cytostatic drug has caused the leukemic process in the bone marrow. During the last 2 years, however, the number of observations on the development of acute leukemia in myeloma patients treated with another alkylating agent (melphalan) has increased rapidly. Also relevant are the observations on the development of acute leukemia in patients with polycythemia vera, who have been treated with radiation and/or alkylating agents. The patient we have described is so far the only known instance of

acute leukemia in a non-malignant condition treated with alkylating agents.

We think that the problem is important from two points of view. 1) Alkylating agents should probably not be used in the treatment of non-malignant conditions such as psoriasis. 2) A close supervision of the further development of patients with psoriasis, and who have been treated with cytostatics, is imperative. If signs of possible oncogenesis are detected they should be reported in the literature.

Reference:

1. Möller, H. & Waldenström, J.: Psoriasis treated with busulphan. *Acta Dermatovener (Stockholm)* 50: 445, 1970.

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