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Letter to the Editor

Superoxide Dismutase Deficiency in Patients with Nitrogen Mustard Therapy-induced Intravascular Hemolysis

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For a long time we have been observing the occurrence of intravascular hemolysis (IVH) in patients afflicted with malignant diseases and undergoing a polychemotherapy regimen including either nitrogen mustard, such as mechlorethamine, or derivatives such as cyclophosphamide and melphalan. IVH usually appears during the fifth course of therapy and surprisingly, in some cases abnormalities usually responsible for hemolysis, such as immunological disorders, carbohydrate metabolism, red cell enzyme deficiency, or infection cannot be detected. In the light of these unexplained IVH's, we decided to determine the red blood cell (RBC) superoxide dismutase (SOD) activity, since SOD is believed to play a central role in protecting the cells against various oxidant stresses [1].

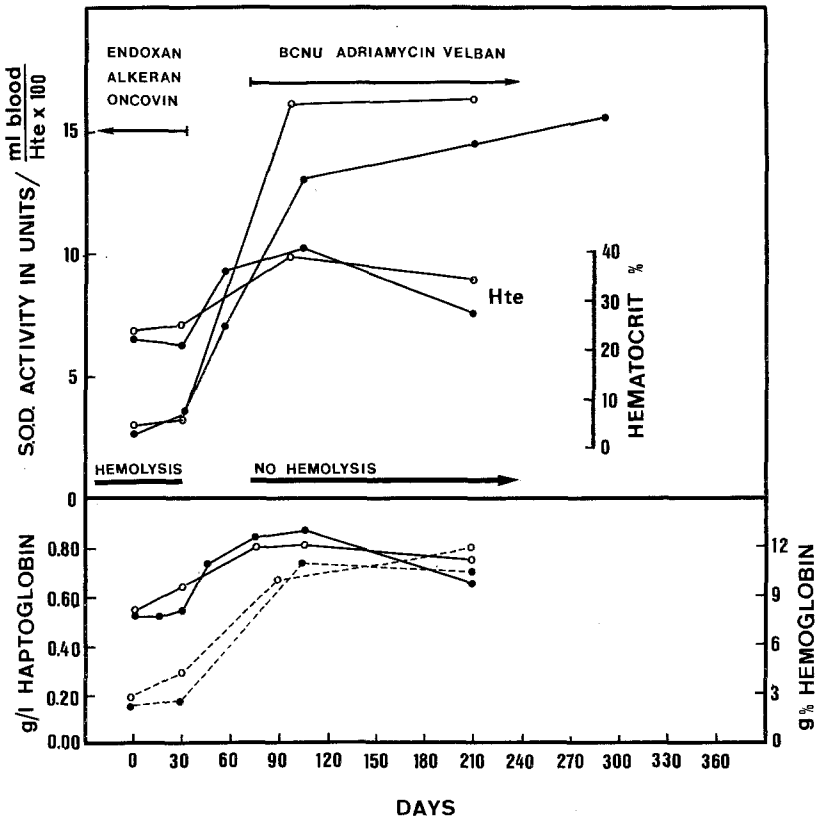

Fig. 1. Relationship between superoxide dismutase deficiency and intravascular hemolysis in two patients with myeloma

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Two groups of patients were investigated. The first group was composed of three patients with myeloma and three patients with Hodgkin's disease, and they were treated with a combination of Alkeran, Endoxan, and Oncovin (AEO) and the MOPP regimen, respectively. Patients in this group exhibited an IVH that was obvious from the marked decline in their hemoglobin level, their hematocrit, and their plasmatic haptoglobin concentration.

The second group was composed of four patients with myeloma and five patients with Hodgkin's disease, undergoing similar treatments but without any symptoms of IVH. RBC SOD activity measured according to a standard assay procedure routinely used in our laboratory [2] was found to be markedly impaired in group I (7.02 ± 3.39)* as compared with group II (12.80 ± 1.44) and with a control group composed of 32 normal subjects (16.00 ± 1.70).

In two patients in group I with myeloma who were undergoing an AEO combination treatment and exhibited IVH, treatment was discontinued and replaced by a BCNU-Adriamycin-Velban combination. RBC SOD was determined before and after the change in treatment. The results summarized in Fig. 1 indicate that the interruption of the nitrogen mustard derivative-containing therapy was followed by a rapid increase in RBC SOD activity, whereas the hemoglobin concentration of the blood, the hematocrit, and the plasmatic haptoglobin level rose to normal. In neither patient was any IVH relapse observed during the course of BCNU-Adriamycin-Velban treatment, and RBC SOD remained within the normal range. From these observations, it may be concluded (1) that in some patients nitrogen mustard therapy induces a marked RBC SOD deficiency; (2) that in accordance with the concept of the protective role of SOD, this deficiency results in hemolysis; and (3) that the measurement of RBC SOD must be included in the investigation of any hemolytic process.

* SOD activity is expressed in units/ml blood/Hte × 100 ± S.D.

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