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Acute Erythroblastic Leukemia Terminating a Very Long-Lasting (27 Years) Hodgkin's Disease

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To the Editor,

Although there is already an ample literature on acute leukemias, usually of myeloid type, complicating treated Hodgkin's disease (HD), the case we present here seems to us very unusual both for the very long-lasting HD (27 years after the diagnosis) and for the arising of an acute erythroblastic leukemia (AEL), rare as a primary disease and even more so as a terminating event in HD, the only recent case reported being that of Larsen and Brincker [4].

The patient (a white woman, M.M.), who died at the age of 49, had the onset of the disease at the age of 22 (laterocervical lymph node involvement). The probable clinical stage at the time was II A. For the first 6 years of her disease the patient was given local radiotherapy of the regions involved (laterocervical, axillary, mediastinal) with regression of the involvement but with subsequent local and distant relapse. Then for about 4 years no relapses of the disease were evident. For the 3 following years she was again treated with radiation therapy and, for the appearance of general signs (fever), with chemotherapy (cyclophosphamide, 3 g).

In 1971, being 39, the patient was first seen by our group. She did not show superficial but lumbar and paraaortic lymph node involvement so that a stage III A was stated: a MOPP combination chemotherapy was started [3] and two cycles were administered but the therapy had to be discontinued owing to an acute hepatitis B. At the recovery from hepatitis complete remission of HD was achieved and the MOPP treatment was stopped.

In 1976 (44 years) another lymphography demonstrated a lymph node involvement below the diaphragm. Histological examination during laparotomic staging suggested a moderate involvement of the spleen; moreover from a gastrointestinal X-ray with a barium meal the suspicion arose of a gastric involvement as well. The MOPP chemotherapy was restarted: 6 cycles were fulfilled and 5 additional cycles were administered as a maintenance therapy achieving again complete remission (even gastrointestinal X-rays with a barium meal and enema were negative). For the following 2 years (1979-1980) no treatment was given.

In January 1981 the patient was hospitalized again: she complained of progressive pallor, mild fever, headache, weakness which had started 1 month before. The general state was seriously

involved, a marked anemia with tachycardia and mild malleolar edema were present while no lymph node involvement was found. The hematological investigation showed hypochromic anemia (Hb 6.9 g/dl; RBC $3 \times 10^{12}/l$), marked leukocytosis ($43 \times 10^9/l$) and a normal platelet count ($160 \times 10^9/l$). In the peripheral blood smear about 95% of the nucleated cells were basophilic erythroblasts; the bone marrow aspirate showed a monomorphic pattern of cells of the erythroid line while the normal myeloid series was virtually absent. On the basis of these findings diagnosis of an AEL (Di Guglielmo's disease) was made. Combination chemotherapy was then started according to the Protocol of the Italian Cooperative Study Group for Nonlymphoblastic Acute Leukemias (daunorubicin plus cytosine arabinoside plus 6-thioguanine). The response to the treatment was good and the patient achieved remission. After a

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phase of marrow aplasia lasting about 20 days, the leukocyte count rose slowly to $5-7 \times 10^9/l$, the blood smears showed circulating erythroblasts not exceeding 5%. While the hematological remission persisted and no signs of leukemic relapse were present, a marked marrow hypoplasia appeared again, fever became resistant to the antibiotics and, after 2 months, the patient died from cardiac failure with the picture of marrow aplasia, no evidence of HD relapse being present. As a final consideration, the quite unusual way of the radiation therapy given at the beginning of the disease reaching a total amount of 18,000 rad, although administered over 9 years, must be taken into account. Undoubtedly such a high amount of radiation together with aggressive chemotherapy (13 MOPP cycles) could have played a causal role for the emergence of a mutant (erythro-)leukemic clone. It is well known that the combination of radio- and chemotherapy in HD shows a relatively high frequency of complicating second malignancies, almost always leukemias [2]. Indeed, it has been reported that in the group of HD patients receiving both radio- and MOPP therapy there is a 15-fold greater incidence of second malignancies, almost entirely due to myelocytic leukemias [1].

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