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Abstracts

Hematologic malignancies

ACUTE NON-LYMPHOCYTIC LEUKEMIA: ONSET AFTER TREATMENT FOR HODGKIN'S DISEASE

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New developments in radiotherapy (RT) and chemotherapy (CT) are helping to improve the overall survival and cure rates of patients with Hodgkin's disease (HD). However, treatment-related complications have taken on enormous clinical importance. As reported in most publications, these include injuries of the gastrointestinal tract, pulmonary function impairment, cardiac toxicity, thyroid dysfunctions, sterility, immunity alterations and the arising of second tumor.^{1–5} Second primary cancer (SPC), particularly acute non-lymphoid leukemia (ANLL), non-Hodgkin' lymphoma (NHL) and secondary solid tumours (ST), are well-known late complications that can occur in patients treated for HD.^{1,4,5} The increase of ANLL risk has been correlated with host-related factors and the type of treatment procedures⁶ and radiation-induced leukemia occurs after a period of time generally exceeding 5 years (Fig. 1). The risk is higher in patients treated with combined RT and CT regimens including mechlorethamine and procarbazine.^{1,6}

With regard to the occurrence of ANLL after RT alone, Coleman⁷ and of Hoppe⁸ has reported, respectively, only one case (A.R. 0.6% at 10 years) of ANLL among 441 patients and 3 cases (A.R. 0.5% at 10 years) among 898 patients treated with irradiation alone. Valagussa et al.⁹ have reported that the ABVD is not associated with acute leukemia occurrence even when combined with radiation. In research carried out by the Cancer Institute in Milan,⁹ only one case of ANLL was recorded after ABVD + RT, with a Cumulative risk of 0.7% (at 15 years), compared with a risk of 9.5% (at 15 years) in patients treated with MOPP + RT ($P = 0.04$). Further studies will make it possible to investigate the occurrence of ANLL after RT + ABVD. Many authors^{4,6,10,11} are in accord on the fact that a higher risk of leukemia from CT including alkylating agents and procarbazine with or without irradiation, compared to the risk factor involved in the use of ABVD or RT alone. Other studies report the potential role of sex, age, splenectomy and spleen irradiation as risk factors in ANLL occurrence.^{3,4,6}

There is controversy regarding the role of splenectomy. Van Leeuwen et al.¹² have reported that splenectomy might predis-

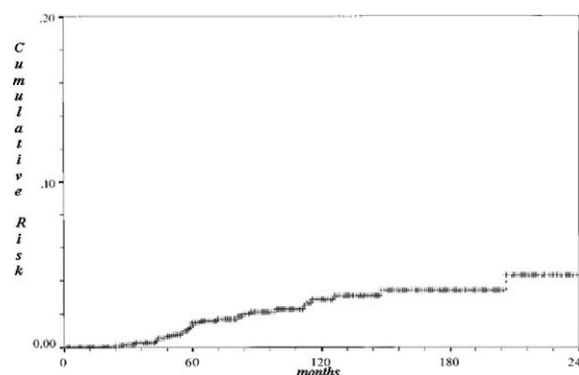


Fig. 1. Cumulative risk of acute non-lymphocytic leukemia (ANLL).

pose to secondary ANLL. For other authors correlation does not exist between splenectomy and onset of leukaemia.^{4,6} In conclusion, treatment with MOPP alone and MOPP plus RT can increase the risk of ANLL. Moreover, the problem of secondary leukemia is probably linked with the prolonged survival of HD patients and the risk of induced cancer is connected both with the type of treatment received and with the related factors. It should also be observed that these results refer to treatment carried out 20 or 25 years ago, when higher CT doses were used and larger volumes of tissue were irradiated. Finally, we must continue to focus attention on long-term survivors of HD patients, to modify our treatment strategy and to identify types of treatment which do not lead to undesirable effects in the future.

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SECOND SOLID CANCER AFTER HODGKIN'S DISEASE: ANALYSIS OF THE RISK AND REVISION OF THE LITERATURE

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At present time, patients with Hodgkin's disease (HD) have a high probability of cure. However, the late sequelae treatment-related have a remarkable clinical importance. An increased of second primary cancers (SPC) has been observed among long-term survivors of HD: particularly, acute non-lymphoid leukemia (ANLL), non-Hodgkin' lymphoma (NHL) and secondary solid tumours (ST).¹⁻⁵ The increase of ANLL risk has been correlated with host-related factors and the type of treatment procedures.^{1,5} Several authors have demonstrated that secondary ANLL was likely with chemotherapy-treatment. NHL has been correlated with the radiochemotherapy treatment: the risk has concentrated in the first year following start of treatment and declined in the subsequent 5 years.⁶ Recently, several studies have been focused attention on the incidence of ST: the appearance risk increases with the length of the follow-up (Fig. 1) and results correlated with the kind of treatment using RT alone or in combination with chemotherapy (CT).^{1,4} The most frequent solid tumor are lung cancer, breast cancer, melanoma skin, gastrointestinal cancer and sarcoma of the bone.

On the occurrence of solid tumours in patients treated with CT alone, the results of BNLI⁷ shows an increased risk of ST after CT alone: further study is required for a better examination of the increase in risk of ST after treatment with CT. Moreover, Maurizi

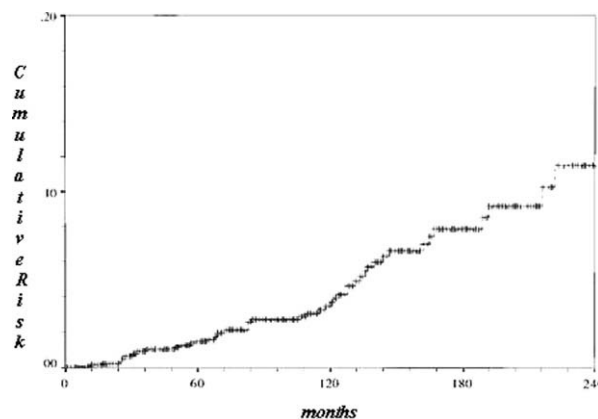


Fig. 1. Cumulative risk of solid tumour (ST).

et al.⁴ show that additional therapy for relapsing patients with CT + RT after initial therapy with RT alone does not increase the risk of ST, while in a recent study⁸ the addition of combined therapy for recurrent disease in patients previously treated with radiotherapy showed a significant increase in the relative risk of ST. In the authors' opinion, it is possible that either the cumulative dose of radiation received after secondary treatment with CT was responsible for a high occurrence of ST or that the increase in ST occurrence was due to initial radiation.

Age is the major risk factor of solid tumours in the HD population, in the same way as age is a major risk factor of almost all solid cancer in the general population. It is uncertain whether this biological phenomenon is related to age or to the HD status of patients or whether it is an undifferentiated effect of treatment (RT or CT or CT + RT).

With respect to the location of ST, no definite relation could be made between the treatment received (radiotherapy alone and radiotherapy with chemotherapy) and the tumor tissue. For example, lung cancer was observed more often in patients who had received RT, but also in patients treated with CT alone. In their detailed analysis of various solid tumours, Kaldor et al.⁹ have pointed out that the occurrence of lung cancer is higher in long-term HD survivors than in the general population. They conclude that this higher risk is due to the cancer-inducing effects of both CT and RT, compared with those produced by other risk factors, e.g. smoking for lung cancer. Van Leeuwen et al.¹⁰ studied a cohort of 1939 patients treated for HD who developed 30 lung cancers and examined the relationship between the carcinogenic effect of smoking and radiation. They conclude that the appearance of lung cancer is related both to the radiation dose received by the lung and to smoking after radiation exposure.

Regarding the occurrence of breast cancer, Van Leeuwen et al.¹¹ and Yahalom et al.¹² reported an increased risk of breast cancer in women who have received radiation therapy for HD at a younger age. Moreover, Yahalom et al.¹² showed that breast cancer following the treatment for HD was bilateral and frequently involved the medial half of the breast, while the prognosis of the disease is similar to that of patients with primary cancer. In Hancock's experience,¹³ the risk after 15 years is equivalent both in women treated with RT alone and in women receiving RT combined with MOPP. For other types of cancer such as cancer of the gastroenteric tract, of the soft tissue and of the nervous system, which have been observed in irradiation, there could be a