Secondary acute myeloid leukemia following treatment with VP16-containing regimens for non-Hodgkin’s lymphoma

ESTER ORLANDI, MARIO LAZZARINO, PAOLO BERNASCONI, CESARE ASTORI, CARLO BERNASCONI
Institute of Hematology, University of Pavia, Division of Hematology, IRCCS Policlinico S. Matteo, Pavia, Italy

We report on two patients who developed a secondary acute myeloid leukemia (sAL) after treatment for non-Hodgkin’s lymphoma (NHL) with regimens containing low to intermediate doses of VP16. Clinical and hematologic features in these two patients were consistent with epipodophyllotoxin-associated sAL. In one case, a rearrangement of chromosome band 11q23 was detected.

Etoposide or VP16 is an epipodophyllotoxin-derivative targeting the enzyme topoisomerase II. In the last few years, a number of reports have focused on the risk of secondary acute myeloid leukemia in patients treated with regimens including epipodophyllotoxins for prior independent malignancy. In patient #1 marrow blasts showed a t(9;11) (p22;q23). At disease progression, he was treated with vincristine plus cyclophosphamide. On the other hand, anthracyclines are administered to relatively low cumulative doses because of their cardiac toxicity, and cyclophosphamide was associated with a nonsignificant increased risk of secondary leukemia in NHL patients. In addition to antineoplastic drugs, our two patients received G-CSF. To date, it is unknown whether this drug may accelerate the development of acute leukemia after genetic damage of hemopoietic stem cells by epipodophyllotoxins.

In conclusion, our data show that VP16-containing regimens currently used in the treatment of NHL may carry a risk of secondary acute leukemia, even after relatively low cumulative exposure to VP16. Although sAL seems an infrequent event, this complication should be considered because of the increasing use of VP16 in the chemotherapy of NHL.

Key words
VP16, secondary leukemia

Correspondence
Dr. Ester Orlandi, Institute of Hematology, University of Pavia, Division of Hematology, IRCCS Policlinico S. Matteo, 27100 Pavia, Italy. Phone: international +39-0382-503596 • Fax: international +39-0382-502250.

References
Pulmonary multinodular relapse of non-Hodgkin’s lymphoma

JOSÉ MARÍA ARGÜXANO, ENCARNACIÓN PÉREZ EQUITZA, ANA MARÍA GOROSQUIETA

Department of Hematology, Hospital de Navarra, Irunlarrea s/n, Pamplona, Spain

We describe here a case of pulmonary multinodular relapse of non-Hodgkin’s lymphoma following autologous stem cell transplantation.

A 44-year-old patient was admitted for autologous peripheral stem cell transplantation. His diagnosis was diffuse large cell B lymphoma, stage II with bulky disease. After an initial complete remission he had relapsed and a second partial remission was achieved with ESHAP chemotherapy.

Transplantation was performed without incidences; in computerized tomography (CT) revealed two small para-aortic lymph nodes, which were evaluated by gallium scan showing their residual nature, thus the patient was considered to have achieved complete remission. Radiotherapy was administered to the bulky zone and a new CT showed no change in the size of residual nodes, but small nodular images appeared in the lung parenchyma. Chest radiography showed a pattern of small, ill-defined nodular images (Figure 1). At this point, six months after transplantation, the patient’s only complaint was mild cough, with no dyspnea or fever. Physical examination yielded no significant findings. The platelet count was 35×10⁹/L, attributed to delayed recovery of platelets after transplantation. Several tests were performed in order to determine the nature of the pulmonary disease.

Except for the platelet count, the rest of the blood count was within normal ranges as were the lactate dehydrogenase concentration and arterial O₂ saturation. Mantoux test and serology for Aspergillus were negative and so, too, was cytomegalovirus antigen detection. Fibrobronchoscopic findings were nonspecific; cytological analysis of bronchoalveolar lavage (BAL) specimens demonstrated a hemorrhagic background and the presence of hemosiderin-laden macrophages. Bacteriologic cultures and fluoroscopy for Mycobacteria were negative. This led to the diagnosis of alveolar hemorrhage, prompting an intensive schedule of platelet support in order to maintain the platelet count above 50×10⁹/L.

Three weeks later, the patient’s status remained unchanged, and a new radiograph showed the growth of nodules. In view of this progression, regardless of the patient’s good status, an open lung biopsy was performed. Histopathologic findings led to the diagnosis of lung infiltration by lymphoma, with a nodu-