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A brief intensive chemotherapy in T-prolymphocytic leukemia

We report the case of a patient with T-prolymphocytic leukemia resistent to deoxycoformycin therapy. As second line therapy, brief, intensive chemotherapy, developed for Burkitt's lymphoma was administered achieving complete remission of the disease. As consolidation therapy, an autologous stem cell transplantation was performed. After a follow-up of 20 months the patient is disease-free.

Sir,

T-prolymphocytic leukemia (T-PLL) is a rare lymphoproliferative disease derived from mature, postthymic T-lymphocytes, as demonstrated by immunophenotypic positivity for either CD4 or CD8, with the former being more often represented, and negativity for Tdt and CD1a.

The prognosis of this disease is considered bad, with poor response to traditional protocols of chemotherapy and a median survival of 7.5 months.[1]

We describe a case of a 53-year old male presented with hepato-splenomegaly, diffuse lymphadenopathy, lymphocytosis of 120×10^9/L, slight thrombocytopenia (130×10^9/L platelets) and normal hemoglobin concentration (13.5 g/dL).

The immunophenotype defined a population of mature T-cells positive for CD3, CD4, CD5, CD7, TCR γ/δ, and negative for TdT, CD1a and CD25.

A diagnosis of the variant with small prolymphocytes of T-PLL was made and therapy with deoxycoformycin (DCF, 7 mg weekly) was started.[1] Because of the lack of response after five cycles, second line chemotherapy was instituted according to a protocol designed for Burkitt-like non-Hodgkin's lymphomas (NHL) (Codox M-Ivac: Codox M regimen: day 1: cyclophosphamide 800 mg/m^2, vincristine 1.5 mg/m^2, doxorubicin 40 mg/m^2; days 2-5: cyclophosphamide 200 mg/m^2; day 8: vincristine 1.5 mg/m^2; day 10: methotrexate 1,440 mg/m^2. Ivac regimen: days 1-5: etoposide 60 mg/m^2, ifosfamide 1,500 mg/m^2, mesna 360 mg/m^2, 7 doses in 24 h; day 1 and 2: cytarabine 2 gm/m^2 for a total of 4 doses. After 2 cycles of combined chemotherapy with the Codox-M-Ivac regimen, complete clinical, morphologic and immunophenotypic remission was obtained and peripheral blood stem cells were harvested after the last cycle of chemotherapy. High dose melphalan (140 mg/m^2) and unfractionated total body irradiation (10 Gy) were administered followed by peripheral stem cell (PBSC) autograft.

This treatment was well tolerated with hematologic reconstitution by day +28 after PBSC infusion. After a follow-up of twenty months, the patient is disease free with normal hematologic and immunophenotypic parameters in the peripheral blood and bone marrow.

Recently, DCF, an inhibitor of adenosine deaminase, has been proposed as first line therapy in T-PLL.[2] However despite 5 cycles of this therapy, our patient showed limited response with recurrence of lymphadenopathy and lymphocytosis between the single cycles.

The choice of the Codox M- Ivac protocol was suggested by the high proliferation rate of the disease, the young age of the patient and the disappointing results reported in the literature with traditional combination chemotherapy.

The Codox-M-Ivac regimen was developed for treatment of Burkitt's or Burkitt-like NHL as brief, intensive chemotherapy, combining two non-cross-resistant protocols.[3]

As already suggested by some authors, this type of brief, intensive protocol may be an option for poor prognosis NHL.[4] The consolidation of the complete remission with autologous PBSC, although experimental, may be a reasonable means to avoid the early relapse frequently seen in T-PLL.[5]

In conclusion, this case illustrates the feasibility and efficacy of a brief intensive chemotherapy program in the management of T-PLL. The disease-free survival of over one year suggests that this is a possible therapeutic approach for younger patients affected by this rare lymphoproliferative disease with a very poor prognosis.

Atto Billio, Norbert Pescosta, Carlo Rosanelli, Pietro Fabris, Paolo Coser

Reparto di Ematologia, Ospedale Regionale, Bolzano, Italy

Key words

T-prolymphocytic leukemia, deoxycoformycin, autologous peripheral blood transplantation.

Correspondence

Atto Billio, M.D., Reparto di Ematologia, Ospedale Regionale, via L. Boehler 5, 39100 Bolzano, Italy. Phone: international +39.0471.908388 – Fax: international +39. 0471.908382 – E-mail: pescosta-n@hotmail.com

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Fulminant hemophagocytic syndrome as presenting feature of T-cell lymphoma and Epstein-Barr virus infection

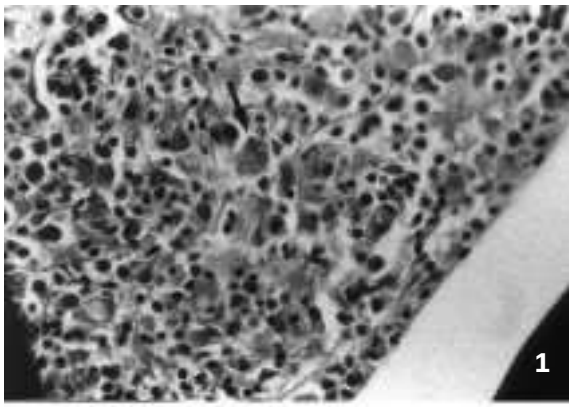
We describe a patient who presented with a fulminant hemophagocytic syndrome. Morphologic and immunohistochemical studies showed infiltration of the marrow and tonsil by neoplastic T-cells. A genomic amplification by means of polymerase chain reaction revealed the presence of EBV DNA in the serum. In spite of aggressive immunosuppression and multiagent chemotherapy this patient died of disseminated intravascular coagulation-induced multiorgan failure.

Sir,

Hemophagocytic syndrome (HPS) is a clinicopathologic entity characterized by systemic proliferation of hemophagocytic histiocytes, fever, cytopenia, deranged liver function, and frequently, coagulopathy and hepatosplenomegaly.[1,2] There are two major clinical subsets of HPS: the aggressive disease known as malignancy-associated HPS and the more benign, reactive hemophagocytic syndromes such as virus-associated HPS.[3] In a few cases HPS presents at the time of initial diagnosis of lymphoma in the absence of any pre-existing disease or immunosuppressive therapy.[4,5] We describe a case of fulminant HPS as the presenting feature of a recent Epstein-Barr virus (EBV) infection and disseminated T-cell lymphoma.

A 50-year old woman was admitted to our hospital with fever, rapid deterioration of her general condition and marked weight loss. Physical examination revealed an ulcerative lesion in the right tonsil, slightly enlarged cervical and axillary lymph nodes, and hepatosplenomegaly. Complete blood count included hemoglobin level of 9.3 g/dL, platelet count of 92×10^9/L, and white blood count of 2.2×10^9/L. Laboratory studies also disclosed the following values: fibrinogen 130 mg/dL, D-dimer 4 µg/mL, alkaline phosphatase 222 U/L, aspartate aminotransferase 83 U/L, alanine aminotransferase 45 U/L, and lactate dehydrogenase 826 U/L. A genomic amplification by means of polymerase chain reaction (PCR) showed a single 54 bp band indicating the presence of EBV DNA in the serum. Bone marrow aspiration and biopsy revealed an increase of reticulin fibers and histiocytic hyperplasia showing fresh, conspicuous hemophagocytosis (Figure 1). Bone marrow biopsy also demonstrated clusters of abnormal lymphocytes. These abnormal cells were small to medium sized lymphoid cells and had a high nuclear to cytoplasmic ratio and irregular hyperchromatic nuclei (Figure 1). Immunohistochemistry showed staining of the abnormal lymphocytes with primary antibodies directed against CD3 and CD45RO but not CD20, CD74 and MB2 (Figure 2). Incisional tonsillar biopsy revealed a diffuse atypical lymphocytic infiltrate underlying the ulcerated and inflamed mucosal lining. Tonsillar lymphoid cells showed similar morphologic and immunophenotypic patterns as the bone marrow lymphoid cells. We evaluated PCR amplification of the rearranged γ T-cell receptor (TCR) from bone marrow samples. Clonal rearrangement for the TCR γ-chain gene was not detected. The patient was first treated with high doses of steroids and when results were consistent with T-cell lymphoma, she was treated with combination chemotherapy that contained adriamycin, cyclophosphamide, vincristine, and prednisolone. However, this patient's HPS was refractory to the chemotherapy, and she died of disseminated intravascular coagulation-induced multiorgan failure on her 20th day in hospital.

HPS has been reported in patients with non-Hodgkin's lymphoma, usually as a terminal compli-



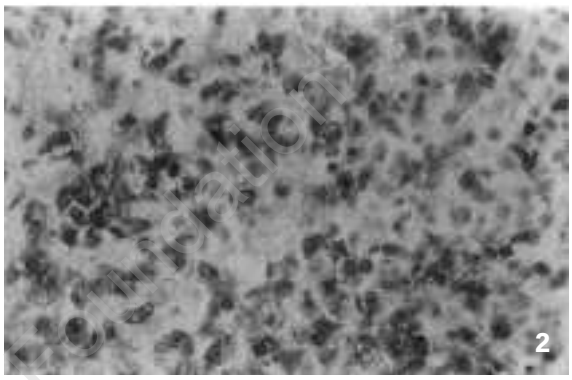


Figure 1. Small and medium sized irregular lymphocytes infiltrating bone marrow and a histiocyte with marked hemophagocytosis (arrow) (x750).

Figure 2. Bone marrow biopsy showing intense membranous CD3 staining in abnormal lymphocyte cells (x500).