Table 2. Response according to the treatment of LGNHL with 2-CdA, CMD or CID.

Treatment	No. of patients	CR	PR	NR
2-CdA	36	4 (11.2%)	9 (25.0%)	23 (63.8%)
CMD	17	2 (11.7%)	5 (29.5%)	10 (58.8%)
CID	5	1 (20%)	1 (20%)	3 (60%)

The differences among the groups treated with the different regimens are not significant (χ^2 test) ($p>0.05$). CR: complete response; PR: partial response; NR: no response.

CMD or CID. Grade 3 or 4 neutropenia developed in 35% and 37% of patients, respectively. Infections occurred in 40% of patients treated with 2-CdA (2 patients died of sepsis) and 38% of patients treated with CMD or CID (1 patient died of sepsis)

There was one fatal neurologic complication in a patient with pre-existing paraneoplastic neurological syndrome, who died of an apparent rapidly progressive sensimotor peripheral neuropathy after completing the treatment with 2-CdA alone.

The results of our study revealed that 2-CdA as monotherapy has significant antitumor activity in previously treated LGNHL patients. The overall response rate was 36.2%. Similar effects have been observed by others.[4,5] It should be stressed that the activity of 2-CdA in previously treated LGNHL seems to be similar to that of another purine analog – fludarabine.[6,7]

There is still little experience on using new purine analogs in combination with other drugs in LGNHL treatment. Impressive results were observed by McLaughlin, using a combination of fludarabine, mitoxantrone and dexamethasone in patients with recurrent or relapsed LGNHL.[8] He recorded a 94% overall response rate with 47% CRs. The combination of 2-CdA with mitoxantrone also resulted in a high (70%) rate of responses.[9] The relatively low rate of responses observed in our patients is probably a consequence of the advanced stage of the disease and the multiple previous therapies.

In conclusion, these preliminary results suggest that addition of mitoxantrone or idarubicin and dexamethasone to 2-CdA in previously treated patients with LGNHL may not be of any advantage over 2-CdA alone.[10] However, randomized studies are necessary to confirm this.

Tadeusz Robak, Joanna Góra-Tybor, Krzysztof Chojnowski

Department of Haematology, Medical University of Lódz, Poland

Key words

Low grade non-Hodgkin's lymphoma, 2-chlorodeoxyadenosine, mitoxantrone, idarubicin, combination chemotherapy

Correspondence

Tadeusz Robak, M.D., Department of Hematology, Medical University of Lódz, 93-513 Lódz, ul. Pabianicka 62, Poland. Phone/fax: international +48.42-6846890 – E-mail: robaktad@psk.2.am.lodz.pl

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Cyclophosphamide / cyclosporin-A treatment of multicentric Castleman's disease with Kaposi's sarcoma

We have used a combination of cyclosporin A and cyclophosphamide to treat a patient with multicentric Castleman's disease (MCD) complicated by visceral Kaposi's sarcoma (KS). Beneficial effects were observed on both MCD and KS lesions: the patient's clinical, radiological and laboratory findings have been stable for 27 months.

Sir,

Multicentric Castleman's disease (MCD) is an uncommon disorder of immune regulation characterized by constitutional symptoms, diffuse lymphoadenopathy, hepato-splenomegaly, mediastinal masses resembling thymoma that may be complicated by non-Hodgkin's lymphomas and Kaposi's sarcoma (KS).[1] The prognosis of MCD is poor with a mean survival of 27 months.[2] Very limited information is available regarding treatment[3] and no consensus exists on optimal therapy.

We describe the case of a 53-year old female whose clinical history began in 1994 with fever, peripheral and mediastinal lymphoadenopathy, and anemia.

Multiple biopsies revealed chronic lymphoadenitis and lymphoepithelial thymoma. After mediastinal radiotherapy the patient was well until January 1996, when fever reappeared together with hepatosplenomegaly and a generalized edematous state. Splenectomy revealed a fibrocongested spleen, abdominal lymph nodes had abundant plasma cells, a liver biopsy was normal. She was treated with antibiotics and steroids, but the fever returned when the prednisone dose was tapered down.

She was referred to our clinic in December 1996, with sustained fever, lymphoadenopathy, and hepatomegaly. Lymph node biopsy established the diagnosis of plasma cell-rich MCD. Physical examination also revealed small, raised, reddish-purple cutaneous nodules on the right knee and both ankles, which had appeared two years before. Histology confirmed the clinical suspicion of KS. Visceral KS localizations were detected on the hard palate and in the stomach. Serum IL-6 levels were extremely high (1,850 pg/mL); serum anti-HHV8 antibodies were present and plasma HHV8 positivity was confirmed by PCR.

The rapid clinical deterioration, irrespective of steroids, prompted us to add a single dose of intravenous (iv) cyclophosphamide (30 mg/kg). An evident clinical and laboratory improvement was complicated by disseminated intravascular coagulation and cerebral hemorrhage. One month later hematologic and neurologic problems were stable; a relapse of MCD led us to restart cyclophosphamide with an iv pulse (25 mg/kg) followed by oral administration (2 mg/kg/die) together with prednisone (1 mg/kg/die). The fever disappeared and the enlarged lymph nodes shrank. Erythrocyte sedimentation rate, C-reactive protein, and liver function all improved; IL-6 dropped to levels seen in normal control subjects (164.6±119.3 pg/mL). Steroids were tapered down to 10 mg/day.

In May 1997 a cutaneous spreading of KS required local radiotherapy. α-interferon was tried briefly, but was stopped because of severe depression. Considering the possibility that the impressive polyclonal plasma cell differentiation of MCD might be under the control of the T-cell system and that the T-cell immunoregulatory circuits might also be abnormal,[4] we added cyclosporin A (CyA 4 mg/kg/die) to oral cyclophosphamide. The palpable lymph nodes did not increase in size and no new nodes appeared. Unexpectedly, we also observed beneficial effects on the KS lesions. Skin and hard palate nodules progressively reduced in size and some disappeared. No new lesions could be detected in the skin or in the stomach. In April 1998, because of the high cumulative dose, cyclophosphamide was interrupted, while CyA was continued at an unvaried dosage. Since then the patient's clinical, radiological and laboratory findings have been stable suggesting that cyclophosphamide and low dose CyA may be used to achieve a satisfactory and prolonged control of both lymphoid and KS cell proliferation in MCD.

Maria Tiziana Bertero, Massimo De Maestri, Federico Caligaris-Cappio

Dipartimento di Scienze Biomediche e Oncologia Umana, Università di Torino, Ospedale Mauriziano Umberto I°, Turin and Istituto per la Ricerca e la Cura del Cancro (IRCC), Candiolo, Italy

Key words

Castleman's disease, Kaposi's sarcoma, treatment.

Funding

This work was supported by the AIRC and by PF Biotecnologie, CNR, Italy.

Correspondence:

Federico Caligaris-Cappio, M.D., Ospedale Mauriziano Umberto I°, largo Turati 62, 10128 Turin, Italy. Phone: international +39-011-5080650 – Fax: international +39-11-5682588 – E-mail: fcaligaris@mauriziano.it

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High-dose ifosfamide and etoposide infusion plus methylprednisolone for refractory or relapsed aggressive non-Hodgkin's lymphoma

The prognosis of patients with aggressive non-Hodgkin's lymphoma (NHL) who fail to achieve a complete remission with first-line anthracycline-containing chemotherapy or who relapse remains poor.[1–4] Many salvage regimens have been reported for these patients with varying effectiveness and very poor chance of long-term survival.[1,2] Ifosfamide has been included in some of these regimens, often in association with etoposide.[1,2,5,6] Improved survival may be obtained with high dose chemotherapy and autologous hematopoietic stem cell transplantation, especially in chemosensitive relapses.[7,8]

Sir,

We designed a novel salvage program including high-dose ifosfamide infusion plus high-dose fractionated etoposide and methylprednisolone (IFOVM), followed by DHAP chemotherapy[9] and subsequent intensive chemotherapy with autologous peripheral blood stem cell transplantation (APBSCT) for patients with refractory or relapsed aggressive NHL.

Between November 1996 and December 1998, 20 consecutive patients were included in this protocol. Patient characteristics at diagnosis are summarized in Table 1. Informed consent was obtained from all patients.

IFOVM induction salvage chemotherapy consisted of ifosfamide (10 g/m^2 as a 72-hour continuous intravenous infusion on days 1-3), etoposide (150 mg/m^2 every 12 hours as a 2-hour i.v. infusion on days 1 to 3), mesnum (20% of the total dose of ifos-