the combination granulocyte colony-stimulating factor (G-CSF) + 2-weekly CHOP allows the clinician to increase dose intensity by delivering chemotherapy every 14 days and decreases the infectious complications, which elderly patients are more exposed to [2]. Two-weekly CHOP + G-CSF significantly improves the complete response and EFS when compared to the traditional CHOP (every 21 days) or to other more complex regimens. As shown in Table 1, there are no significant differences in the results achieved with R-CHOP or with 2-weekly CHOP + G-CSF.

Although the results are comparable, 2-weekly CHOP + G-CSF shows a reduced toxic death rate and a shorter duration of the treatment. As shown in Table 1, we calculated and compared the cost of these two treatments at our institution, finding a significantly lower cost in 2-weekly CHOP + G-CSF. Of note, in R-CHOP cost-assessment, we have not included the additional expense for the G-CSF eventually delivered during this treatment (employed in more than one-third of patients) [1].

Waiting for the ongoing trials comparing these two approaches, the current data in the literature and the estimate of expenses seem to suggest the use of 2-weekly CHOP + G-CSF in the treatment of aggressive lymphomas in the elderly.

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Coronary ischemia related to alemtuzumab therapy

Alemtuzumab is a humanized monoclonal antibody targeted to lymphocytes through the CD52 receptor. This agent has been demonstrated to reduce the amount of malignant lymphocytes in patients with chronic lymphocytic leukemia (CLL), and, in turn, to achieve a 33% response in patients previously treated with alkylating agents and who have failed fludarabine therapy [1, 2]. Common side-effects have been described related to drug infusion, such as rigors, fever, nausea, vomiting and rash. In addition, dyspnea, hypotension and hypoxia may occur [2]. The use of the subcutaneous route has been associated with less severe reactions [3]. Herein, we present the case of a male patient with CLL who developed an acute coronary event during alemtuzumab administration.

A 58 year-old patient was diagnosed with B-CLL in 1994. He initially received six cycles of fludarabine, and due to a relapse, he was placed on melphalan and prednisone for a period of 4 years. Because of no response he received other lines of chemotherapy: chlorambucil, CVP (cyclophosphamide, vincristine and prednisone) and cladribine. During the last 3 months, there has been a progressive rise in his lymphocyte count which in May 2003 reached 180,000 cell/mm³. At that time, he presented with enlargement of cervical adenopathies and skin lesions; a biopsy revealed CLL. A bone marrow core biopsy showed diffuse infiltration of CLL.

The patient had a history of coronary bypass at 37 years of age and two coronary angioplasties in 1998 and 2001. After that, he remained asymptomatic.

Treatment with alemtuzumab was planned and informed consent was obtained from the patient. The white cell count was 147,000 cell/mm³. Dyphenhydramine and acetaminophen were administrated prior to infusion. He tolerated well the first intravenous dose of 3 mg and a dose of 10 mg was given on the following day. Right after the second infusion of alemtuzumab, the patient developed severe chills and fever, followed by shortness of breath, typical chest pain, hypotension and became hypoxemic. An electrocardiogram showed a depression of the ST segment in

Table 1.

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>No. of patients</td>
<td>202</td>
<td>153</td>
</tr>
<tr>
<td>Median age, years</td>
<td>69</td>
<td>67</td>
</tr>
<tr>
<td>Median follow-up, months</td>
<td>24</td>
<td>40</td>
</tr>
<tr>
<td>CR</td>
<td>76%</td>
<td>77%</td>
</tr>
<tr>
<td>EFS</td>
<td>52%</td>
<td>53.4%</td>
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<tr>
<td>Toxic deaths</td>
<td>10.4%</td>
<td>3.5%</td>
</tr>
<tr>
<td>Treatment duration (theoretical)</td>
<td>21 days × 8 cycles (168 days)</td>
<td>14 days × 6 cycles (84 days)</td>
</tr>
<tr>
<td>Cost ($/m²)a</td>
<td>9718 €</td>
<td>2975.4 €</td>
</tr>
</tbody>
</table>

aCurrent cost at our institution.

CR, complete response; EFS, event-free survival; G-CSF, granulocyte colony-stimulating factor; R-CHOP, Rituximab + CHOP.

References


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the lateral aspect. A chest radiography showed pulmonary edema. The increase of the MB fraction of creatine kinase (CK-MB) confirmed the diagnosis of non-ST elevation myocardial infarction. Echocardiographic evaluation revealed segmental hypokinesia but with normal ejection fraction, and a moderate aortic stenosis. The patient improved and two more doses of alemtuzumab 10 mg were administered subcutaneously. The following week, 30 mg was administered by the same route and 7 h after the infusion the patient developed chest pain and dyspnea. Electrocardiographic changes were observed and the patient was admitted to the coronary unit where he recovered without complications. Subcutaneous infusion of alemtuzumab was reinitiated at a dose of 10 mg and nitroglycerine patches were placed simultaneously with each injection. With this intervention no further symptoms appeared and the patient completed six more doses. One month after the beginning of therapy, the patient presented fever and had to be admitted to hospital. His white cell count was 2100 cells/mm³, blood cultures were positive for Pseudomonas aeruginosa and a thorax computed tomographic scan showed multiple pulmonary infiltrates. The patient developed progressive respiratory insufficiency and died 1 week after admission. No autopsy was obtained.

Damaj et al. have reported a patient with CLL without a history of coronary heart disease who suffered an acute myocardial infarction after alemtuzumab infusion [4]. As proposed by these authors, cardiac vasospasm elicited by cytokines could be the cause of coronary ischemia. A cytokine-release syndrome has been described for intravenous therapy with rituximab, another monoclonal antibody [5]. However, our patient had chest pain even though we used the subcutaneous route. Thus, close cardiovascular monitoring should be recommended for patients receiving alemtuzumab, regardless of the route of administration.

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