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Brief report

Prognostic impact of anthracyclines in the treatment of aggressive lymphoma in patients over 70 years☆

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ABSTRACT

Background and objective: The optimal treatment of aggressive non-Hodgkin lymphoma (NHL) in elderly patients remains controversial. We aimed to evaluate the impact of age and use of anthracyclines.
Patients and method: Retrospective analysis of patients with aggressive NHL aged over 70 years old.
Results: One hundred and twenty-eight patients with a median age of 76 years (70–91). Eighty-eight percent received chemotherapy, and 72% received anthracyclines. The overall response rate was 70%, 51% with a complete response (CR)/uncertain complete response and 19% with a partial response (PR). Overall survival (OS) was 28 months (95% confidence interval 18–78). In the diffuse large B-cell lymphoma group, progression-free survival (PFS) and OS were significantly better in patients who achieved CR versus PR. The use of anthracyclines was associated with CR, the international prognostic index (IPI) was associated with both survival and response, and age showed no association.
Conclusions: In patients aged ≥70 years with aggressive lymphoma who received chemotherapy, the IPI but not age and the use of anthracyclines showed a prognostic impact. Therefore, in elderly patients with aggressive lymphomas, the use of anthracyclines should be considered and therapeutic decisions should not be based on age exclusively.

Impacto pronóstico de las antraciclinas en el tratamiento de pacientes mayores de 70 años con linfoma agresivo

Palabras clave:
Linfoma no hodgkiniano
Antraciclinas
Índice pronóstico internacional
Edad

RESUMEN

Fundamento y objetivo: El tratamiento óptimo de los linfomas no hodgkinianos (LNH) agresivos en ancianos es controvertido. El objetivo de este estudio fue evaluar el impacto de la edad y de las antraciclinas en pacientes ancianos con LNH.
Pacientes y método: Análisis retrospectivo de pacientes con una edad > 70 años, con LNH agresivo.
Resultados: Se incluyeron 128 pacientes, con una mediana de edad de 76 años (extremos 70-91). El 88% se trató con quimioterapia, y un 72% recibió antraciclinas. La tasa global de respuesta fue del 70%, con un 51% de respuestas completas (RC)/respuestas completas inciertas y un 19% de respuestas parciales (RP). La supervivencia global (SG) mediana fue de 28 meses (intervalo de confianza del 95% 18-78). En los pacientes con linfoma difuso de células grandes B, la supervivencia libre de progresión y la SG mediana fueron significativamente mejores en los que alcanzaron RC en comparación con los que alcanzaron RP. Las antraciclinas se asociaron a RC, el índice pronóstico internacional (IPI) se asoció tanto a supervivencia como a respuesta, y la edad no mostró ninguna asociación.

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Conclusiones: En los pacientes con edad ≥ 70 años con linfomas agresivos de nuestro centro que recibieron quimioterapia, tanto el IPI como el uso de antraciclinas mostraron impacto pronóstico, pero no la edad. Por tanto, creemos que el tratamiento de los pacientes ancianos con linfomas agresivos debería contemplar el uso de antraciclinas, y que la decisión terapéutica no debe basarse exclusivamente en la edad.

Introduction

Incidence of non Hodgekins lymphomas (NHL) has notably increased in the last few decades, particularly in the elderly.[1] Standard treatment of clinically aggressive NHL is chemotherapy with cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP), associated with anti-CD20 (rituximab) monoclonal antibody if tumour cells express CD20.[2] Anthracyclines are an essential element in this chemotherapy regime.[3,4] Unfortunately, it is not always possible to administer them in the elderly due to comorbidities which limits the use of intensive chemotherapies, and to the higher risk of adverse events, thus lowering therapeutic success probabilities.[3–6] In this context, the treatment of aggressive lymphomas with curative intent is still open to controversy.

We carried out a retrospective study aimed at examining the treatments used in our standard clinical practice in elderly patients with aggressive lymphomas and to assess the impact of the use of anthracyclines on these populations.

Patients and method

All patients ≥70 years of age with aggressive NHL were retrospectively assessed in our hospital between 2002 and 2012.

Demographic data were recorded for each patient, as were histological type and clinical and biological characteristics such as haemogram values, lactate dehydrogenase serum levels and beta-2-microglobulin, Ann Arbour staging, the presence of voluminous mass and extra lymph node involvement. The International Prognostic Index was calculated (IPI).[7] The type of treatment performed was recorded, as was the response, time of relapse/disease progression or death and the disease status during the last check-up.

Treatment response and survival, considered in terms of overall response (OR), complete response (CR), uncertain complete response (uCR), partial response (PR), overall survival (OS) and progression free survival (PFS), were evaluated by Cheson et al. criteria.[8]

The incidence of infections, the use of anti-biotic prophylaxis, use of the *granulocyte colony-stimulating factor* (G-CSF <9 and the appearance of other relevant adverse clinical events were reported.

Statistical analysis

The Kaplan–Meier method was used for survival curves. For multivariate analysis the Cox model was used and a logistic regression model for factors associated with response. The variables introduced were: age (70–75, 76–80 and over 80), IPI (high IPI [4 or 5 points] and the others [1, 2 and 3 points]) and use of anthracyclines.

Results

128 patients (59 males and 69 females) were identified, with a median age of 76 (extremes 70–91). One hundred and nine patients (85%) presented with diffuse large B-cell lymphoma (DLCL-B), 8 Patients (6%) with mantle cell lymphoma (MCL), 8 Patients (6%) with peripheral T-cell lymphoma, and 3 patients (2%) with Burkitt lymphoma. The clinical characteristics are shown in Table 1. 96% of patients completed the extended study. 88% of patients were treated with chemotherapy, 3% received other treatments (surgery and/or radiotherapy) and 9% received no treatment.

Of the 113 patients treated with chemotherapy, the regimes used were: CHOP every 21 days with or without rituximab (CHOP21±R) in 27 patients, CHOP14±R in 5 patients, etoposide, cyclophosphamide, doxorubicin, vincristine and prednisone±R in 5 patients, cyclophosphamide, non-pegylated liposomal adriamycin, vincristine and prednisone±R in 40 patients, cyclophosphamide, vincristine and prednisone±R in 15 patients, gemcitabine+R in one patient, and carmustine, methotrexate, cytarabine) in another patient. Thus 72% of patients received regimes with anthracyclines, although in 60% of cases dose adjustments were required. Prophylaxis with G-CSF and antibiotics was administered in 95% of patients.

OR rate of patients treated with chemotherapy was 70%, 51% of CR/uCR and 19% of PR. In 3% of patients the disease was stabilised, and in 15% there was disease progression. In 10 patients (14%) response could not be assessed, mostly due to premature death.

With median follow-up of 28 months, median OS was 28 months (confidence interval of 95% [CI 95%] 18–78). OS by histological subgroup at 2, 4 and 6 years was: DLCL-B 50% (CI 95% 41–61), 45% (CI 95% 35–57) and 34% (CI 95% 23–51); MCL 75% (CI 95% 50–100), 50% (CI 95% 20–100) and 25% (CI 95% 5–100), and T-cell NHL 15% (CI 95% 2–89), 0% and 0%, respectively.

In DLCL-B treated subgroup (n = 100), median PFS was significantly better in the patients with CR compared with those with PR (not attained compared with 3.5 months; $P < 0.0001$), which led to

Table 1
Demographic and clinical characteristics of the 128 patients aged ≥70 years diagnosed with clinically aggressive non Hodgkins lymphoma.

	Patients (n = 28)
Type of lymphoma	
Diffuse large B-cell lymphoma	109 (85)
Mantle cell lymphoma	8 (6)
Peripheral T-cell lymphomas	8 (6)
Burkitt lymphoma	3 (2)
Gender	
Male	59 (46)
Females	69 (54)
Age	
70–75	40 (31)
76–80	60 (47)
>80	28 (22)
Ann Arbour staging	
I	26 (20)
II	25 (20)
III	14 (11)
IV	63 (49)
B symptoms	72 (56)
ECOG (performance status)	
0–1	53 (41)
≥2	75 (59)
International prognosis index	
1–3	76 (59)
4–5	52 (41)

Data expressed as n (%).