Treatment of Cutaneous B-Cell Lymphoma, Leg Type, With Age-Adapted Combinations of Chemotherapies and Rituximab

In contrast with most primary cutaneous B-cell lymphomas, primary cutaneous large B-cell lymphomas, leg type (PCLBCLs-LT) are often life-threatening. Owing to their occurrence in elderly patients (many patients aged > 80 years), these lymphomas have often been treated with radiotherapy alone or palliative chemotherapies, resulting in 5-year survival rates around 50%. Recently, the addition of rituximab to the standard CHOP regimen (cyclophosphamide, doxorubicin, vincristine, and prednisone) (R-CHOP) was found to prolong survival in 60- to 80-year-old patients with nodal diffuse large B-cell lymphomas (DLBCLs). Although this result was not directly applicable to older patients with PCLBCL-LT, it rapidly led to a significant shift in French practice, consisting in using the classic R-CHOP regimen in patients younger than 80 years and in generally good condition, and less intensive combinations of rituximab and polychemotherapies (R-PCTs) in the oldest and/or frailest patients. To our knowledge, such an approach has never been evaluated.

Methods. All consecutive patients registered in the French Study Group of Cutaneous Lymphomas for a PCLBCL-LT and treated with R-PCT between January 2002 and June 2007 were included in the study. Medical records were reviewed and comprehensive data were collected, including baseline characteristics, type of R-PCT regimen, adverse events, response to therapy, relapse, extracutaneous progression, subsequent therapies, and final status. Follow-up data were collected from referent dermatologists and from general practitioners, when necessary, until the final evaluation period (January 1 to March 31, 2008). The study was approved by the institutional review board of Reims University Hospital, Reims, France.

Results. Twenty-five patients, aged 44 to 96 years (median age, 76 years), were included in the study (Table). For 11 cases (1, 2, 3, 5, 6, 9, 10, 12, 21, 24, and 25), preliminary data and short-term outcomes were previously reported. Twenty patients had lesions located on the leg at presentation, whereas 5 had a PCLBCL-LT at sites other than the leg. Seventeen patients (group 1) received R-PCT.
as first-line therapy, and 8 (group 2) received R-PCT as second-line therapy for refractory skin lesions (n = 5) or visceral dissemination (n = 3) to the central nervous system (case 21), lung and bone (case 22), or bone marrow and mesenteric nodes (case 16). The R-PCT was R-ACVBP (doxorubicin, cyclophosphamide, vindesine, bleomycin, and prednisone) in 1 case, a standard R-CHOP regimen in 14 cases, an R-CHOP regimen with lower doses (R-miniCHOP) in 7 cases, and a less intensive R-PCT without anthracycline in 4 cases.

All 17 patients in group 1 and 6 of 8 in group 2 achieved a complete response, but 10 experienced relapse in the skin (n = 8), the skin and lymph nodes (n = 1), or the central nervous system (n = 1). Four patients had multiple successive cutaneous relapses. Treatment of relapses included surgery (1 case), radiotherapy (4 cases), rituximab (1 case), ibritumomab tiuxetan (1 case), and/or various chemotherapies (4 cases). No patient was lost to follow-up. After a 33-month median follow-up, 20 patients were alive (including 13 in complete remission), 3 had died of lymphoma, and 2 had died of unrelated causes. The 3-year disease-specific survival rate was 87%.

Nine patients (36%) had at least 1 grade 3 or higher adverse event, including grade 3 (n = 2) or grade 4 (n = 5) neutropenia, grade 4 thrombocytopenia (n = 1), grade 4 neutropenic sepsis (n = 1), grade 3 cardiac failure (n = 1), grade 3 pneumonia (n = 1), and grade 3 venous thrombosis (n = 1; this patient had a catheter). One patient died of neutropenic septicemia.

These 25 patients treated with R-PCT were compared with a historic series of 47 patients with PCLBCL-LT who received other therapies only, as detailed in a previous study.2 The 2 groups did not differ by classic prognostic factors,2 including age (median ages, 76 vs 78 years) (P = .30), location of skin lesions, clinical stage at diagnosis, performance status, or lactic dehydrogenase level. However, the percentage of patients who achieved a complete response (92% vs 64%) (P = .01) and the 3-year specific survival rates (87% vs 50%) (P = .004) were much higher in patients treated with R-PCT.

Comment. We report for the first time to our knowledge a complete response rate greater than 90% and a 3-year survival rate greater than 80% in patients with PCLBCL-LT. Despite the retrospective design of the study, these results and the comparison with a historic series of patients treated earlier with other therapies only strongly suggest that the prognosis of these life-threatening lymphomas may be dramatically improved by the use of age-adapted R-PCT. Response and survival rates in our patients were higher than those reported in elderly patients with DLBCL treated with standard R-CHOP,4,5 suggesting that PCLBCL-LT could in fact be less aggressive than their systemic counterparts. Patients older than 80 years (n = 9; 36%) and those with a poor general condition received less-intensive R-PCT with overall favorable results. Main adverse events in the entire series were neutropenia and consecutive infections, suggesting that granulocyte-colony stimulating factor should be systematically used when treating PCLBCL-LT with R-PCT, as recommended in at-risk elderly patients with DLBCL.5 Recurrences were frequent but were often limited to the skin and were responsive to subsequent treatments. These data provide a basis for prospective clinical trials. Further studies could compare standard R-CHOP to less intensive R-PCT and/or investigate the optimal number of R-PCT cycles and the role of a maintenance therapy with rituximab to prevent recurrences.

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Ultrasound Therapy for Lipodermatosclerosis

L ipodermatosclerosis (LDS) consists of lower-leg inflammation and woody induration in patients with chronic venous or lymphatic hypertension.1 Acute LDS may be painful and is frequently misdiagnosed as cellulitis. While compression stockings2 may be helpful, therapeutic options are limited. Ultrasound treatment of LDS was reported once more than 25 years ago;2 we now report 16 legs treated with this technique.


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