To the editor:

Central nervous system prophylaxis in peripheral T-cell lymphoma

The role of central nervous system (CNS) prophylaxis in diffuse large B-cell lymphoma (DLBCL)[1,2] and mantle cell lymphoma[3,4] has been addressed in recent *Blood* issues. The role of CNS prophylaxis is still controversial, particularly after the introduction of immunochemotherapy. Despite lack of proven efficacy and concern about toxicity, the National Comprehensive Cancer Network (NCCN) guidelines still recommend CNS prophylaxis in a subset of patients with aggressive B-cell lymphomas.

The role of CNS prophylaxis in peripheral T-cell lymphomas (PTCL) is more questionable. Except for sporadic case reports, few articles have focused on the topic and little is known about the practice of CNS prophylaxis in PTCL worldwide. According to the NCCN guidelines the only entity in which prophylaxis with intrathecal chemotherapy is recommended is adult T-cell leukemia/lymphoma (ATLL).

To further address this issue, we retrospectively analyzed 447 patients with T-cell lymphomas seen at the University of Texas M. D. Anderson Cancer Center from 1996 to 2009. Patients with cutaneous T-cell lymphomas, primary CNS T-cell lymphoma, or initial involvement of CNS were excluded from the analysis. A total of 250 patients with PTCL were available for the analysis. All cases were reviewed at our institution for confirmation of diagnosis. CNS relapses in PTCL proved to be an extremely rare event, occurring in only 6 patients (2.4%). Patients' characteristics are shown in Table 1. All patients were stage IV at diagnosis, and 4 of them had bone marrow involvement. Lactic dehydrogenase was elevated in 4 of them, with a median of 1207 IU/L (range: 428-3312). Relapses occurred concomitant or after systemic recurrence in 5 of 6 patients, all presenting with refractory disease. Except for 1 patient, who is still in treatment, all patients died of progressive disease. No CNS events occurred in patients with angioimmunoblastic T-cell lymphoma (n = 40), hepatosplenic T-cell lymphoma (n = 10), or enteropathy-associated T-cell lymphoma (n = 4).

As there are no data allowing clear recommendations for CNS prophylaxis in PTCL, it is left to the physician's discretion whether to administer intrathecal chemotherapy. Fourteen patients received CNS prophylaxis at our institution, based on the presence of marrow involvement (n = 8), paraspinal mass (n = 2), more than 2 extranodal sites (n = 1), or multiple factors (n = 2). One patient with $CD4^+/CD56^+$ hematodermic neoplasm received CNS prophylaxis based only on histology. Of these 14 patients, only 1 had CNS relapse. Despite the small number of patients, CNS prophylaxis was not statistically proven to be effective ($P = .33$) in preventing CNS relapse. When applying the NCCN criteria for CNS prophylaxis in DLBCL to our patients with PTCL (paranasal sinus, testicular, epidural, bone marrow, ≥ 2 extranodal sites, or HIV lymphoma), 99 patients had indication for CNS prophylaxis. As CNS recurrence occurred in only 6, 93 patients would be exposed to unnecessary and potentially harmful intrathecal chemotherapy.

In our experience, CNS relapses is a rare event in PTCL. When it occurs, it usually manifests as a terminal event in patients with refractory disease. Moreover, with the limitation of a retrospective review, CNS prophylaxis does not appear to have an impact in preventing events, and the NCCN criteria for CNS prophylaxis in DLBCL may not be indicated for patients with PTCL.

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Table 1. Characteristics of patients with PTCL presenting with CNS relapse

Patient	Diagnosis	CNS prophylaxis	Type of CNS relapse	Marrow involvement	Survival after CNS involvement, d
1	PTCL-NOS	No	Leptomeningeal/ cauda equina	Yes	72
2	PTCL-NOS	No	Leptomeningeal	Yes	30
3	$CD4^+/CD56^+$ hematodermic neoplasm	No	Leptomeningeal/eye	Yes	47
4	ALCL	Yes	Leptomeningeal	Yes	65
5	ATLL	No	Leptomeningeal	Yes	48
6	ATLL	No	Leptomeningeal	No	Not reached

PTCL-NOS indicates peripheral T-cell lymphoma, not otherwise specified; ALCL, anaplastic large cell lymphoma; and ATLL, adult T-cell leukemia/lymphoma.