Complete response of relapsed angioimmunoblastic T-cell lymphoma following therapy with bevacizumab

A 54-year-old woman presented with slow-growing cervical lymph nodes, weight loss and disseminated skin rash in February 2006. Biopsies from skin and cervical node revealed angioimmunoblastic T-cell lymphoma (AILT), stage IVB. She received chemotherapy with cyclophosphamide, doxorubicin, vincristine and prednisone, with a transient improvement of the skin rash and cervical nodes, followed by progression after three cycles. Second line with etoposide, methylprednisolone, cytarabine and cisplatin was tried, and again a short response followed by a rapid progression was observed, together with an important decrease in performance status and pancytopenia. She then started weekly oral methotrexate (20 mg) and daily prednisone (15 mg). After 3 months on treatment with disease stabilization, progression in skin, lymph nodes and bone marrow was observed. Her clinical condition was poor, developing deep venous thrombosis, pancytopenia and fever.

At this point, fourth-line chemotherapy or alemtuzumab was felt not possible, and therapy with the monoclonal anti-vascular endothelial growth factor (VEGF) antibody bevacizumab was started in September 2006 at a dose of 10 mg/kg every 14 days. After three doses, blood counts rose to normal values and her general condition improved. She maintained low-dose prednisone (5 mg daily) and then switched to 30 mg daily for 5 days after every bevacizumab administration. Quality of life and tolerance were excellent, with only arterial hypertension grade 3 requiring combination antihypertensive agents as relevant toxicity. A complete response with total disappearance of enlarged lymph nodes and bone marrow infiltration, assessed by bone marrow biopsy and computed tomography scan, was observed after 3 months of therapy, lasting for 10 months. However, in July 2007, a new disseminated relapse occurred and the patient died in a few weeks.

Initially described as angioimmunoblastic lymphadenopathy, AILT is now recognized as a distinct subtype of T-cell lymphoma and incorporated in the World Health Organization classification of lymphoid tumors [1]. This rare lymphoma accounts for <1.5% of all non-Hodgkin’s lymphoma (NHL), tends to occur in adult patients and presents with systemic symptoms, frequently associated with hypergammaglobulinemia and autoimmune features. Prognosis for AILT is poor, and standard anthracycline-based chemotherapy achieves response rates of up to 50%, but most of the patients relapse, resulting in a 5-year survival of 30% and a median survival time of only 3 years [2].

In an effort to improve the poor outcome of these patients, there have been interests in novel therapeutic strategies including immunomodulatory agents such as cyclosporine and antiangiogenic agents such as thalidomide and bevacizumab [3]. It has been demonstrated that AILT shows high levels of VEGF-A expression on both lymphoma cells and endothelial cells, and the most prominent vascular component among lymphoma [4]. For these reasons, antiangiogenic therapy seems very attractive for this disease. Although antiangiogenesis is now a part of the treatment strategies in a variety of neoplasms such as colon, breast, kidney, lung cancer and multiple myeloma, such approach is still been tested in clinical trials for lymphoma. The experience with those agents in AILT is scarce, with only anecdotal cases reported. In a previous report from Bruns et al. [5], the authors presented a patient with refractory AILT been treated with bevacizumab (5 mg/kg every 14 days). A complete response after eight doses of bevacizumab in lymph nodes and bone marrow was achieved, lasting for 6 months. Before therapy, the lymph nodes and bone marrow showed expression of VEGF-A on lymphoma cells as well as on the endothelium. After therapy with bevacizumab,
histopathology of the bone marrow revealed the disappearance of VEGF-expressing lymphoma cells and a decrease of bone marrow vascularization.

Our case report indicates that bevacizumab can induce prolonged response in refractory AILT previously treated with conventional chemotherapy, with an excellent tolerance and toxicity profile for the patient. However, we need to wait until ongoing clinical studies finish to determine whether or not bevacizumab will be an active agent in the management of NHL, improving the outcome for our patients and, why not, for those with AILT.

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doi:10.1093/annonc/mdm579