Hepatosplenic gammadelta T-cell lymphoma successfully treated with a combination of alemtuzumab and cladribine

A 41-year-old female patient suffering from fatigue due to haemolytic Coombs-negative anaemia was admitted to our department in November 2001. Computed tomography scans and sonography solely displayed a marginal hepatosplenomegaly. Bone marrow trephine biopsy (BM-TB) revealed a hypercellular marrow presenting few small nodular lymphomatous infiltrates, >50% reactive with antibodies to CD19, CD20, CD21 and bcl2. Also, numerous CD3-positive T cells, but no monoclonal T-cell receptor (TCR) rearrangement could be detected initially. Using primers for the immunoglobulin heavy chain rearrangement, a slight band was detected suggestive of B-cell monoclonality. Together with the morphology of the infiltrate, follicular lymphoma was hypothesised. Cytogenetics revealed a normal female chromosomal pattern. The follicular lymphoma international prognostic index was judged as high risk. Consequently, three cycles of R-CHOP (rituximab–cyclophosphamide–doxorubicin–vincristine–prednisolone) were administered leading to a good partial remission. None the less, transfusion-dependent haemolytic anaemia and neutropenia reoccurred 1 year later and was symptomatically treated by repetitive red blood cell transfusions—108 units within 1 year. Concomitantly, massive hepatosplenomegaly in conjunction with B-type symptoms developed. At that time, the BM-TB showed a hypercellular marrow with multiple nodular lymphomatous infiltrates revealing the typical hepatosplenic gammadelta (γδ) T-cell lymphoma-specific phenotype: CD2+, CD3+, CD4−, CD5−, CD7+, CD8− and a bright CD52 positivity. PCR-based analysis of the TCR γδ chain rearrangement by two
different methods revealed a clear positive band on gel electrophoresis in peripheral blood as well as bone marrow specimens and a confirmative monoclonal peak in the automated fluorescent fragment analysis. These findings established the diagnosis of hepatosplenic γδ T-cell lymphoma. Because of the rarity of this lymphoma type, no published guidelines for the treatment of this entity exist. Since a bright CD52 expression had been observed, we chose the anti-CD52 antibody alemtuzumab in combination with cladribine, a nucleoside analogue with a pronounced cytotoxic and T-cell depletory activity [3].

A total of six cycles were given. Cladribine was administered at a dose of 0.12 mg/kg body weight by i.v. infusion over 2 h and alemtuzumab at a dose of 10 mg absolute by i.v. infusion over 1 h, both on days 1–3 of each cycle, repeated every 4 weeks. This treatment was followed by alemtuzumab maintenance therapy (10 mg by i.v. infusion over 1 h, three times a week) for a further 18 weeks. Premedication for alemtuzumab consisted of mephenamic acid and dimethindene maleate. Pneumocystis jiroveci pneumonia and herpes virus prophylaxis was administered as outlined in the manufacturer’s recommendations.

Shortly after start of chemotherapy, the transfusion demand dropped and was entirely suspended at the beginning of alemtuzumab maintenance. Since harvest of CD 34-positive stem cells was insufficient, high-dose therapy with autologous stem cells was insufficient, high-dose therapy with alemtuzumab has recently been started. Nevertheless, to date no such combination treatments have been employed yet in this entity [1, 2, 5]. By combining both alemtuzumab and cladribine, a continuing lasting clinical and molecular remission, of more than 2 years, was be achieved in this aggressive lymphoma.

However, to confirm the promising results of this therapy, further evaluation in more patients is necessary.

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