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Case Report

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Biweekly cladribine and rituximab in a patient with hairy cell leukemia and severe renal failure

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Abstract

Hairy cell leukemia (HCL) is a rare indolent lymphoproliferative disorder usually clinically characterized by pancytopenia and splenomegaly. It is very sensitive to purine analogues cladribine and pentostatin which are both primarily excreted by kidneys and registration labels bear warnings against their use in patients with severe renal insufficiency. We report a patient with HCL and severe renal failure who was successfully treated with five subcutaneous injections of cladribine 0.14 mg/kg and six biweekly infusions of rituximab 375 mg/2 iv. This regimen was tolerated remarkably well without cumbersome side–effects. Our case-report suggests that cladribine can be efficaciously and safely used in patients with severe renal insufficiency if administered in standard doses once every two weeks.

Case presentation

Hairy cell leukaemia (HCL) is a rare indolent lymphoproliferative disorder usually clinically characterized by pancytopenia and splenomegaly [1]. Small mature lymphoid cells with hairy cytoplasmic projections expressing B-cell markers, CD22, CD11c, CD103, CD25, CD123, DBA44, FMC-7 and negative for CD10 and CD5 are found in the bone marrow and spleen. Most cases harbor B-raf mutations. HCL is extremely sensitive to purine analogues cladribine and pentostatin [2-4]. After a single treatment cycle more than 90% of patients obtain remissions lasting more than 5 years. Overall, 10-year survival exceeds 90%. Both drugs are primarily excreted by kidneys [5,6] and registration labels bear warnings against their use in patients with severe renal insufficiency [7,8]. The European Medical Agency label for cladribine mentions severe renal insufficiency as a contraindication for its use, therefore treatment of HCL patients with kidney failure remains a challenge. Here we report such a patient successfully treated with the combination of cladribine and rituximab.

A 75-year old man was admitted to our hospital for evaluation of severe kidney failure and preparation for chronic dialysis. His creatinine clearance was 10 ml/min and proteinuria 0.35 g/day. He had pancytopenia (WBC 2.67 × 10^9/L with 53% lymphocytes, RBC 2.64 × 10^{12}/L, Hgb 82 g/L, platelets 59 × 10^9/L) without hepatosplenomegaly or lymphadenopathy. Kidneys were small, consistent with chronic renal disease. A trephine biopsy was performed and HCL diagnosed. The patient was treated with five subcutaneous injections of cladribine 0.14 mg/kg and six biweekly infusions of rituximab 375 mg/2 iv. Toxicity was acceptable; granulocytopenia and thrombocytopenia were brief and mild; RBC transfusions were given twice. Neither infections nor other non-haematological toxicities occurred. A repeated trephine biopsy showed complete clearance of tumour cells. At follow-up 8 years after treatment the patient is still in complete remission, on chronic dialysis. Interestingly, he was treated for 2 non-melanoma skin cancers a few years after HCL treatment with cladribine.

Purine analogues used in HCL are excreted through kidneys, 80% of the total administered dose of pentostatine and around 30% of cladribine are found in the urine [5,6]. In patients with renal failure, the area under the curve of cladribine is larger than in patients with normal kidney function resulting in more prolonged pancytopenia. Data suggest that weekly administration of cladribine is similarly effective as daily administration [9]. We speculated that more widely spaced dosing would reduce the risk of drug accumulation, enable us to follow haematological toxicity more closely and if necessary, stop the treatment before the total planned amount of cladribine was administered. Any reduction in antitumor effect of cladribine could be countered by rituximab which is not excreted by kidneys, but less active as monotherapy than purine analogues [10]. The treatment was tolerated remarkably well without cumbersome side–effects. This case-report suggests that cladribine can be efficaciously and safely used in patients with severe renal insufficiency if administered in standard doses once every two weeks.

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Conflicts of interest

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