change of blast cell percentage, which suggests that some inherent changes might also exist during the transformation of CML.

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Fludarabine therapy in chronic lymphocytic leukemia-associated severe nephrotic syndrome

We present a rare case of leukemia-associated membranous nephropathy presenting as severe nephrotic syndrome. Fludarabine treatment was successful in inducing an effective remission from the chronic lymphocytic leukemia and complete resolution of proteinuria.

Sir,

While the majority of patients with chronic lymphocytic leukemia (CLL)-associated nephrotic syndrome (NS) have been found to have membranoproliferative glomerulonephritis, about 20% have either membranous glomerulonephritis or minimal change disease.[1] Available evidence suggests that NS associated with CLL is related to immune-complex disease. Remission induction of glomerular disease with successful treatment of the leukemia provides further indirect evidence that testifies to the paraneoplastic nature of the glomerular involvement.[2] A 56-year old previously healthy female was seen for evaluation of leukocytosis. Physical examination revealed cervical lymphadenopathy. A hemogram showed a white blood cell (WBC) count of 41.4×10^9 cells/L with an absolute lymphocyte count (ALC) of 32.7×10^9/L, hemoglobin of 13.8 g/dL, and platelet count of 346×10^9/L. A peripheral blood smear showed mature lymphocytosis and smudge cells. Flow cytometry of peripheral blood lymphocytes demonstrated a clonal B-cell process consistent with CLL. She was observed with frequent monitoring of her blood counts. Two years later, she presented with a rapid ten-kilogram weight gain, peripheral edema and hypertension. Serum albumin was 2.6 g/dL, creatinine 3.8mg/dL, and cholesterol 406 mg/dL. A 24-hour urine collection contained 19.2 g of proteins. Urine electrophoresis failed to identify monoclonal protein excretion. Percutaneous renal biopsy revealed membranous glomerulopathy. Her WBC count was 73.3×10^9/L (ALC: 61.6×10^9/L), and hemoglobin was 9.9 g/dL. The patient was treated with three courses of intravenous fludarabine 25 mg/m^2 daily for 5 days repeated every 4 weeks. The patient showed a remarkable response to therapy. One month after the third dose, she had complete resolution of edema, WBC count decreased to 3.7×10^9/L (ALC: 1.11×10^9/L), and urinary protein excretion dropped to 3.4/g/day (Figure 1). Serum creatinine had decreased to 2.0/mg/dL, serum cholesterol decreased to 253/mg/dL and serum albumin increased to 3.8/g/dL. One year after therapy, the urinary protein excretion is 102/ mg/day and ALC is stable around 2.3×10^9/L. About 35% of patients refractory to previous cytostatic treatment and about 75% of untreated patients obtain complete remissions with fludarabine.[3] Fludarabine, a purine analog, appears to be an effective initial induction therapy with a reasonable safety profile for patients with CLL.[4] In resting lymphocytes the accumulated triphosphate fludarabine derivatives result in defects in the repair of DNA, DNA strand breaks, activation of endogenous nucleases, depletion of nicotinamide adenine dinucleotide

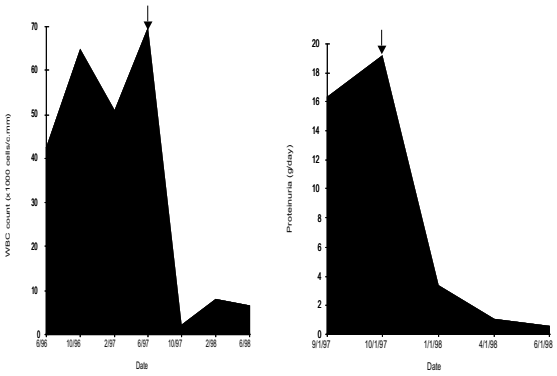

Figure 1. The response of white blood cell count (left) and proteinuria (right) after initiation of fludarabine therapy (arrows) in October 1997.

(NAD) and apoptotic cell death. In dividing lymphocytes these agents inhibit the ribonucleotide reductase that ultimately leads to inhibition of DNA synthesis.[5] As a result of its cytotoxic activity, fludarabine induces a profound lymphocytopenia. A marked decrease in CD4 lymphocytes occurs that may persist for several years, while affecting other mononuclear cell populations (CD5), which recover more rapidly.[6] Although this case and a previous case[6] showed that fludarabine may be considered as a reasonable and efficacious alternative to traditional alkylator-based therapy in patients with severe membranous glomerulopathy coexistent with CLL, general conclusions can not be definitely made, and further clinical evaluation is required to define the role of this drug in the treatment of CLL-associated NS.

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8q24 translocations in blastic transformation of mantle cell lymphoma

We report four cases of blastic transformation of mantle cell lymphoma (MCL), cytogenetically characterized by 8q24 karyotypic abnormalities in addition to t(11;14), suggestive of *c-myc* deregulation. Three patients developed blastic disease in lymph nodes, peripheral blood and bone marrow, after one to seven years, and died after 1 to 3 months. One patient presented with blastic MCL and died after 15 months. We propose that *c-myc* activation may be another cell cycle deregulation event leading to aggressive transformation in MCL.

Sir,

Mantle cell lymphoma (MCL) is characterized by relentless disease progression.[1] Blastic presentations are associated with poor survival.[2] Blastic histology is also recognized on serial biopsies.[3] We report four cases of blastic transformation of MCL, characterized by 8q24 karyotypic abnormalities.

Case #1. A 58-year old man with stage IIIA MCL reached a complete remission (CR) with oral chlorambucil. Two years later, he presented with progressive lymphadenopathy, jaundice, and circulating blasts, and died despite combination chemotherapy.

Case #2. A 45-year old man with stage IA MCL reached remission with VACOP-BP chemotherapy and radiotherapy (RT). Seven years later he presented with rapid lymph node enlargement and abundant large circulating blasts. He died after one month's treatment with chlorambucil.

Case #3. A 67-year old woman presented with a jaw mass and chest X-ray opacity. Fine-needle aspirate cytology diagnosed metastatic small

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