Hairy Cell leukemia, a disease characterized by splenomegaly without adenopathy, by pancytopenia, and by circulating malignant cells with prominent cytoplasmic projections requires therapy in most cases. The manifestations of hairy cell leukemia result from a balance between (1) leukemic infiltration of the red pulp of the spleen by hairy cells, which leads to hypersplenism, and (2) leukemic infiltration of the bone marrow, which leads to decreased production of bone marrow elements and to peripheral blood cytopenia(s). In most cases, the hypersplenism can be corrected by splenectomy, however, approximately one-third of the patients have progressive disease in the bone marrow, which manifests itself either by a leukemic phase with various associated cytopenias or by progressive pancytopenia. In four earlier patients, we originally suggested treatment with chlorambucil for these manifestations of progressive disease. Five additional patients have subsequently been treated with chlorambucil. All of these nine patients are the subjects of this report.

MATERIALS AND METHODS

Since the completion, in November 1978, of a study of four postsplenectomy hairy cell leukemia patients with progressive disease who were treated with chlorambucil, five additional patients have developed progressive disease and have been placed on single-agent chemotherapy. Treatment consisted of administration of chlorambucil, 4 mg/day, which was decreased to 2 mg/day when a response could be documented. Allopurinol, 300 mg daily, was started prophylactically simultaneously with chlorambucil administration in each case. A 6-mo trial of chlorambucil therapy was required to make a patient evaluable unless a distinct improvement in blood counts was obtained earlier and chlorambucil was electively discontinued by the treating physician.

RESULTS

The characteristics and clinical course of four of the new patients (patients 5–8), who received chemotherapy for at least 6 mo, are shown in Fig. 1. Patients 5 and 6 had dramatic responses. Patient 5 developed the leukemic phase of the disease approximately 1 yr postsplenectomy. He was extremely sensitive to chlorambucil, and his WBC dropped in 6 wk from 27,000/cu mm with 80% hairy cells to 2000/cu mm, with less than 50% hairy cells. From a platelet count of 48,000/cu mm, he achieved normal levels within 4 mo, or almost 6 mo after starting chlorambucil. Although leukopenia persists, his absolute granulocyte count has improved. A bone marrow biopsy (Table 1) in April 1980 showed distinct improvement over one in May 1979, when chlorambucil was started; the cellularity was decreased, the percentage of hairy cells was lower, and normal blood elements were regenerating. Patient 6 became increasingly pancytopenic approximately 1 yr postsplenectomy. A bone marrow biopsy showed 100% cellularity with 90% hairy cells. Daily therapy with 4 mg of chlorambucil eliminated the need for transfusions and resulted in return of a platelet count of 25,000/cu mm to a normal count of 367,000/cu mm within 7 mo after the initiation of therapy. Although leukopenia has persisted, the percentage of granulocytes has improved. A bone core biopsy in April 1980 demonstrated a cellularity of 40%, with 80% hairy cells and regenerating normal blood elements.

Patient 7 developed the leukemic form of hairy cell leukemia approximately 7 mo postsplenectomy, with a WBC of 32,400/cu mm and 75% hairy cells. Treatment with chlorambucil resulted in a progressive decrease in his WBC and stabilization of his hematocrit and platelet count. In June 1979 he developed daily fever up to 40°C. A progressive pulmonary infiltrate was biopsied, but no bacteria or opportunistic organisms were found, and the patient was started on six-drug antituberculosis therapy. Two weeks later he had cardiac arrest, after a period of hypotension, and died. A premortem blood culture was positive for...
**Pseudomonas aeruginosa.** The culture from the open lung biopsy eventually grew *Mycobacterium kansasii*.

Patient 8 had progressive anemia and thrombocytopenia within 3 mo after splenectomy. Six months of chlorambucil therapy failed to improve his pancytopenia, and his referring physician elected to discontinue the chemotherapy.

The ninth patient received chlorambucil for only 2.5 mo before it was stopped at the onset of hepatitis, which was thought to be due to recent transfusions. There was no significant improvement in her blood counts during the period of chlorambucil treatment. She expired 6 wk later of an interstitial pneumonitis, which was presumed to be viral in nature as no organisms were recovered. Examination of her liver revealed only mild infiltration of hairy cells in the portal triads.

Thus, of the eight evaluable patients (patients receiving at least 6 mo of chlorambucil treatment), seven (three in the recent group and four in the earlier...
group) have had an objective response. Of the seven responders, two have died of intercurrent infection, one (patient 2) of pseudomonas sepsis and the other (patient 7) of disseminated atypical Mycobacterium kansasii infection with preterminal pseudomonas sepsis. Of the five remaining patients, one (patient 4) had to stop chlorambucil therapy because of persistent leukopenia and fever. During the time without chlorambucil, vasculitis developed, and the patient was maintained on high-dose prednisone alone in various amounts for 8 mo. He suddenly developed fever, became septic, and expired within 24 hr of the onset of the acute illness. He survived 33 mo after his chlorambucil therapy had been initiated. The remaining four patients (patients 1, 3, 5, 6) are still receiving low doses of chlorambucil and, as of June 1980, continued to work full-time at their various occupations.

DISCUSSION

Since our first report in 1979 on the treatment with chlorambucil of patients with progression of hairy cell leukemia after splenectomy, we have treated four additional patients, two in a progressive leukemic phase and two in a progressive pancytopenic phase with few circulating hairy cells. The fact that seven of the eight treated patients (the ninth was treated only briefly) had objective responses suggests that low-dose chlorambucil chemotherapy can be used effectively in postsplenectomy patients with progressive disease.

However, it should be noted that there appears to be little, if any, benefit in the number of circulating granulocytes; only three patients ended up with a granulocyte count of >1000/cu mm. Thus, the majority of patients treated with chlorambucil still remain at risk for a life-threatening infection. Although our treatment strategy appears hopeful, an alternative one has been suggested for patients in the leukemic phase. One might consider repeated leukopheresis, as the low labeling index reported by Braylan et al. suggests that these cells are not rapidly proliferating. Fay et al. have shown that significant amounts of hairy cells can be removed mechanically, and that the improvement in blood counts can last for several years. Use of this approach could postpone the need for chemotherapy in the patients who progress with the leukemic form of the disease, but more patients need to be evaluated.

However, patients with the pancytopenic form of progressive hairy cell leukemia postsplenectomy probably cannot benefit from repeated leukopheresis. Three of our eight patients had this form, and two of these benefited from chlorambucil chemotherapy. Perhaps the persistent leukopenia that these patients have even with chemotherapy could be ameliorated by administration of lithium carbonate, but this remains to be proved.

Although several case reports have demonstrated objective responses and improved granulocyte counts after intensive chemotherapy and long periods of aplasia, the initial therapy of postsplenectomy patients with progressive hairy cell leukemia disease does not require such an aggressive approach. Our current recommended therapy for these patients is low-dose chlorambucil chemotherapy for at least a 6-mo period; our experience suggests that the great majority (87.5%) of patients will respond.

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REFERENCES


Progress report on chlorambucil therapy in postsplenectomy patients with progressive hairy cell leukemia

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