Chronic granulocytic leukaemia in a patient with chronic renal failure on dialysis

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SUMMARY A diagnosis of chronic granulocytic leukaemia was made in a man who had been haemodialysed for three years. The association between leukaemia and chronic renal failure is rare.

Several authors¹⁻⁴ have reported an increase in the incidence of malignancy in patients with chronic renal failure. The phenomenon was discussed in detail by Kjellstrand,⁵ who, after studying the United States and European Dialysis Transplant Registries, concluded that the incidence of malignancy is increased by chronic uraemia and that there is a higher incidence of death related to malignancy among uraemic patients than among those who have had a successful kidney transplant, thereby exonerating immunosuppressive drugs as a causal agent of the neoplastic change.

Our patient had renal failure and was being treated by haemodialysis when he developed chronic granulocytic leukaemia. The case is being reported in order to emphasise the relationship between uraemia and cancer. One case with some similar features has been reported previously.⁶

Case report

The diagnosis of chronic renal failure was made in a 27-year-old man when he was admitted to hospital with lobar pneumonia in 1967. His creatinine clearance was 42 ml/mm. In 1974 he began dialysis to relieve the symptoms of uraemia. His haemoglobin was 7.6 g/dl and his white cell count $7.0 \times 10^9/l$, neutrophils $5.3 \times 10^9/l$, lymphocytes $1.1 \times 10^9/l$, monocytes $0.4 \times 10^9/l$, and eosinophils $0.2 \times 10^9/l$.

He received his first renal transplant in March 1975 but the graft was rejected after eight days and was removed. He received azathioprine and prednisone in conventional doses. After this, haemodialysis was continued at home.

In July 1977, a routine white cell count was $43.7 \times 10^9/l$. The differential white cell count and bone marrow morphology were typical of chronic granulocytic leukaemia, and the Philadelphia chromosome was demonstrated. Treatment with

busulphan was started but had to be stopped after a second transplant in October 1978 when his platelet count fell to $35 \times 10^9/l$. This second transplant failed within six days of the operation because of renal vein thrombosis secondary to infection. The transplanted kidney was removed and immunosuppressive therapy was withdrawn. He was moderately well on haemodialysis but treatment with busulphan was not started again until June 1979 when his white cell count had risen to $68.5 \times 10^9/l$. It was stopped in October 1979 when he was pancytopenic: haemoglobin 5.2 g/dl, WCC $2.7 \times 10^9/l$, neutrophils $2.0 \times 10^9/l$, lymphocytes $0.6 \times 10^9/l$, eosinophils $0.1 \times 10^9/l$, platelets $17 \times 10^9/l$. A bone trephine showed focal myeloid hyperplasia due to residual chronic granulocytic leukaemia with very few erythroid precursors and virtually no megakaryocytes. The picture was not that of leukaemic transformation but was thought to be one of marrow depression.

He deteriorated clinically, requiring frequent transfusions and remaining both leucopenic and thrombocytopenic until his death in January 1980, which was attributed to aplastic anaemia, probably the consequence of busulphan therapy.

Discussion

There is an increased incidence of malignancy in patients with uraemia¹⁻⁴ and also in those receiving chemical immunosuppression after renal transplantation.⁷ Matas *et al.*³ calculated that there was a sevenfold increase in the incidence of malignancy in their series of 78 patients on chronic haemodialysis compared with an age-matched normal population. Of the 47 patients of Miach *et al.*,⁴ none of whom had had immunosuppressive drugs, six developed cancer. In neither this series nor the series of Kinlen *et al.*² did any patient develop leukaemia, though non-Hodgkin's lymphoma, hypernephroma, and skin cancer were relatively common. Sutherland *et*

al.⁶ diagnosed malignancy in four of 120 non-chemically immunosuppressed uraemic patients. One of these patients had chronic granulocytic leukaemia. He died of leukaemia two years after the disease had been diagnosed. He was in advanced renal failure but had never been dialysed (MJ Farr, personal communication).

There is experimental evidence to show that cell-mediated immunity is impaired in uraemia. Smiddy *et al.*⁸ demonstrated prolongation of skin allograft survival in acutely uraemic rabbits, and Elves *et al.*⁹ suggested that the defect resided in the lymphocytes by demonstrating the poor response of uraemic lymphocytes in the mixed lymphocyte culture test and poor transformation of lymphocytes under the influence of phytohaemagglutinin. The uraemic defect appears to be due to a dialysable factor because lymphocyte function reverts to normal when the cells are washed in normal serum.¹⁰ Wilson *et al.*¹¹ found reduced cell-mediated immunity, lymphopenia, and thymic atrophy to be common in 45 patients with irreversible renal failure. Burnet¹² suggested that reduced cell-mediated immunity impaired the immune surveillance for neoplastic mutant cells.

The aetiology of chronic granulocytic leukaemia is unknown, and there is certainly no hypothesis that can satisfactorily explain why one immunosuppressed patient develops skin cancer, another lymphoma, and yet another leukaemia. Of the various neoplasms that arise in uraemic patients, leukaemia of any type is relatively uncommon. This is the second reported example of chronic granulocytic leukaemia developing in a patient with chronic uraemia.

References

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