CASE REPORT

The use of rituximab and bendamustine in treating chronic lymphocytic leukaemia (CLL) in end-stage renal disease (ESRD)

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SUMMARY

A patient with a history of type 2 diabetes mellitus and chronic lymphocytic leukaemia has renal failure with large kidneys. The patient refused kidney biopsy to determine the aetiology of her renal failure. She uses peritoneal dialysis to treat renal failure. She received rituximab and bendamustine to treat chronic lymphocytic leukaemia. Adenopathy resolves with treatment and she does not experience any electrolyte disturbances or decrease in urine output as a result of chemotherapy in the setting of renal failure. Renal function did not recover with chemotherapy.

TREATMENT

She receives peritoneal dialysis to manage kidney failure with nephrotic range proteinuria. The patient was treated with bendamustine 90 mg/m² intravenous on days 1 and 2 and rituximab 3.75 mg/m² on day 1 and pegfilgrastim 6 mg on day 3 of 28 cycles up to 6 cycles.

OUTCOME AND FOLLOW-UP

Subsequent CT scan for repeat staging after completion of rituximab and bendamustine showed significant improvement (Figures 1A,B, 2A,B and 3A,B).

BACKGROUND

With many chemotherapeutic agents known to have nephrotoxic effects, the choice of specific drug regimen must be taken into consideration. This case reviews the use of rituximab and bendamustine in treating chronic lymphocytic leukaemia (CLL) in a patient with end-stage renal disease (ESRD) on peritoneal dialysis.

CASE PRESENTATION

A 58-year-old woman with a history of diabetes mellitus type 2, hypertension, chronic kidney disease stage 5 on peritoneal dialysis, hyperlipidaemia and asthma initially presented for evaluation of recurrent axillary lymphadenopathy. She noted to have cervical adenopathy in the past 2 years and intermittent fevers and night sweats for the past 6 months.

INVESTIGATIONS

Finding from the right cervical lymph node biopsy was consistent with CLL/small lymphocytic lymphoma. Subsequent bone marrow biopsy was significant for 60–80% bone marrow involvement by B-cell CLL. CD5, CD23, CD 19, CD20 dim, CD22 dim, ZAP70 and CD 38 were noted to be positive. CT showed extensive, bulky lymphadenopathy in the visualised chest, abdomen and pelvis with most predominantly at axillary, subcarinal, porta hepatitis celiac axis, and external iliac lymph node stations.

Kidney biopsy was not performed to evaluate nephrotic range proteinuria. Abdominal ultrasound showed the right kidney of 13.2 cm and the left of 13.1 cm.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for renal failure included diabetes mellitus and lymphocytic infiltration, both associated with a large kidney size.

Figure 1 (A) Nodes seen on CT scan pretreatment. (B) Nodes absent on CT scan after treatment.

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Figure 2 (A) Nodes seen on CT scan pretreatment. (B) Nodes absent on CT scan after treatment.

A 3-month average white cell count prior to chemotherapy was $18 \times 10^6/l$ with 91% lymphocyte count, while postchemotherapy it was $3.3 \times 10^6/l$ with 27.3% lymphocyte count.

Tumour lysis syndrome was anticipated with worsening of renal function. We also expected electrolyte disturbances such as hyperkalaemia, hyperuricaemia, hyperphosphataemia because of ineffective electrolyte clearance by peritoneal dialysis. Fortunately for the patient, there were no significant changes in serum potassium, uric acid, phosphorus, magnesium, blood urea nitrogen, creatinine or bicarbonate concentrations when comparing levels prior to initiation of treatment, during chemotherapy and after completing six cycles of chemotherapy. Urine output did not diminish as a result of chemotherapy.

DISCUSSION

With many chemotherapeutic agents known to have nephrotoxic effects, the choice of specific drug regimen must be taken into consideration. In this case, rituximab and bendamustine were used to treat CLL in an ESRD patient on peritoneal dialysis.

This patient was noted to have renal failure at the time of diagnosis of CLL. Renal failure has been noted in CLL. This has been attributed to lymphocytic infiltration. The lymphocytes

Figure 3 (A) Abdominal node seen on CT scan pretreatment. (B) Abdominal node size reduced with treatment.

have been found to occlude the renal microvasculature and the glomerular capillaries. Markers of lymphocytes have shown that the lymphocytes in the interstitial infiltration were identical to the peripheral lymphocytes.¹ With treatment of CLL, renal failure improved in cases published.²

Rituximab and bendamustine were used in this case. Rituximab has been long used as a monotherapy or in combination with other chemotherapy agents for treating acute and chronic leukaemias. The anti-CD20 monoclonal antibody, rituximab, has been shown to have activity against B-cell CLL.³ Bendamustine, an alkylating agent with purine-analogue properties, induces apoptosis through activation of DNA-damage stress response and inhibition of mitotic checkpoints. It has been approved for the treatment of CLL and has been a favourable agent in treating relapsed or refractory B-cell CLL due to its minimal cross resistance with other alkylating agents.^{4 5} The manufacturer of bendamustine does not recommend its use in patients with creatinine clearance less than 40 ml/min. Studies on rituximab and bendamustine side effects have not noted significant renal impairment and have been well tolerated in study groups.^{3 4}

This patient did not experience any excessive cellular substance release to cause hyperkalaemia, hyperphosphataemia or

hyperuricaemia, which could be problematic in the setting of poor excretion due to renal failure. Unfortunately, the patient did not recover renal function after chemotherapy, suggesting renal failure was unlikely to be related to lymphocytic leukaemia.

This case demonstrates a favourable response of CLL to rituximab and bendamustine with minimal adverse effects in the setting of renal failure.

Learning points

- ▶ Chronic lymphocytic leukaemia can cause renal failure by lymphocytic infiltration.
- ▶ Chronic lymphocytic leukaemia responds favourably to rituximab and bendamustine, even in patients with end-stage renal disease.
- ▶ Judicial use of chemotherapeutic agents and dose adjustment for renal failure results in minimal side effects.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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