CASE REPORT

Pulmonary leucostasis in a patient with chronic lymphocytic leukaemia

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SUMMARY

A 71-year-old woman with no chronic medical problems presented to the emergency room with a 24-month history of chronic non-productive cough, malaise, increasing fatigue and weight loss. On physical examination, she had significant cervical and axillary lymphadenopathy with no organomegaly. She was diagnosed with chronic lymphocytic leukaemia (CLL) due to her lymphocyte count of $1789.4 \times 10^9/L$ on admission. A few days after hospitalisation, she developed respiratory failure requiring intubation. A chest X-ray showed interstitial markings. The abnormally high number of mature lymphocytes could have caused leucostasis in the lungs of this patient with CLL.

BACKGROUND

Chronic lymphocytic leukaemia (CLL) is the most common type of leukaemia, with nearly 10 000 new cases a year in the USA alone.¹ There is limited research on indications for leucopheresis in patients with CLL. It has been shown that white cell count as high as $500 \times 10^9/L$ may not cause leucostasis in patients with CLL.¹ In CLL there is a predominance of mature lymphocytes, which usually does not result in occlusion of microvasculature. Leucostasis in the lungs of a patient with CLL has been rarely documented in the literature to our knowledge.

CASE PRESENTATION

A 71-year-old Caucasian woman presented to the emergency department with a chronic non-productive cough, malaise, increasing fatigue and weight loss.

The patient was in her usual health until approximately 24 months earlier, when she was advised by her dentist to follow-up with her primary physician for significant cervical lymphadenopathy. She did not establish such care until presentation to the emergency department.

On examination, her vital signs were normal though her weight was 85 kg, which was 10 kg less than 1 month earlier. She had generalised cervical and axillary bulky lymphadenopathy. The abdomen was without organomegaly. She had no lower extremity edema.

The patient had no known medical history and was not on any medications. She had not seen a physician in over 20 years. She reported that her mother had an unknown type of leukaemia.

INVESTIGATIONS

On admission, complete blood count with differential showed: red blood count $3.97 \times 10^{12}/L$ ($3.87-5.08 \times 10^{12}/L$), white cell count $>1789.4 \times 10^9/L$

($3.3-10.7 \times 10^9/L$), haemoglobin 7.6 g/dL (12.1–15.0 g/dL), haematocrit 20.5% (35.4–44.2%), platelets $298 \times 10^9/L$ ($150-400 \times 10^9/L$), lymphocytes $1789.4 \times 10^9/L$ ($1.1-4.0 \times 10^9/L$) and neutrophils $<0.1 \times 10^9/L$ ($1.6-7.2 \times 10^9/L$).

On day 1 of admission, haematology and oncology specialists were consulted and the patient started on bendamustine and rituximab. The patient was also on prophylaxis allopurinol for tumour lysis syndrome. Her lymphocytes started to trend down.

On day 7, she was noted to have hypoxia and her lymphocytes was $953 \times 10^9/L$. Chest X-ray demonstrated hilar lymphadenopathy, bilateral hilar, mediastinal lymphadenopathy, right middle lobe atelectasis and prominent interstitial markings. Her hypoxia progressively worsened requiring intubation on the eighth day of hospitalisation. Her haemoglobin was 6.9 g/dL and her lymphocytes $870 \times 10^9/L$ at the time of intubation.

She received 2 units of blood on day 9, there was no increase in the haemoglobin levels. CT was ordered to look for evidence of bleeding. CT showed bilateral rectus sheath haematoma and right pelvic haematoma. Heparin was stopped and surgery was consulted to evaluate the patient. Surgery decided to conservatively manage the patient rather than perform surgery.

All other common causes of respiratory failure were eliminated by work up. The patient failed to improve on broad spectrum antibiotics, ruling out community-acquired pneumonia. An echocardiogram on day 14 showed enlarged right ventricle and enlarged right atrium. Left ventricle and atrium were normal.

A CT angiogram ruled out the possibility of a pulmonary embolism.

There was strong suspicion of leucostasis based on unexplained interstitial markings with respiratory failure. The patient was not leucopheresed. It was certainly brought up and considered but was never carried out.

DIFFERENTIAL DIAGNOSIS

Diagnosis of CLL is based principally on flow cytometry of peripheral blood. Our patient's flow cytometry was reported as follows: 98% of total cells were small κ monotypic B cells, expressing the following antigens: CD5, CD19, CD20 (dim), CD22 (very dim), CD23, CD45 and dim κ light chain. The B cells were negative for CD10, CD38 and CD79b. Diagnosis of CLL was confirmed in this patient.

Prognostic indicators in patients with CLL include lymphocyte doubling time and molecular/chromosomal markers. Owing to lack of follow-up

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of our patient, lymphocyte-doubling time was not known at her initial presentation. Molecular/chromosomal markers were reported as ATM and MYB gene deletions as well as del (13q). Deletion of ATM gene is associated with extensive adenopathy, progressive disease and shorter survival.

Congestive heart failure was ruled out by the echocardiogram, which showed mild enlargement of the right ventricle and atrium. CT angiogram ruled out pulmonary embolism as a cause of hypoxia and shortness of breath. The patient received blood transfusion after the chest X-ray findings, ruling out transfusion-related lung injury.

TREATMENT

Current therapies for CLL do not offer a cure. The objective of management of CLL is palliative. There are guidelines providing indications for treatment. These include weight loss, anaemia, thrombocytopenia, repeated infections and splenomegaly, lymphadenopathy or patient preference, to initiate treatment.²

Many palliative therapies have been used in CLL. Rituximab in combination with bendamustine achieved treatment response of 88% in a multicentre phase II trial of a CLL study group.³ Based on this trial our patient was started on bendamustine and rituximab.

The patient was mildly hypotensive and was subsequently started on midodrine. Lasix 80 mg was started for worsening bilateral lower extremity edema that started on day 13 of admission along with bibasilar rales. On discharge, the patient was normotensive and euvoletic with trial off midodrine and lasix. With regard to her anaemia, she was symptomatic with shortness of breath and worsening fatigue with a haemoglobin count of 7.3 g/dL. Thus, she received 2 units of packed red blood cells and haemoglobin remained stable thereafter.

Unfortunately, she developed acute kidney injury presumed to be secondary to nephrocalcinosis. She became oliguric and required transient haemodialysis. She was also started on aranesp for anaemia due to chronic kidney disease. Despite a creatinine level of 0.9 mg/dL on discharge, the aranesp was continued in order to aid in augmenting the patient's haemoglobin rise. Her course was also complicated by new deep venous thrombosis in her upper extremities during her hospital stay. She was started on coumadin and had an inferior vena cava filter put in.

OUTCOME AND FOLLOW-UP

The patient's course was complicated by tumour lysis syndrome, however, her respiratory status improved. On day 7 of therapy

she was extubated. After 24 days of hospitalisation she was discharged to a rehabilitation facility. It is our hypothesis that this patient developed respiratory failure secondary to leucostasis. All other common causes of respiratory failure were eliminated by the work up.

DISCUSSION

This case report demonstrates that leucostasis should be considered in the pathophysiology of patients with CLL who present with excessive lymphocytes. It is conceivable that in patients such as this, leucopheresis may be of therapeutic benefit. Additional studies need to be made of patients with CLL who present with symptomatic hyperleucocytosis to find speedy diagnostic methods and immediate treatments.

Learning points

- Unexplained respiratory failure with lung interstitial marking in patients with chronic lymphocytic leukaemia (CLL) might be due to leucostasis.
- Additional studies need to be made of patients with CLL who present with symptomatic hyperleucocytosis.
- Bendamustine and rituximab offer significant therapy to patients with CLL.

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