Uncommon simultaneous diagnosis of multiple myeloma and chronic myeloid leukaemia

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Abstract

Chronic myeloid leukaemia (CML) is a clonal hematopoietic stem cell disorder. The annual incidence of CML is 1.5 cases per 100,000 individuals. Multiple myeloma (MM) represents a malignant proliferation of plasma cells derived from a single clone. The co-occurrence of two rare malignancies CML and MM in the same patient is an extremely rare incident, and simultaneous diagnosis of CML and MM is reported in only five cases in the literature. A 75-year-old male presented with complaints of easy fatigability, loss of appetite and unquantified weight loss of four months' duration. On evaluation he was found to have normocytic normochromic anaemia, leucocytosis, elevated serum-calcium concentration and azotaemia. Peripheral blood for the BCR-ABL fusion gene product was positive by fluorescence in situ hybridisation (FISH). However, bone marrow biopsy revealed CD138 positive, 15% plasma cells. Thus the diagnosis of CML and MM was established. Although we can't be certain regarding the cause of CML and MM in our patient, the hypothesis that they evolved from common malignant pluripotent hematopoietic stem cells still holds. However, at the age of 75 years, it might be just due to chance.

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Introduction

Chronic myeloid leukaemia (CML) is a type of myeloproliferative disorder. It is caused by the mutation in the BCR-ABL1 gene which results in a reciprocal balanced translocation between the long arms of chromosomes 9 and 22, t (9; 22) (q34.1; q11.2), known as the Philadelphia chromosome (Ph). CML constitutes 15% of all cases of blood cancer. It is commonly diagnosed in fifth or sixth decade of life.[1] Multiple myeloma (MM) is a disorder of plasma cell proliferation derived from a single clone. The malignant plasma cells infiltrating the bone marrow and other organ systems, their products and the body's response to them results in the various clinical manifestations of the disease. MM is a disease of the elderly and is usually diagnosed in seventh decade of life. The co-occurrence of these two rare disorders, CML and MM is an exceptionally rare event and review of the literature suggests that only 20 cases have been reported worldwide. We present a similar case of a patient who was diagnosed simultaneously with CML and MM, and succumbed shortly after starting treatment due to a likely unrelated event like acute coronary syndrome.

Case presentation

A 75-year-old male with a past medical history of hypertension presented with complaints of easy fatigability, loss of appetite and weight loss of four months' duration. On general physical examination only pallor was present. On examination of the abdomen, it was soft with no evidence of hepatosplenomegaly and bowel sounds were present. Initial laboratory workup showed a haemoglobin level of 96g/l, haematocrit of 25.9%, mean corpuscular volume (MCV) of 83.3fl, white blood cell count of 40 x 10^9/l, and a platelet count of 433 x 10^9/l. Peripheral blood smear (PBS) was suggestive of normocytic normochromic anaemia with 3% myelocytes, 3% metamyelocytes, and 1% blasts with rouleaux formation. Initial biochemical workup revealed serum creatinine value of 132.6 micromol/l, corrected total serum calcium concentration of 2.6 mmol/l, with the total protein of 73g/l and albumin of 31g/l. His initial serum uric acid value was 565.06 micromol/l. He underwent ultrasonography of the abdomen which was negative for hepatosplenomegaly. The skeletal survey for lytic lesions was negative. Peripheral blood sample was sent for BCR-ABL

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Figure 1 Bone marrow biopsy, 40x, immunostain for CD 138, shows CD 138 positive plasma cells.

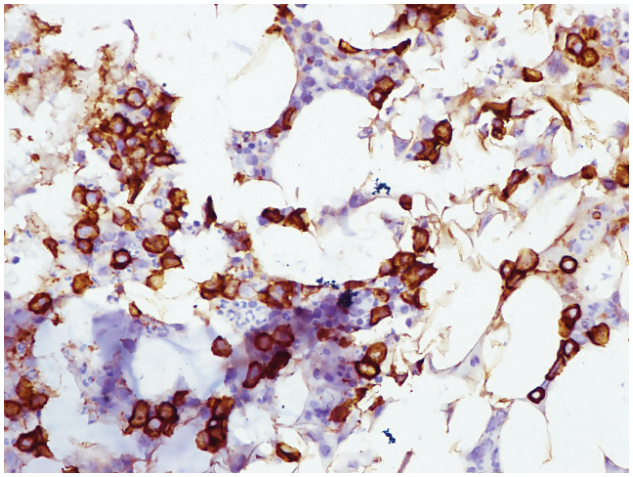
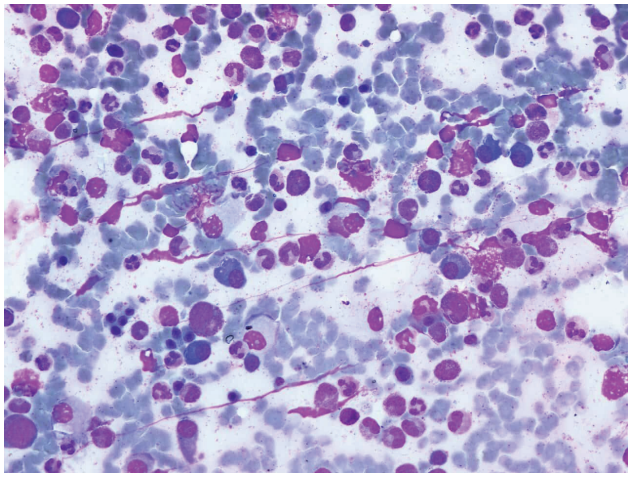


Figure 2 Bone marrow aspirate smear H & E 40x, showing an increase in the number of plasma cells (15 %)



t (9; 22) translocation assay by FISH which showed fusion signals for BCR-ABL in 148/200 (74%) of interphase nuclei. The sample was reported as positive for t (9; 22) (q34, q11.2). He was started on capsule imatinib 400 mg once a day. The patient was subjected to bone marrow aspiration and biopsy, which was not consistent with the diagnosis of CML and was suggestive of MM (Figures 1, 2). Subsequently serum protein electrophoresis was performed which showed an M band of 20 g/l in the gamma globulin region. Two days after starting selective tyrosine kinase inhibitor (TKI) therapy the patient developed acute-onset dyspnoea with chest heaviness. Urgent electrocardiograph showed ST-elevation inferior wall myocardial infarction. While awaiting transfer to the intensive care unit, the patient's condition deteriorated and he succumbed to his illness and could not be revived despite the cardiopulmonary resuscitation efforts.

Discussion

The co-occurrence of these two rare disorders, CML and MM is an exceptionally rare event. Out of the 20 cases reported in literature, only in five cases were both malignancies diagnosed simultaneously.[2-5] In our patient CML was diagnosed first; even that was unusual in the absence of splenomegaly. Moreover, other than anaemia, our patient did not have any of the myeloma defining events. It was the bone marrow which showed 15% plasma cells. A logical speculation is that CML and MM may originate from the same pool of malignant pluripotent hematopoietic stem cells.[2] It is clearly established that CML arises from pluripotent hematopoietic stem cells which have the capacity to differentiate into other cell types including immunoglobulin-synthesising B lymphocytes.[6] Besides this, it has been clearly established that the BCR-ABL fusion gene product is continuously active tyrosine kinase which is responsible for the proliferation of the cells, and leads to malignant transformation of the disease.[6] This hypothesis can explain the simultaneous occurrence of CML and MM in our patient. Although we can't be certain regarding the cause of CML and MM in our patient, the hypothesis that they evolved from common malignant pluripotent hematopoietic stem cells still holds.

Conclusion

This case highlights the importance of bone marrow examination even though the diagnosis of CML was clear after PBS and FISH report. However, at the age of 75 years, it might be just due to chance.

References

1 Rohrbacher M, Berger U, Hochhaus A et al. Clinical trials underestimate the age of chronic myeloid leukemia (CML) patients. Incidence and median age of Ph/BCR-ABL-positive CML and other chronic myeloproliferative disorders in a representative area in Germany. *Leuk* 2009; 23: 602–4.

2 Ide M, Kuwahara N, Matsuishi E et al. Uncommon case of chronic myeloid leukemia with multiple myeloma. *Int J Hematol* 2010; 91: 699–704.

3 Schwarzmeier JD, Shehata M, Ackermann J et al. Simultaneous occurrence of chronic myeloid leukemia and multiple myeloma: evaluation by FISH analysis and in vitro expansion of bone marrow cells. *Leukemia* 2003; 17: 1426–8.

4 Alvarez-Larrán A, Rozman M, Cervantes F. Simultaneous occurrence of multiple myeloma and chronic myeloid leukemia. *Haematologica* 2001; 86: 894.

5 Tanaka M, Kimura R, Matsutani A, et al. Coexistence of chronic myelogenous leukemia and multiple myeloma. Case report and review of the literature. *Acta Haematol* 1998; 99: 221–3.

6 Savona M, Talpaz M. Getting to the stem of chronic myeloid leukaemia. *Nat Rev Cancer* 2008; 8: 341—50.