Atypical chronic myeloid leukaemia: cytogenetic and molecular testing—a clincher to final diagnosis

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DESCRIPTION

A 66-year-old woman presented with melena for 5 months with an episode of haematemesis. Ultrasonography revealed hepatosplenomegaly. Her complete blood count showed anaemia (haemoglobin of 44 g/L), hyperleucocytosis (total leucocyte count $323.99 \times 10^9/L$) and thrombocytopenia (platelets of $40 \times 10^9/L$). Peripheral blood showed hyperleucocytosis with neutrophil and myelocyte bulge with complete differential count of neutrophils: 47.0%, lymphocytes: 2.5%, eosinophils: 1.5%, monocytes: 1.5%, basophils: 1.5%, metamyelocytes: 4.5%, myelocytes: 37.5%; blasts: 4.0 %; and thrombocytopenia (figure 1A). Bone marrow aspirate (figure 1B) was hypercellular showing myeloid hyperplasia with 5% blasts (myelogram: blasts: 5.0%, myelocytes: 23.6%, metamyelocytes: 4.4%, neutrophils: 57.4%, eosinophils and its precursors: 0.2%, lymphocytes: 1.4%, monocytes: 0.2%, plasma cells: 0.2%, erythroid precursors: 7.2%, basophils: 0.4%). Trilineage dysplasia was also noted. Bone marrow biopsy was hypercellular showing myeloid hyperplasia with small focal areas of increase reticulin fibrosis. Karyotype showed 47,XX, trisomy 8 (figure 1C). Fluorescence in situ hybridisation (FISH) was negative for t(9;22)/BCR-ABL1 (figure 1D). Real-time PCR for p210, p230 and p190 BCR-ABL1 transcripts was also negative. Molecular studies for JAK2, CALR and MPL were also found negative. A final diagnosis of atypical chronic myeloid leukaemia (aCML) was

made. Atypical CML belongs to the group of myelodysplastic/myeloproliferative neoplasms (MDS/MPN). Although a definite cytogenetic or molecular signature is absent in aCML, most common karyotypic changes reported in aCML include trisomy 8 and del (20q). Abnormalities involving other chromosomes such as 12, 13, 14, 17, 19 and 21 have also been described.¹ Persistent leucocytosis without monocytosis with absence of Philadelphia (Ph) chromosome and BCR/ABL fusion gene suggests a diagnosis of aCML. Evidence of marked multilineage dysplasia is an important morphological finding indicating aCML. Differential diagnosis of aCML is CML, myelofibrosis, chronic neutrophilic leukaemia (CNL) and chronic myelomonocytic leukaemia (CMML).^{2,3} CML is mostly characterised by hyperleucocytosis with prominence of myelocytes (usually >20%), basophilia, presence of BCR-ABL1 without significant dyshaematopoiesis. In contrast to that, aCML does not show myelocyte prominence (myelocytes are usually 10%–20%) with the presence of granulocytic dyspoiesis; and without basophilia and BCR-ABL1 translocation. Myelofibrosis shows

Figure 1 (A) Peripheral blood showed hyperleucocytosis with neutrophil and myelocyte bulge and dysgranulopoiesis. (B) Bone marrow aspirate hypercellular showing myeloid hyperplasia with trilineage dysplasia. (C) Karyotype showed 47,XX, trisomy 8. (D) Fluorescence in situ hybridisation showed negative for t(9;22)/BCR-ABL1.

Patient's perspective

Two months ago, I was suffered from melena, hematemesis and hepatosplenomegaly. I am feeling better now and we would like to thank technologists, consultants of diagnostic and clinical department for their excellent technical assistance. I am also indebted to the inpatient nursing teams and support staff for the excellent care they provided.

Learning points

- ▶ In the WHO 2016 classification, atypical chronic myeloid leukaemia (aCML) is defined as myelodysplastic/myeloproliferative neoplasms disease with an incidence approximately 100 times lower than the incidence of BCR-ABL1-positive CML.
- ▶ No specific chromosomal abnormality is associated with aCML.
- ▶ Other myeloproliferative neoplasms pose diagnostic dilemma for aCML; however, the presence of a granulocytic proliferation associated with marked dysgranulopoiesis and the absence of BCR-ABL1 translocation are the defining features of aCML.

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leucoerythroblastic anaemia with the presence of tear drop cells, increase marrow fibrosis and JAK2, CALR or MPL mutation. CMML is characterised by monocytosis $>1 \times 10^3/\mu\text{L}$ and CNL is characterised by neutrophilia with immature granulocytes $<10\%$ and no dyshaematopoiesis. In our case, due to the presence of marked hyperleucocytosis (>3 lakh/ μL) with myelocyte bulge without monocytosis, the closest differential diagnosis was CML in chronic phase. However, presence of dyspoiesis on morphological evaluation with absence of Ph chromosome on karyotype and FISH, and BCR/ABL fusion gene on real-time PCR, clinches the diagnosis.

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and its interpretation, and contributed to subsequent revisions of the manuscript. All authors have seen and agree with the final version.

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