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

Smeeta Gajendra,1 Anil Yadav,2 Manorama Bhargava2

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 x 10^9/L) and thrombocytopenia (platelets of 40 x 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 increased 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. 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 (CML).

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.
leucocytosis with the presence of tear drop cells, increase marrow fibrosis and JAK2, CALR or MPL mutation. CMML is characterised by monocytosis >1×10³/μL and CNL is characterised by neutrophilia with immature granulocytes <10% and no dysnaematopoiesis. In our case, due to the presence of marked hyperleucocytosis (>3lakh/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.

**Contributors** SG conceived and drafted the first manuscript. AY performed FISH and karyotyping. SG and MB diagnosed the case, worked on the acquisition of data, and its interpretation, and contributed to subsequent revisions of the manuscript. All authors have seen and agree with the final version.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent for publication** Obtained.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**REFERENCES**