CASE REPORT

Acute myeloid leukaemia with t(8;21)(q22;q22.3) and loss of the X chromosome

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SUMMARY

Cytogenetic abnormalities occur in approximately 60% of newly diagnosed patients with acute myeloid leukaemia (AML) and are useful in the risk stratification of AML. Translocation between chromosomes 8 and 21—t(8;21)—(q22;q22.3), which carries a favourable prognosis, is found in approximately 5% to 10% of all patients with AML. Additional chromosomal abnormalities have been described in patients with AML with t(8;21), which may impact on the favourable prognosis. We report a patient who had AML with t(8;21)(q22;q22.3) and loss of the X chromosome.

BACKGROUND

Patients with acute myeloid leukaemia (AML) with t(8;21) generally carry a favourable prognosis, in terms of disease response and long-term survival. Additional chromosomal abnormalities have been described in such patients and these may have an impact on the good prognosis, which is described in this article.

CASE PRESENTATION

A 40-year-old woman attended the emergency department of our hospital with acute onset of large bruises on the skin and gum bleeds of 10 days duration. She did not have any comorbid illness in the past and she was not on any regular medications. She was a non-smoker and rarely consumed alcohol. Her family history was unremarkable. On general examination, generalised purpuric spots and ecchymosis were noted. There was no palpable organomegaly or lymphadenopathy and systemic examinations were unremarkable.

INVESTIGATIONS

Full-blood counts showed pancytopenia with haemoglobin of 98 g/L, white cell count of $2.2 \times 10^9/L$, neutrophil count of $0.5 \times 10^9/L$, platelet count of $45 \times 10^9/L$ and occasional blasts in the blood film. Her coagulation parameters were within normal limits. Bone marrow biopsy showed marked hypercellularity with 70% leukaemic blasts; the majority of them were large with granular and basophilic cytoplasm. Normal haematopoiesis was markedly suppressed with granulocytic maturation of 22% (figure 1, Wright's stain $\times 1000$ magnification). Flow cytometric analysis demonstrated expression of surface markers CD13, CD33, CD34, human leukocyte antigen-DR (HLA-DR) and myeloperoxidase (MPO) on the blasts. These morphological and immunophenotypic features were consistent with AML with maturation. Bone

marrow chromosomal analysis revealed a translocation between chromosome 8 and chromosome 21, along with loss of the X chromosome in 80% of metaphases. The karyotype was 46,XX,t(8;21)(q22;q22.3)(2)/45,sl,-X/(16)/46,XX(2) (figure 2). The diagnosis was AML with recurrent genetic abnormalities according to WHO classification of tumours of haematopoietic and lymphoid tissues.¹

TREATMENT

The patient was admitted to the acute haematology unit, and chemotherapy with cytosine arabinoside 100 mg/m² for 7 days and daunorubicin 50 mg/m² for 3 days was administered for remission induction. She underwent complete remission, with bone marrow biopsy at day 28 showing <1% blasts and restoration of normal haematopoiesis. Chromosomal analysis on remission bone marrow demonstrated normal karyotype (46 XX) with complete disappearance of the abnormalities t(8;21) and deletion of X chromosome.

OUTCOME AND FOLLOW-UP

After achievement of complete remission, the patient received two cycles of consolidation therapy with high-dose cytosine arabinoside (HiDAC). During this period, she had an uneventful course, with no major complications. She remained healthy and continued to be in complete remission until the last review, 2½ years after the initial diagnosis.

DISCUSSION

Cytogenetic abnormalities occur in approximately 60% of newly diagnosed patients with AML and are useful in the risk stratification of AML. The

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Figure 1 Bone marrow aspirate showing large myeloblasts with granular cytoplasm (Wright's stain $\times 1000$ magnification).

Figure 2 Bone marrow cytogenetics showing t(8;21)(q22;q22.3) with loss of X chromosome.

translocation between chromosomes 8 and 21 (t(8;21)) leads to fusion of the *AML1* gene (*RUNX1*) on chromosome 21 and the *ETO* (*RUNX1T1*) gene on chromosome 8.¹ The t(8;21) abnormality is found in approximately 5% to 10% of all patients with AML and 10% to 20% of AML with maturation. The t(8;21), inversion of chromosome 16 (inv(16)) and translocation between the long and short arms of chromosome 16 (t(16;16)) belong to the category of core binding factor AML, which carries a good prognosis.² Patients with AML with t(8;21) have a favourable prognosis after intensive chemotherapy, with low relapse rates. In a study, it was observed that patients with AML with t(8;21) demonstrated a complete response rate (CRR) of 97% and 10-year overall survival (OS) of 61%, when compared to CRR of 90% and OS of 38% in patients with a normal karyotype AML.³ Although t(8;21) is a favourable prognostic marker, relapse of AML can occur in approximately 30% of patients. Detection of fusion transcripts by reverse transcriptase-PCR is a highly sensitive technique that can identify leukaemic cells in 10⁵–10⁶ normal cells. Interphase fluorescence in situ hybridisation, although less sensitive, can also be used to detect minimal residual disease.²

In general, the WHO diagnostic criterion for AML is the presence of 20% or more blasts in the bone marrow. However, according to the WHO classification, bone marrow blasts of less than 20% should also be diagnosed and treated as AML, if associated with t(8;21) abnormality.⁴ The common morphological features in t(8;21) AML are the presence of large leukaemic blasts with basophilic cytoplasm and plenty of azurophilic granules. Auer rods are also commonly seen. The bone marrow frequently shows granulocytic maturation to promyelocytes, myelocytes and mature neutrophils with or without dysplastic changes such as abnormal nuclear segmentation (eg, pseudo-Pelger-Huet anomaly). These blasts typically express the surface markers CD13, CD33, CD34 and HLA-DR, and are positive for myeloperoxidase. The lymphoid markers, namely, CD19 and cytoplasmic CD79a, can also be aberrantly expressed in the blasts.¹ Myeloid sarcoma can occur in approximately 15% of patients with t(8;21) AML, commonly involving the skin and lymph nodes.⁵

Additional chromosomal abnormalities have been described in patients with AML with t(8;21) and may have prognostic implications. Loss of the X chromosome (–X) occurs in 30–40% of females and loss of Y chromosome (–Y) occurs in approximately 50% of males with AML associated with t(8;21). While the loss of X chromosome does not appear to influence the good prognosis of AML with t(8;21), loss of Y chromosome is known to improve the prognosis. Other chromosomal abnormalities such as trisomy 4, trisomy 8, deletion 9q or tetraploidy, can rarely accompany t(8;21), and their prognostic impact is not known. The frequency of complex cytogenetic abnormalities in t(8;21) AML varies between 9% and 23% and will have an adverse prognostic impact in such patients.^{2–6} It has been observed that molecular abnormalities such as *KIT* mutations and *FLT-ITD* can also lead to an adverse prognosis if they coexist with t(8;21).⁷

Learning points

- ▶ Cytogenetic abnormalities occur in approximately 60% of newly diagnosed patients with acute myeloid leukaemia (AML) and are useful in the risk stratification of AML.
- ▶ Additional chromosomal abnormalities have been described in patients with AML with t(8;21) and may have prognostic implications.
- ▶ Loss of X chromosome does not appear to influence the good prognosis of AML with t(8;21).

Contributors MM was the doctor who treated the patient and wrote the manuscript. KD was the cytogeneticist who performed and reported the bone marrow cytogenetics test and edited the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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