

# CAP TODAY

PATHOLOGY ♦ LABORATORY MEDICINE ♦ LABORATORY MANAGEMENT

## Acute myeloid leukemia with hyperdiploidy

CAP TODAY and the Association for Molecular Pathology have teamed up to bring molecular case reports to CAP TODAY readers. AMP members write the reports using clinical cases from their own practices that show molecular testing's important role in diagnosis, prognosis, and treatment. The following report comes from Aga Khan University in Karachi, Pakistan. If you would like to submit a case report, please send an email to the AMP at [amp@amp.org](mailto:amp@amp.org). For more information about the AMP and all previously published case reports, visit [www.amp.org](http://www.amp.org).



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**Case.** An 87-year-old male with a clinical history of hypertension and sick sinus syndrome presented with a one-month history of fever, generalized weakness, and weight loss. There was no lymphadenopathy or hepatosplenomegaly on physical examination. Bone marrow examination was performed to evaluate for cytopenias. Complete blood counts showed hemoglobin of 9.0 g/dL, hematocrit 27.0 percent, WBC  $1.92 \times 10^9/L$ , ANC  $0.23 \times 10^9/L$ , and platelets  $82 \times 10^9/L$ . Peripheral blood film showed leukopenia with 21 percent blast cells. Also seen were anisopoikilocytosis, macrocytosis, and polychromasia of red blood cells, and thrombocytopenia.

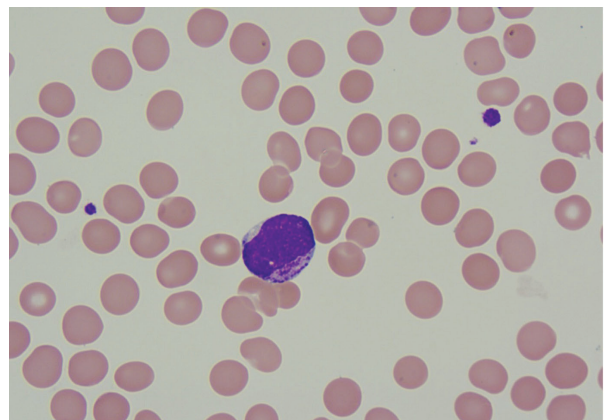
Bone marrow aspirate showed 24 percent blast cells in total nucleated nonerythroid cell population. Blasts were medium to large with moderately abundant cytoplasm containing pink granules, open nuclear

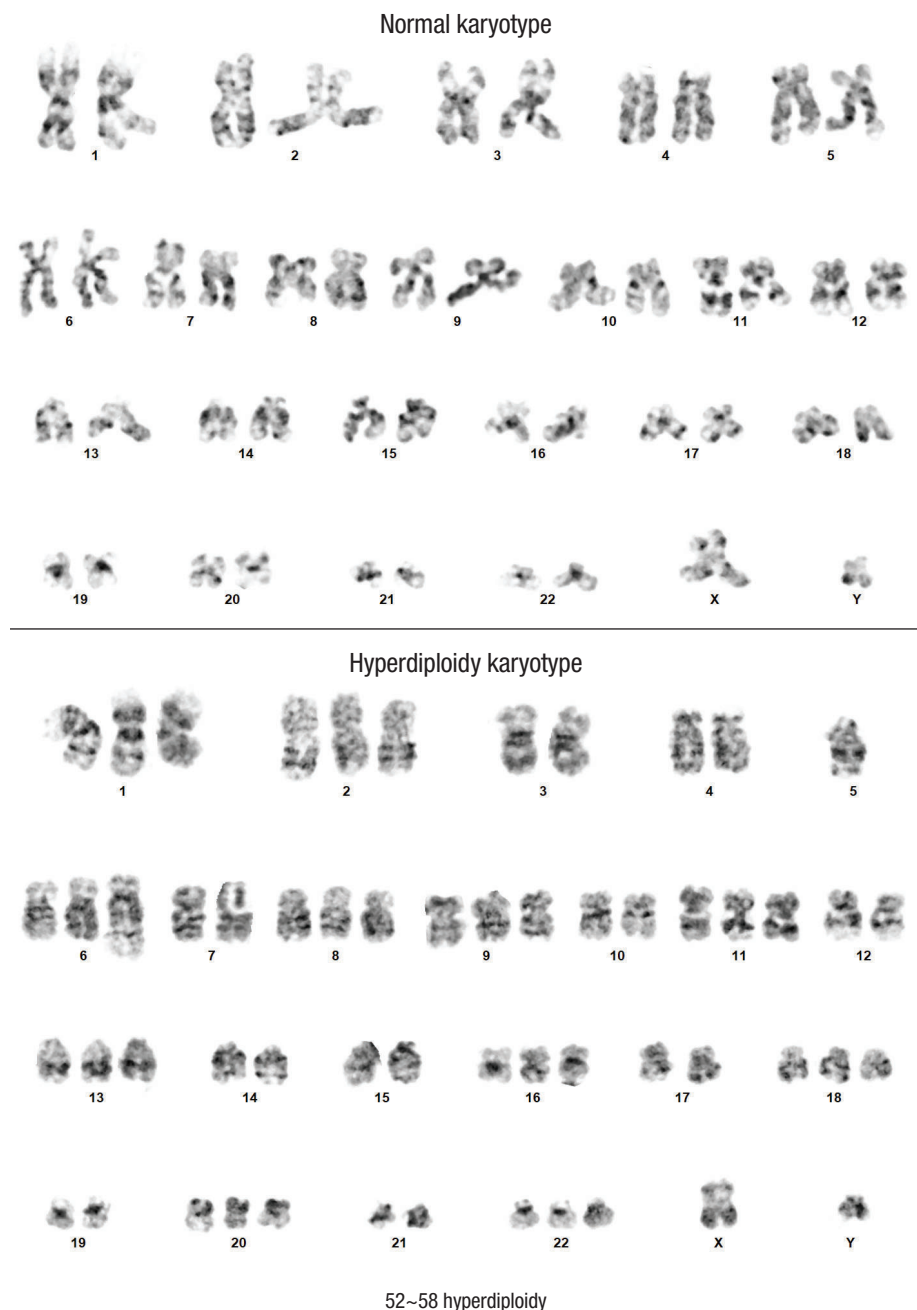
chromatin, and prominent nucleoli (Fig. 1). Normal hematopoiesis was seen in the background. Bone trephine was hypercellular and showed interstitial infiltration with blast cells. Immunophenotyping of blast cells by flow cytometry showed reactivity to CD13, CD33, cytoplasmic MPO, HLA-DR, CD117, and CD34. Bone marrow cytogenetic analysis was reported as 52~58, XY, add(6)(q27)[16]/46,XY[04]. The following chromosomes were gained: 1, 2, 6, 8, 9, 11, 13, 16, 18, 20, and 22 (Fig. 2). FISH assays for 5q deletion and trisomy 8 were positive (Figs. 3a and 3b). *NPM1*, *FLT3-ITD*, and *D835* mutations by conventional PCR were not detected. The case was diagnosed as acute myeloid leukemia. The patient has thus far received one cycle of azacitidine chemotherapy; venetoclax was held after the first dose because of abnormal serum creatinine levels.

**Discussion.** This report depicts a case of AML with hyperdiploidy, which is not specifically defined as a

subtype of AML under the WHO fifth edition of 2022 or the International Consensus Classification (ICC). Hyperdiploid karyotype is defined as greater than 49 chromosomes. Hyperdiploidy is an unusual phenomenon in AML with an incidence reported in the literature to be less than two percent of AML cases.<sup>1</sup> The commonly involved chromosomes are trisomy 8, 21, and 22, which are primarily encountered in de novo AML. Iyer, et al., reported a low remission rate and short survival in this group,<sup>2</sup> while Shetty, et al., reported a minor trend of better outcome as compared with AML with complex cytogenetics.<sup>1</sup> However, Chilton, et al., suggested that such patients not be categorized in an adverse prognostic group by default.<sup>3</sup> Those with specific adverse cytogenetic features, such as monosomy 5 or 5q- and monosomy 7 or 7q-, can be assigned to an adverse risk group. Those with only numeri-

**Fig. 1.** Myeloblast exhibiting intracytoplasmic granules

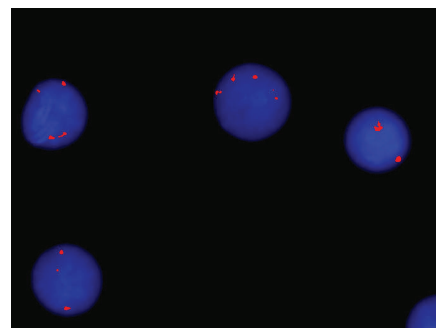
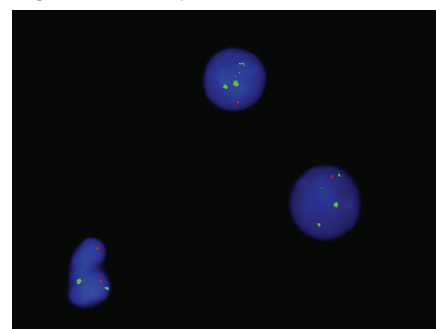


**Fig. 2.** Bone marrow karyotype: 52~58, XY, add(6)(q27)[16]/46,XY[04]

cal increment can be classified as intermediate risk.

Deletion of the long arm of chromosome 5 has a favorable prognostic implication in myelodysplastic syndrome but an unfavorable implication in AML. It often involves the loss of genetic material, impacting critical genes involved in hematopoiesis and cell cycle regulation. The 5q deletion was detected by FISH but not by conventional cytogenetics in this patient. Cryptic deletions,

which may not be readily apparent under standard cytogenetic analysis, may pose diagnostic challenges but are increasingly recognized with advanced genomic techniques. These deletions are associated with distinct clinical and prognostic implications, influencing the disease course and treatment outcomes. The identification of cryptic 5q deletions is crucial for risk stratification, potentially guiding therapeutic decisions and possibly tailoring treat-

**Fig. 3a.** FISH trisomy 8**Fig. 3b.** FISH 5q Del

ment strategies, such as the use of novel targeted therapies.<sup>4</sup> Despite harboring this unfavorable chromosomal change, our patient initially responded well to azacitidine and showed improvement in his blood counts with clearance of blast cells in the peripheral blood.

In conclusion, the exact prognostic significance of hyperdiploidy in myeloid malignancies is undetermined. Paving the way forward, the information provided in the current study contributes to potentially helping to predict the outcome of patients with similar abnormalities and to build the global repository of such unusual genetic changes. □

1. Shetty A, Cortes JE, Ravandi F, et al. Hyperdiploidy in AML: outcomes of acute myelogenous leukemia (AML) patients (pts) with a hyperdiploid karyotype. *J Clin Oncol*. 2014;32(15)(suppl):7088.

2. Iyer RV, Sait SNJ, Matsui S, et al. Massive hyperdiploidy and tetraploidy in acute myelocytic leukemia and myelodysplastic syndrome. *Cancer Genet Cytogenet*. 2004;148(1):29–34.

3. Chilton L, Hills RK, Harrison CJ, Burnett AK, Grimwade D, Moorman AV. Hyperdiploidy with 49–65 chromosomes represents a heterogeneous cytogenetic subgroup of acute myeloid leukemia with differential outcome. *Leukemia*. 2013;28(2):321–328.

4. Rea B, Aggarwal N, Yatsenko SA, Bailey N, Liu YC. Acute myeloid leukemia with isolated del(5q) is associated with *IDH1/IDH2* mutations and better prognosis when compared to acute myeloid leukemia with complex karyotype including del(5q). *Mod Pathol.* 2020;33(4):566–575.

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## Test yourself

*Here are three questions taken from the case report. Answers are online now at [www.amp.org/casereports](http://www.amp.org/casereports) and will be published next month in CAP TODAY.*

- 1.** Trisomy of which chromosome(s) is the most common in acute myeloid leukemia?
  - a. Chromosomes 8, 11, 13, 21, and 22.
  - b. Chromosomes 2, 5, 9, and 10.
  - c. Chromosome 12.
  
- 2.** Which of the following is true regarding cytogenetic and molecular markers of AML and its risk stratification?
  - a. Recurrent translocations and unbalanced cytogenetics are used by the WHO to classify AML as favorable, unfavorable, and intermediate risk.
  - b. Hyperdiploid karyotype defines a distinct subtype of de novo AML under the WHO classification.
  - c. *MLL* and *TP53* gene mutations are of favorable prognostic significance in AML patients.
  
- 3.** The characteristic translocation seen in acute promyelocytic leukemia is:
  - a. t(15;17)
  - b. t(5;17)
  - c. t(11;17)