Mixed phenotypic acute leukemia

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ABSTRACT

Mixed phenotypic acute leukemias (MPALs) are a heterogeneous group of rare leukemias constituting about 1% to 5% of all leukemias. MPAL is defined as an acute leukemia that demonstrates expression of a combination of antigens of different lineages so that it is not possible to assign a single lineage to that leukemia. These leukemias have been characterized by relative therapeutic resistance. We present a case of a woman with an acute MPAL diagnosed as a B/myeloid leukemia.

KEYWORDS B/myeloid leukemia; mixed lineage leukemia; mixed phenotypic acute leukemias

CASE REPORT

A 53-year-old white woman presented to the emergency room after referral by her primary care physician because of a platelet count of 16 K/ μ L. She had been experiencing easy fatigability, dyspnea on exertion, and easy bruising. Her past medical history was noncontributory. On examination a diffuse petechial rash was noted. Her white blood cell count was 21.8 K/ μ L, hemoglobin 11.9 g/dL, hematocrit 34.3%, and platelet count 14 K/ μ L. The peripheral blood differential count included 62% blasts (*Figure 1a*). A subsequent bone marrow sample was 100% cellular with 90+% blasts (*Figure 1b*). Flow cytometry revealed the blasts to be positive for CD19 (*Figure 1c*), CD10, CD20, CD22, CD34 with equivocal myeloperoxidase. A myeloperoxidase stain on the bone marrow biopsy showed approximately 50% positive blasts (*Figure 1d*). Thus, the criteria were met for a B/myeloid mixed phenotype acute leukemia (MPAL; *Table 1*). Fluorescent in situ hybridization was positive for the BCR/ABL gene rearrangement, and quantitative reverse transcription polymerase chain reaction was positive for the t(9;22)BCR/ABL-1 minor (p190) fusion transcript. Treatment was started with R-Hyper CVAD (rituximab, cyclophosphamide, vincristine, dexamethasone, methotrexate, cytarabine) and dasatinib.

DISCUSSION

Mixed phenotypic acute leukemias are characterized by having the presence of antigens of more than one lineage.^{1–3} These leukemias have been historically labeled acute leukemias of ambiguous lineage and called various names such as mixed lineage leukemia, bilineal leukemia, and biphenotypic leukemia, the criteria for which have often been arbitrary. These are rare leukemias constituting 1% to 5% of all leukemias.³ The European

Group for Immunological Classification of Leukemias addressed this disorder by assigning scores for specific myeloid or lymphoid antigen expressed on blasts.⁴ The 2001 World Health Organization (WHO) classification incorporated the European Group for Immunological Classification of Leukemias scoring system when defining acute leukemias of ambiguous lineage.⁵ In 2008, the WHO classification proposed a more simple diagnostic algorithm based on fewer more specific lineage markers (*Table 1*).⁶ The new 2016 WHO revision will contain no new entities in this subgroup.⁷ The WHO recognizes two distinct categories: MPAL with the t(9;22)(q34;q11)/BCR/ABL1 and MPAL with t(v;11q;11q23)/MLL rearrangement. In those cases that have the t(9;22)(q34;q11) translocation, the breakpoint will be p210 in about two thirds of cases and p190 in the other third. Cases without these particular rearrangements are designated as MPAL NOS (not otherwise specified).⁸

The rarity of MPAL and the lack of diagnostic criteria applied in previously reported cases have made it difficult to determine whether these leukemias have distinct characteristics and which is the best therapeutic regimen for these patients. Although the putative cell of origin in MPAL is unknown, it is possible that this leukemia arises in a very early hematopoietic progenitor cell with potential to undergo either a myeloid or lymphoid differentiation or rarely B and T cell differentiation. One large reported series of MPAL (100 cases) revealed the following breakdown of cases: B⁺myeloid 58%, T⁺myeloid 38%, B⁺T 4%, B⁺T⁺myeloid 2%.⁹ In adult patients, MPAL has been characterized by relative therapeutic resistance that may be attributed in part to the high percentage of patients with adverse cytogenetic abnormalities and p-glycoprotein overexpression.^{1,9,10} Limited available data suggest that an acute lymphoblastic leukemia–like regimen followed by allogeneic stem cell

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Figure 1. (a) Peripheral blood, Wrights stain $\times 1000$; (b) bone marrow aspirate, Wrights stain $\times 1000$; (c) flow cytogram-B lymphoblasts (CD19 expression); (d) blasts expressing myeloperoxidase $\times 400$.

Table 1. MPAL lineage assignment criteria

Lineage	Criteria
Myeloid	Myeloperoxidase + (flow cytometry, immunohistochemistry, or cytochemistry) or Monocytic differentiation (at least two of the following: nonspecific esterase cytochemistry, CD11c, CD14, CD64, lysozyme)
T	Strong cytoplasmic CD3 (with antibodies to CD3 ϵ chain) or surface CD3
B	Strong CD19 with a least one of the following strongly expressed: CD79a, cytoplasmic CD22 or CD10 or Weak CD19 with at least two of the following strongly expressed: CD79a, cytoplasmic CD22 or CD10

transplant may be a first choice if a donor is available.¹⁰ Addition of a tyrosine kinase inhibitor in patients having the t(9;22) translocation has also been suggested.¹⁰ The role of immunophenotypic and genetic markers in guiding therapy as well as the utility of targeted therapies in the non-Ph1-positive MPALs is unknown at this time.

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