

## Case 251

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### History

45-year-old male with recent history of shingles on right face one month prior to presentation. Patient then noted night sweats and gum swelling. Hematologic testing at that time revealed a leukocyte count of  $50 \times 10^9/L$  with circulating blasts. At the time of the bone marrow collection, CBC data revealed the following:

#### Normal Ranges for Laboratory

|        |                             |                |
|--------|-----------------------------|----------------|
| WBC    | 69.3 $\times 10^9/L$ [H]    | ( 3.8 - 10.6)  |
| RBC    | 3.69 $\times 10^{12}/L$ [L] | ( 4.13 - 5.57) |
| Hgb    | 12.5 g/dl [L]               | ( 12.9 - 16.9) |
| Hct    | 36.6 % [L]                  | ( 38.0 - 48.8) |
| MCV    | 99.2 fL [H]                 | ( 82.6 - 97.4) |
| MCH    | 33.8 pg [H]                 | ( 27.8 - 33.4) |
| MCHC   | 34.1 gm/dL                  | ( 32.7 - 35.5) |
| RDW    | 15.4 % [H]                  | ( 11.8 - 15.2) |
| PLT    | 114 $\times 10^9/L$ [L]     | ( 156 - 369)   |
| POLYS  | 2.0 % ( 1.39) [L]           | ( 2.24 - 7.68) |
| BANDS  | 1.0 % ( 0.69)               | ( 0.10 - 0.80) |
| META   | 1.0 % ( 0.69)               |                |
| LYMPHS | 8.0 % ( 5.54) [H]           | ( 0.80 - 3.65) |
| MONOS  | 31.5 % ( 21.83) [H]         | ( 0.30 - 0.90) |
| EOS    | 1.0 % ( 0.69) [H]           | ( 0.00 - 0.40) |
| BLASTS | 55.5 % ( 38.46)             |                |

### Details

Blood smear review showed marked leukocytosis with numerous blasts and abnormal monocytic or myelomonocytic cells. (Image1) Rare cells with probable short Auer rods were also seen (not illustrated).

Bone marrow is 60% cellular with blasts (66%) and monocytic cells (17%), with a few scattered maturing myeloid forms, erythroid precursors, and occasional megakaryocytes. No prominently increased eosinophil population or abnormal eosinophilic cells with basophilic granules were noted. (Images 2 and 3).

### Immunohistochemistry and Flow Cytometry

Flow Cytometry and Cytochemistry:

Flow cytometric evaluation of bone marrow aspirate showed two prominent cell populations:

1) 41% CD34+ myeloblasts marking as follows:

CD34+, dim CD45+, CD13/33+, CD14-, CD36 (partial+), CD64+, CD117+, CD15 (partial+), HLA-DR+, CD33+, CD56-, CD13+, CD11b (partial+), partial MPO+.

2) 37% CD14+ monocytes marking as follows:

CD34-, bright CD45+, CD13/33+, CD14+, CD36+, CD64+, CD117-, CD15+, HLA-DR+, bright CD33+, CD56-, CD13 (partial+), CD11b+, probable partial MPO+.

One or both of these populations was also weakly CD4+ (61% of total events are CD3-/dim CD4+). In some scatter plots, the two populations are also not clearly distinct (i.e. form a spectrum of cells that merge together). Representative scatter plots shown in Image 4 (red = CD34+ blasts, green = monocytic / myelomonocytic cells).

Neither population stains for CD2, CD3 (surface or cytoplasmic), CD5, CD7, CD19, CD20, CD22, CD10, or TdT.

Cytochemistry staining showed reactivity of leukemic cells for alpha-naphthyl-acetate esterase, chloroacetate esterase, and myeloperoxidase. (Images 5 and 6).

## **Cytogenetic Findings**

Karyotype: 46,XY,t(6;11)(q27;q23) [20/20 metaphases]

FISH: Positive (break-apart probe) for MLL gene rearrangement. [89 / 107 cells counted]

## **Molecular Findings**

PCR positive for FLT3 internal tandem duplication.

PCR negative for FLT3 D835 mutation.

PCR negative for NPM1 mutation.

## **Interesting Features/Discussion**

This case illustrates a classic AML-M4 morphology and appears to fall within the category of AMLs with a t(6;11)(q27;q23) that involves the MLL gene locus at 11q23. Several studies (subsets of cases from larger series mostly) have indicated that these cases may form a unique subgroup with adverse clinical behavior (Cancer 2004;101:1420-7; Blood 2010;116:354-365). This subset is not currently recognized as a specific subset in 2008 WHO blue book.

## **Proposed Diagnosis**

Acute Myeloid Leukemia with t(6;11)(q27;q23).

Per 2008 WHO: Acute Myeloid Leukemia, NOS, NPM1 unmutated (AML-M4 morphology).

## **Consensus Diagnosis**

Acute myeloid leukemia with t(6;11)(q27;q23)

Per 2008 WHO: Acute myelomonocytic leukemia