CASE REPORT

Absent or Extremely Low Neutrophil Alkaline Phosphatase Activity Levels in Patients with Myelodysplastic Syndromes

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Abstract

Three patients with myelodysplastic syndrome (MDS) had absent or extremely low levels of neutrophil alkaline phosphatase (NAP) activity (arbitrarily defined as an NAP score <10). All patients showed varying degrees of hypogranulation in neutrophil morphology. The NAP activity levels transiently normalized following the administration of granulocyte colony-stimulating factor (G-CSF) in two cases. No patients experienced any severe infectious episodes. These results suggest that NAP activity is not central to the neutrophil function.

Key words: neutrophil alkaline phosphatase, myelodysplasia

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Introduction

Myelodysplastic syndrome (MDS) is a diverse group of hematopoietic disorders characterized by dysplasia, peripheral cytopenia, and the risk of progression to acute myeloid leukemia and death. Cellular dysfunction and/or cytopenia of the neutrophilic lineage contribute to infections, a known cause of morbidity and mortality in patients with MDS (1). The neutrophil alkaline phosphatase (NAP) activity level is one of the practical measurements used to evaluate the neutrophil functions. We herein report three cases with absent or extremely low levels of NAP activity.

Case Reports

Case 1

An 81-year-old man presented with a progressive anemia (Hb 8.1 g/dL). His white blood cell (WBC) and platelet counts were normal, although myelocytes (14%) were present in the peripheral blood (PB), and the NAP activity was nil (Table). The patient’s bone marrow (BM) was hypercellular with an M/E (myeloid/erythroid) ratio of 10.3. Marked hypogranulation with a pelgeroid nuclear chromatin pattern was seen in the myeloid series (Figure 1A), although blast cells accounted for only 1.6% of BM (Figure 1B). T(3;17)(q26.2;q23) and +8 chromosomal abnormalities were present, in 18 and two metaphases, respectively, out of 20 metaphases examined. The WBC count subsequently rose to 140×10^3/μL and remained elevated thereafter. However, the number of blast cells showed no increases in either the PB or BM. The predominant cell types were immature myeloid cells. Although BCR-ABL was not examined, a diagnosis of chronic myelogenous leukemia (CML) was excluded due to the cytogenetic findings. The patient was diagnosed as having myelodysplasia/myeloproliferative neoplasm (MDS/MPN) according to the revised WHO classification (2). His IPSS-R (Revised International Prognostic Score) was high (3). He has been doing well under 5-azacytidine treatment and has shown a slight improvement in red cell transfusion dependence.

Case 2

An 83-year-old man was referred to us for an evaluation of macrocytic anemia. His laboratory data were as follows: Hb: 7.2 g/dL, MCV: 105 fL, WBC: 2.8×10^3/μL, and platelets: 17.3×10^4/μL. His neutrophil count was 33% with an ex-

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Table. Clinical, Laboratory and Neutrophil Cell Surface Characteristics of Patients

<table>
<thead>
<tr>
<th>Case</th>
<th>Age &amp; Sex</th>
<th>MDS types</th>
<th>IPSS-R risk</th>
<th>NAP score</th>
<th>Flow cytometric expression (PB neutrophils)</th>
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<td>RCMD</td>
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<tr>
<td>3</td>
<td>78 F</td>
<td>RCMD</td>
<td>intermediate</td>
<td>3</td>
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</tbody>
</table>

MDS: myelodysplastic syndromes, MPN: myeloproliferative neoplasms, RCMD: refractory cytopenia with multilineage dysplasia, IPSS-R: revised international prognostic scoring system, NAP: neutrophil alkaline phosphatase, PB: peripheral blood, CD: cluster of differentiation

Figure. Photomicrographs of bone marrow smears stained with May-Giemsa. Original magnification×1,000. Profound hypogranulation and pelgeroid nuclear chromatin in the myeloid series in Case 1 (1A). The arrow indicates blast cells in Case 1 (1B). Hypogranulation in the myeloid cells (2A) and an erythroblast with megaloblastoid changes in Case 2 (arrow, 2B). Hypogranulation in both immature and mature myeloid cells (3A, 3B).

tremely low level of NAP activity (Table). Serum chemistry revealed a high erythropoietin level (728.1 mIU/mL) and normal levels of ferritin, B12, and folate. The patient’s BM was cellular with an M/E ratio of 11.77 and blast cells totaling 1.8%. The myeloid cells showed varying degrees of hypogranulation (Figure 2A). Erythroid cells were sparse, although some megaloblastoid changes were found (Figure 2B). In addition, 15% of the erythroblasts were PAS positive. Dysplastic megakaryocytic cells such as micro-megakaryocytes and cells with multiple round nuclei were seen. The results of a cytogenetic study were normal. A diagnosis of refractory cytopenia with multilineage dysplasia (RCMD) (2) and a risk categorization of a low IPSS-R (3) was made. The patient has been given occasional red cell support.

Case 3

A 78-year-old woman had pancytopenia with an Hb level
of 6.4 g/dL, a WBC count of 3.3×10^9/μL and a platelet count of 1.1×10^11/μL. The neutrophil count was 44% with an extremely low level of NAP activity (Table). Her serum erythropoietin level was 72.3 mIU/mL and her ferritin level was 809 ng/mL. Her BM was cellular with an M/E ratio of 11.7 and blast cells totaling 0.2%. Hypogranulation was seen in both immature and mature myeloid cells (Figure 3A, 3B). Some micromegakaryocytes were noted. A narrow cytogenetic study revealed trisomy 8 in all metaphases analyzed. A diagnosis of RCMD with an IPSS-R categorization of intermediate risk was made (2, 3). The patient has been given red cell and platelet transfusions.

All three patients showed an orderly expression of myeloperoxidase (MPO) as assessed with standard staining (data not shown).

Discussion

The abnormally low NAP activity levels observed in the present three cases were not due to technical errors, since the NAP activity levels remained unchanged in repeat examinations and in parallel examinations carried out at The Clinical Hematology Laboratories, Kyoto University Hospital. The control samples always yielded normal activity levels on each occasion.

The abnormal neutrophil functions present in patients with MDS reported to date include defective migration, superoxide production and microbial killing activity (4-6). The NAP activity shows no consistent pattern in MDS patients, although it is known to often be low. In fact, MDS is the only condition associated with decreased NAP scores besides CML, although the scores are not as low as those observed in CML (7). The present three MDS cases were unique in their extremely low levels of NAP activity, far lower than that observed in CML patients in the chronic phase. The NAP activity level has no significant correlation to the MPO activity level (7), as confirmed in the current report. A literature review found only two cases of MDS with extremely low NAP activity levels still retain the capacity to respond to G-CSF and show significant elevations of NAP activity.

In conclusion, MDS patients with absent or extremely low levels of NAP activity show varying degrees of hypogranular neutrophil morphology; however, such cases are not necessarily associated with frequent infectious complications.

The authors state that they have no Conflict of Interest (COI).

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References

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