Studies on Mitochondrial and Cytoplasmic Malate Dehydrogenase in Childhood Myelodysplastic Syndrome

By Hiromu Muchi and Yoshifumi Yamamoto

Three cases of uncommon childhood hematologic disorders are reported. At presentation, one patient had refractory anemia with an excess of blasts (RAEB) with partial 7-monosomy and was reclassified into RAEB “in transformation” thereafter. Another case was diagnosed as acute myelogenous leukemia with complete 7-monosomy. The other case was diagnosed as RAEB “in transformation” without chromosome aberrations. The cytogenetic studies of the patients with 7-monosomy revealed abnormal karyotypes on bone marrow cells, but normal karyotypes on peripheral blood cells. Polymorphonuclear cells from the two patients with 7-monosomy revealed reduced mitochondrial malate dehydrogenase activity, but those from the patient with RAEB “in transformation” without chromosome aberrations did not. Cytoplasmic malate dehydrogenase activity, having been defined as located on chromosome 2, was within the normal range in those three patients. The decreased mitochondrial enzyme activity in the two patients with 7-monosomy would be a dosage effect of the chromosome aberration, but not caused by their hematologic disorders. The level of mitochondrial enzyme activity in the patients with 7-monosomy was reduced in polymorphonuclear cells, but not in mononuclear cells in peripheral blood. This fact would indicate that such chromosome evolution had involved myeloid cells only, but not lymphoid cells. Both enzymes from leukemic cells of four patients with active disease showed much higher activities than controls, an expression of partially enhanced oxidative phosphorylation.

Hitherto, the definition and classification of preleukemia or hematopoietic dysplasia was still unclear. Recently, myelodysplastic syndrome (MDS) was proposed with new diagnostic criteria in association with partial modification of the definition of acute myelogenous leukemia (AML) by Bennet et al. MDS is a marrow stem cell disorder with clinically characterized hematologic abnormalities that may precede the development of AML, and which, including refractory anemia with an excess of blasts (RAEB), are rare in childhood. Cytogenetic studies in preleukemic syndrome revealed a high incidence of chromosomal aberrations, among which 8-trisomy and 7-monosomy were the most frequent expressions. Sieff et al. concluded that 7-monosomy was the diagnostic criterion of one of the relatively common myeloproliferative disorders and had a high risk of progression to AML. Patients with 7-monosomy plus a myeloproliferative disorder are classified as 7-monosomy syndrome. The genes for mitochondrial malate dehydrogenase (mMDH), which converts malate to oxaloacetate in tricarboxylic acid (TCA) cycle, are located on chromosome 7. This should be noted because the transformation of tumor cells is accompanied by altered enzyme activities and mitochondrial ultrastructure. The objectives of this article are (1) to describe the clinical and laboratory findings of three cases of MDS in childhood, (2) to determine the activities of mMDH and cytoplasmic (extramitochondrial) MDH in MDS and in other hematopoietic disorders, (3) to answer the question of whether reduced mMDH activity is a dosage effect of 7-monosomy, (4) to elucidate the relationship among the cells from the patients with 7-monosomy and mMDH, and (5) to compare the activities of mMDH and cytoplasmic MDH (cMDH) in each disorder, including leukemias.

CASE HISTORIES

Case 1

N.A., a 9-yr-old boy, was admitted in June 1979 with a 1-yr history of anemia and easy bruising. He was the only child of healthy parents. Physical examination revealed petechiae, ecchymoses, and marked hepatomegaly. The patient was anemic (hemoglobin 7.5 g/dl, RBCs 2,430 x 10^6/liter) and leukopenic (2.0 x 10^9/liter). Bone marrow was normocellular with increased immature myeloid cells, suggesting impaired maturation (20% of total nucleated cells were myeloblasts and promyelocytes). Erythroid precursor cells were hypoplastic, but lacked morphological abnormalities (Fig. 1). Myeloblasts with Auer rods were not revealed either in bone marrow aspirate or in peripheral blood. Ringed sideroblasts were not seen. The number of megakaryocytes was reduced. The patient was diagnosed as RAEB and received sequential blood transfusions. Treatment with prednisone or cytotoxic drugs was not tried. Leukemic transformation has not been observed for more than 4 yr.

Case 2

K.U., an 8-yr-old girl, had been diagnosed as having refractory anemia and had received frequent whole blood transfusions for a...
year. She was transferred because of infiltrative shadow on the right lung. Physical examination on admission revealed pallor and hepatomegaly. Bone marrow aspirate at that time was hypocellular, and immature myeloid cells were relatively increased (37%). The patient's condition rapidly progressed to overt leukemia, and she died of sepsis, without improvement, in spite of comprehensive chemotherapy with adriamycin, cytosine arabinoside, 6-mercaptopurine, and prednisone. It was concluded that the patient suffered from MDS at first, which was transformed to AML. Bone marrow CFU-c incidence was remarkably reduced. However, defective chemotaxis and random mobility were not observed.

Case 3

Y.S., an 8-yr-old girl, was admitted in August 1981 with pallor and cervical lymphadenopathy. Neither petechiae, ecchymoses, nor hepatosplenomegaly were present. Bone marrow was hypercellular and erythroid precursor cells were hyperplastic and morphologically abnormal (Fig. 3). The patient was anemic, with normal leukocyte and thrombocyte counts. Myeloblasts with Auer rods were often seen in peripheral blood (13%) and bone marrow smears. Ringed sideroblasts were not observed. The patient, classified as RAEB "in transformation," has not developed overt leukemia, and has been maintained in good condition by serial blood transfusions alone (Fig. 4). Infectious episodes have not been life threatening, as in the other two patients with 7-monomosity. The number of blasts have not increased for more than a year. Bone marrow CFU-c incidence was markedly decreased. Chemotaxis and random mobility were normal.

MATERIALS AND METHODS

Cell Preparation

Blood and bone marrow were drawn into heparinized plastic tubes from controls, from the patients with MDS, and from patients with other hematopoietic malignancies. The separation of mononuclear cells (MN) and polymorphonuclear cells (PMN) was performed using Ficoll-Hypaque centrifugation. PMN were separated from the cell pellets after sedimentation of erythrocytes with 3% dextran, followed by lysis of remaining erythrocytes in 0.83% NH₄Cl-Tris HCl (pH 7.45). These fractionated cells were sonicated with a Sonifier cell disruptor (Heat Systems-Ultrasonic Inc.) and centrifuged. Supernatant cytosol fractions were used for enzyme assays.
Chemotaxis and Random Mobility

Chemotaxis and random mobility were measured according to Boyden's method.7

mMDH Assay8

Principally, mMDH activity was measured spectrophotometrically by the increase in absorption at 340 μm due to NAD+ conversion to NADH in the presence of 1-malate. The reaction mixture consisted of 2.5 ml of 0.12 M glycine-NaOH (pH 10.0), 0.3 ml of 0.85 M 1-malate (pH 7.5), and 0.2 ml of 37.5 mM NAD+ (pH 6.5). The reaction, carried out at 28–30°C, was initiated by addition of a sample solution, i.e., enzyme-rich cytosol fraction diluted with 0.1 M potassium phosphate buffer (pH 7.4). The rate of NADH formation was followed for 10 min at 340 μm with a HITACHI 139 spectrophotometer. Specific activity was defined as the number of micromoles per milligrams of protein per minute. Protein was measured by the methods of Lowry et al.,9 crystalline bovine serum albumin being used as the standard.

cMDH Assay10

Enzyme activity was measured spectrophotometrically by the decrease in absorption at 340 μm due to NADH oxidation in the presence of oxaloacetate. Assays were carried out at 30°C, containing 2.5 ml of triethanolamine-EDTA buffer, 0.3 ml of 1.25 mM oxaloacetate, and 0.2 ml of 2.25 mM NADH. The reactions were started by the addition of enzyme-rich cytosol fraction diluted with 0.1 M potassium phosphate buffer (pH 7.4). Decreasing absorbancy at 340 μm was measured with a HITACHI 139 spectrophotometer for 10 min. Specific activity and protein were measured as previously described.

Cytogenetic Studies

Chromosomes from bone marrow cells were prepared using a modification of the method Tjio and Whang.11 Peripheral white blood cells were cultured in the presence of phytohemagglutinin (PHA), and chromosome preparations from those cultures were made after a 72-hr incubation. All metaphase preparations were stained using the trypsin-Giemsa banding technique.12,13

Case 3  Course and Blood Values

![Fig. 4. Clinical course and blood values in case 3.](image-url)
mMDH AND cMDH IN CHILDHOOD MDS

RESULTS

Clinical and Laboratory Findings (Table 1)

Hepatomegaly was present in cases 1 and 2, while lymphadenopathy was not noted in all three cases. Anemia was the noteworthy finding at presentation. Mild leukopenia with relative monocytopsis was observed in case 1, but leukocytosis was present in cases 2 and 3. Thrombocytopenia was not remarkable at presentation. Immature myeloid cells were less than 30% of nucleated bone marrow cells in cases 1 and 3, but more than 30% in case 2. Neutrophil alkaline phosphatase (NAP) was within the normal range at diagnosis, but gradually decreased in case 1. Neutrophil function was abnormal in case 1, showing defective chemotaxis and random mobility, but normal in cases 2 and 3. Recurrent infections were seen in cases 1 and 2, and led, in case 2, to septicemia followed by death. Case 1 was diagnosed as RAEB at first and reclassified into RAEB “in transformation,” case 2 as AML developed from MDS, and case 3 as RAEB “in transformation.”

Cytogenetic Studies

Cytogenetic studies of bone marrow cells in case 1 (Table 2) revealed a preponderance of abnormal karyotypes of 46, XY, r(7), (p11, q21), which would be expressed as partial 7-monosomy (Fig. 5). Lymphocyte cultures showed a normal karyotype. In case 2, complete 7-monosomy was found in bone marrow cells; most of the cells were leukemic at that time. In case 3, however, chromosome aberrations were not observed either in bone marrow cells or peripheral blood cells.

### Table 1. Laboratory Findings at Diagnosis of 3 Patients With MDS

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>RBC (10^6/cumm)</th>
<th>Hb (g/dl)</th>
<th>WBCt (/cumm)</th>
<th>Blast (%)</th>
<th>Neutro (%)</th>
<th>Lympho (%)</th>
<th>Eosino (%)</th>
<th>Baso (%)</th>
<th>Mono (%)</th>
<th>Platelet (10^4/cumm)</th>
<th>NAP (score)</th>
<th>Chromosome</th>
<th>TdT activity</th>
<th>Chemotaxis</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>9</td>
<td>Male</td>
<td>216</td>
<td>6.7</td>
<td>3,000</td>
<td>0</td>
<td>14</td>
<td>68</td>
<td>2</td>
<td>6</td>
<td>10</td>
<td>12.8</td>
<td>168</td>
<td>46,XY,r(7)</td>
<td>Not increased</td>
<td>Defective</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>Female</td>
<td>271</td>
<td>8.7</td>
<td>12,600</td>
<td>37.0</td>
<td>37.5</td>
<td>19</td>
<td>4.5</td>
<td>0.5</td>
<td>1.5</td>
<td>29.0</td>
<td>216</td>
<td>45,XX, r(7)</td>
<td>Not increased</td>
<td>Normal</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>Female</td>
<td>139</td>
<td>4.4</td>
<td>11,700</td>
<td>13</td>
<td>31</td>
<td>48</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>11.2</td>
<td>327</td>
<td>46,XX</td>
<td>Not increased</td>
<td>Normal</td>
</tr>
</tbody>
</table>

*Erythrocyte.
†Leukocyte.
‡Neutrophil alkaline phosphatase.
§Terminal deoxynucleotidyl transferase.

mMDH Assays

mMDH activities of peripheral PMN and MN from normal controls were 47.74 ± 5.82 (mean ± standard deviation) and 19.57 ± 9.57, respectively. In the two patients with 7-monosomy, the enzyme activity of their PMN was 16.84 (case 1) and 14.46 (case 2). The enzyme activity of their MN, however, was 14.68 (case 1) and 36.27 (case 2). In case 1, most MN were lymphocytes. However, in case 2, myeloblasts occupied 80%–90% of MN in peripheral blood, as her blood was examined after leukemic transformation had occurred. In case 3, mMDH activity was 55.08 in PMN and 30.77 in MN, which included not only lymphocytes but also immature myeloid cells, as seen in case 2. The enzyme activities in case 1 were measured using bone marrow cells aspirated in April 1982. Lymphocytes and erythroid precursor cells were scarce, and 29.8% of the total nucleated cells in the bone marrow were myeloblasts. This fact would indicate that mMDH activity of MN in bone marrow was an expression of immature myeloid cells in case 1. The enzyme activities of PMN and MN in the bone marrow from case 1 were 12.22 and 52.38, respectively (Table 3). Leukemic cells from three patients with acute leukemia and a patient with chronic myelogenous leukemia in lymphoid crisis revealed extremely high values of the enzyme activity levels (Table 4).

cMDH Assay (Table 5)

cMDH activities of PMN and MN from controls were 48.28 ± 13.97 and 293.05 ± 58.41, respectively. The enzyme activity of PMN was 52.26 in case 1 and 51.48 in case 3, and that of MN was 241.92 and 238.32, respectively. In a patient with acute lympho-
cytic leukemia (S.W.), the enzyme activity of leukemic cells was 382.98.

DISCUSSION

There is considerable confusion regarding the classification of a variety of hematologic disorders. The classification has been employed to bridge the gap between overt AML and less acute syndromes initially characterized by varying manifestations of inadequate maturation of marrow elements. Preleukemia syndrome and hemopoietic dysplasia were expedient terms used to categorize less characterized disorders. Most of the patients with "preleukemia syndrome" were male and 50 yr of age or older when their hematologic abnormalities began. Keihauser reported that preleukemia occurrence in childhood was extremely rare and that clinical features in childhood were almost the same as those in adults. The clinical courses and laboratory findings of these three patients were compatible with those of the patients in previous reports. In this study, the term myelodysplastic syndrome (MDS) was selected to describe the clinical courses of these three patients. However, it is difficult to connect expedient terms commonly used with the recently modified classification for MDS, because in the article by Bennet et al. there was no description corresponding to the preleukemia syndrome. Case 1, who had anemia, thrombocytopenia, and 20% blasts in bone marrow aspirate at presentation, was classified into RAEB and thereafter was reclassified into RAEB "in transformation," as blasts exceeded 5% in peripheral blood. Cytogenetic studies of bone marrow cells revealed partial 7-monosomy. Case 2, who had suffered from refractory anemia for a year and then developed overt leukemia and died, was diagnosed as AML with complete 7-monosomy. In case 3, myeloblasts in bone marrow as well as in peripheral blood ranged from 10%–30%, and Auer rods were often seen. The patient was classified into RAEB "in transformation" without any chromosome aberrations.

At the First International Workshop on Chromosomes in Leukemia in Helsinki, Finland, it was shown that the group of patients with AML and monosomy-7 had a distinctly increased susceptibility to bacterial infections, as compared with other patients with similar diseases. Recently, Gahmberg et al. reported that in two patients with 7-monosomy syndrome and a patient with deletion of the distal half of the long arm of chromosome 7, granulocyte chemotaxis was reduced, and the major labeled surface glycoprotein (GP 130) of normal human blood cells was markedly reduced. Chemotactic ability and random mobility of neutrophils were markedly decreased in case 1, but they were within the normal range in case 2 with complete 7-monosomy. This fact suggested that 7-monosomy or deletion of the long arm would relate to the impaired function of granulocytes, but other factors would contribute. Infectious episodes in "preleukemia syndrome" were not uncommon.

Previous studies by Benn et al. indicated that the genes for mMDH were located on the region pter–q22 of chromosome 7. The relationship of chromosome aberration and certain enzymes has been established by trisomy-21 and superoxide dismutase, i.e., excess enzyme activity in trisomy-21. The fact was expressed as dosage effect. The activities of mMDH were reduced in PMN from the patients with 7-monosomy, but not reduced in PMN from a patient without any chromosome aberrations. The activities of two other leukocyte enzymes, adenosine deaminase and purine nucleoside phosphorylase, which have been

<table>
<thead>
<tr>
<th>Source</th>
<th>Method</th>
<th>Number of Cells Analyzed</th>
<th>Results</th>
<th>Number of Cells Identified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral blood</td>
<td>+ PHA 72 hr culture</td>
<td>20</td>
<td>46XY</td>
<td>20</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>Direct</td>
<td>30</td>
<td>46XY</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>46,XY,r(7)(P11q21?)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4;4n with ring</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>without ring</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 5. Karyotype of bone marrow metaphased with 7-monosomy in case 1.
The activities of cMDH were determined also. It has been reported that the decreased mMDH activity in the patients with 7-monosomy is related to the chromosome aberration. In contrast, cMDH activities were quite similar in normal subjects, two patients with 7-monosomy, a patient with RAEB “in transformation” without any chromosome aberrations, and a patient with acute lymphocytic leukemia (ALL). It has been determined that the gene for cMDH is located on chromosome 2.20 It appears that cMDH was not involved either with MDS or 7-monosomy.

The activities of mMDH and cMDH of leukemic cells revealed much higher values than controls. De Bersaques et al.21 reported that mMDH activity was generally increased in human epidermoid tumors. Adenosine triphosphate (ATP) is derived from respiration-linked oxidative phosphorylation in most tumor cells. Therefore, a substitute respiratory substrate is necessary to fuel tumor cells by oxidative phosphorylation. It is proposed by Laviates et al.22 that glucose is replaced by glutamate as the major respiratory precursor. An abbreviated, but efficient, TCA cycle results from this substitution. Cederbaum and Rubin23 measured several enzyme activities of the TCA cycle in a series of rat hepatomas and found elevated CO2 production from a-ketoglutarate, succinate, and malate, whereas oxidative decarboxilation of acetate did not increase concurrently. These findings may suggest that the elevated mMDH activity in those cells is an expression of at least partially enhanced oxidative.

### Table 3. Mitochondrial Malate Dehydrogenase Activity in 3 Patients With MDS

<table>
<thead>
<tr>
<th>Patient</th>
<th>Chromosome Karyotype</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Sample</th>
<th>mMDH (μM/mg prot/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N.A.</td>
<td>7-Monosomy</td>
<td>11</td>
<td>Male</td>
<td>PB</td>
<td>16.84</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PMN</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BM</td>
<td>14.68</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MN</td>
<td>12.22</td>
</tr>
<tr>
<td>K.U.</td>
<td>7-Monosomy</td>
<td>8</td>
<td>Female</td>
<td>PB</td>
<td>14.46</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PMN</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BM</td>
<td>52.38</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>MN</td>
<td>36.27</td>
</tr>
<tr>
<td>Y.S.</td>
<td>Normal (46XX)</td>
<td>8</td>
<td>Female</td>
<td>PB</td>
<td>55.08</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PMN</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BM</td>
<td>30.77</td>
</tr>
</tbody>
</table>

Normal control (mean ± standard deviation): PMN — 47.4 ± 5.84; MN — 19.51 ± 9.47.

PB, peripheral blood; BM, bone marrow; PMN, polymorphonuclear cells; MN, mononuclear cells.

The activity of mMDH in PMN in patients with 7-monosomy was absolutely reduced, but not in MN in peripheral blood. It is said that hemopoiesis is regulated by a variety of factors determining proliferation, differentiation, amplification, and maturation of stem cells and their committed progenies. Sequential changes of their characteristics on surface markers in myeloid cells were studied following their differentiation from precursor cells to neutrophils. The fact that cytogenetic studies of bone marrow cells in case 1 revealed 7-monosomy, in spite of a normal karyotype in peripheral blood cells, would suggest that such chromosome aberration occurred on myeloid precursor cells but not lymphoid cells. Our results regarding mMDH activities in the patients with 7-monosomy would confirm that the chromosome aberration had involved only myeloid precursor cells. Moderate elevation of the activities of mMDH in MN in cases 2 and 3 was caused by contamination of immature myeloid cells. Myeloid precursor cells expressed relatively higher activities of mMDH than mature neutrophils in case 1.

### Table 4. Mitochondrial Malate Dehydrogenase Activity in 4 Leukemic Patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Chromosome Karyotype</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Sample</th>
<th>mMDH Activity (μM/mg prot/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T.Y.</td>
<td>CML, lymphoid crisis</td>
<td>Ph1 positive</td>
<td>11</td>
<td>Female</td>
<td>BM*</td>
<td>122.05</td>
</tr>
<tr>
<td>S.W.</td>
<td>Non-T, non-B ALL</td>
<td>Normal</td>
<td>8</td>
<td>Male</td>
<td>BM*</td>
<td>195.06</td>
</tr>
<tr>
<td>Y.S.</td>
<td>AML (M2)</td>
<td>8–21 translocation</td>
<td>14</td>
<td>Male</td>
<td>BM*</td>
<td>190.48</td>
</tr>
<tr>
<td>M.H.</td>
<td>T-All</td>
<td>Normal</td>
<td>8</td>
<td>Female</td>
<td>PB*</td>
<td>250.00</td>
</tr>
</tbody>
</table>

Normal control (mean ± standard deviation): PMN — 47.4 ± 5.82; MN — 19.51 ± 9.47.

CML, chronic myelogenous leukemia.

*Leukemic cells.
phosphorylation accompanying malignant transformation.

CONCLUSION

Three cases of MDS in childhood were reported. One was RAEB at presentation with parital 7-monosomy and was reclassified as RAEB “in transformation” thereafter. Another was AML with complete 7-monosomy, who had suffered from refractory anemia for a year. The last was RAEB “in transformation” without chromosome aberrations. Reduced mMDH activity in PMN from patients with 7-monosomy would be a dosage effect of the abnormal karyotype. The fact that, in case 1, PMN had reduced mMDH activity but MN in peripheral blood did not confirm that chromosome aberration occurred only in myeloid precursor cells. Cytoplasmic enzymes do not take a part either in 7-monosomy or in MDS. The fact that cMDH and mMDH from leukemic patients revealed much higher levels than those from controls would be an expression of partially enhanced oxidative phosphorylation.

REFERENCES


Table 5. Cytoplasmic Malate Dehydrogenase Activity in Patients With MDS and a Patient With ALL

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Chromosome Karyotype</th>
<th>Sex</th>
<th>Sample</th>
<th>c MDH Activity (µM/mg prot/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N.A.</td>
<td>RAEB in transformation</td>
<td>46, XY, r (7)</td>
<td>M</td>
<td>PMN</td>
<td>52.26</td>
</tr>
<tr>
<td>Y.S.</td>
<td>RAEB in transformation</td>
<td>46, XX</td>
<td>F</td>
<td>PMN</td>
<td>51.48</td>
</tr>
<tr>
<td>S.W.</td>
<td>Non-T, non-B ALL</td>
<td>46, XY</td>
<td>M</td>
<td>Leukemic cells</td>
<td>382.98</td>
</tr>
</tbody>
</table>

Normal control (mean ± standard deviation): PMN — 48.28 ± 13.97; MN — 293.05 ± 58.41.
Studies on mitochondrial and cytoplasmic malate dehydrogenase in childhood myelodysplastic syndrome

H Muchi and Y Yamamoto