Transient Leukemia in a Case of Mosaic Trisomy 21

Chein-Wei Line, Ying-Yao Chen, Shu-Ming Lin, Pao-Chin Chiou, Kai-Sheng Hsieh, Hung-Bo Wu*

The incidence of leukemia in Down syndrome is 10 to 20 folds higher than that in the general population. If the leukemia occurs in a newborn, 30% to 50% are transient leukemia and will spontaneously go into remission. We describe here a female neonate who presented with an elevated white blood cell counts, associated with a high percentage of blast cells. A cytochemical stain of the bone marrow revealed properties of acute myeloblastic leukemia, which is rare in childhood. Although the baby had a nearly normal phenotype, chromosome analysis revealed constitutional mosaicism for trisomy 21. Supportive management was given without use of chemotherapeutic agents. Complete remission occurred within 2 months.

Key words: transient leukemia, mosaic trisomy 21, congenital leukemia

Leukemia is very rare in a neonate. If it does occur in a newborn, it is usually associated with trisomy 21. Thirty to fifty percent of these leukemias are transient. Although the clinical course is generally transient and benign, it may also be a preleukemic disorder and need regular follow up. Identification of transient leukemia (TL) and differentiating it from congenital leukemia can prevent unnecessary chemotherapy.

Case Report

A female neonate was born by vaginal delivery to a gravida 2 para 2 mother after 36 weeks of gestation. The mother had been healthy in the past. During this pregnancy, she suffered from pregnancy-associated hypertension. This baby had a healthy 4 year-old brother. The patient was transferred to our hospital due to tachypnea and abdominal distension at 2 days of age. The initial physical examination findings were pulse 130-140 per minute, respiratory rate 60-70 per minute, and blood pressure was 65/45 mmHg. Her body weight, body height and head circumference were appropriate for gestational age. Facial features showed a mildly depressed nose and normally formed and placed ears. No epicanthal fold was noted. No lymph node enlargement was seen. She had a grade 2/6 pansystolic murmur over the pulmonic area. The cardiac echo revealed a patent ductus arteriosus about 0.3 cm in diameter. The abdomen was distended and the liver and spleen were palpable at 5 cm below the costal margin. Her four limbs were freely moveable. She had normal palmar creases and no clinodactyly. Skin examination revealed erythematous patches over the trunk. The initial blood cell count was white blood cells $154 \times 10^3/\mu L$ with 97% blast cells, hemoglobin 9.5 gm/dL and platelets $82 \times 10^3/\mu L$. Biochemical examination documented an elevated lactate dehydrogenase (LDH) level of 3663U/L, normal uric acid level of 5.8 mg/dL and normal levels of electrolytes and liver enzymes. A cytochemical stain of a bone marrow aspiration revealed properties of acute monocytic leukemia (M5). Cytogenetic analysis revealed mosaicism of trisomy 21 (mos 47, XX, + 21 [7] / 46, XX [33]). Except for the tachypnea and hepatosplenomegaly, the patient was well, had good activity and good feeding tolerance. No cell lysis crisis or leukostasis were noted during the hospital course. The white cell count gradually normalized by 2 months (table). We followed this patient periodically. A repeat cytogenetic analysis was done at 5 months and trisomy 21 cells were still present in her peripheral blood (mos 47, XX, + 21 [9] / 46, XX [31]). When she was 14 months old, her body weight, body height and head circumference were in the normal range. Her face showed no obvious stigma of Down syndrome except for a mildly depressed nose. She walked well and had appropriate psychosocial development for her age.

Discussion

Down syndrome is the most common autosomal chromosomal abnormality in liveborn infants. The average incidence of leukemia is 1/150, which is 10-20 fold higher than in the general population. The peak ages of onset are bimodal and include the newborn stage and the period from 3 to 6 years old [1,3]. If it occurs in the new...
mon in TL (50% vs 1%) [14,15]. A skin biopsy can make this more common in congenital leukemia and less common in TL [12,13].

It is referred to blue nodules, referred to as “blueberry muffin”. It is abnormal myelopoiesis, pseudoleukemia and ineffective regulation of granulopoiesis. Trisomy 21 acts as an important predisposing factor in the genesis of transient leukemia [5].

When marked leukocytosis is documented in a newborn, congenital leukemia, TL and sepsis with leukemoid reaction should be considered. Examinations for sepsis can exclude the leukemoid reaction. The clinical course, cytogenetic analysis, pathology and cell cultures help clinicians distinguish congenital leukemia from TL [2,6-17].

Compared to the fatal form of congenital leukemia, TL has a relatively benign clinical course with the possibility of complete and spontaneous resolution. Using the French-American-British (FAB) classification, congenital leukemia may be considered acute myelomonocytic leukemia (M4) or acute monocytic leukemia (M5) dominant. But TL is usually erythroleukemia (M6) or acute megakaryoblastic leukemia (M7) dominant [12-17]. Cytogenetic analysis revealed that the leukemic cells in mosaic trisomy 21 patients have a higher rate of spontaneous remission and the decrease in blast cells parallels the decrease of trisomy 21 cells in the peripheral blood and bone marrow [13]. Patients with constitutional trisomy 21, trisomy 21 with other abnormalities or hyperdiploidy have a higher rate of acute leukemia [10,11]. Normal colony formation in bone marrow cell cultures favors TL while an abnormal pattern of colonies favors congenital leukemia [6-9]. Clinical manifestations of TL are petechiae, purpura and hepatosplenomegaly. Lymphadenopathy is not a frequent finding [13]. Leukemic cutis is leukemic clusters which infiltrate the skin and appear as red to blue nodules, referred to as “blueberry muffin”. It is more common in congenital leukemia and less common in TL (50% vs 1%) [14,15]. A skin biopsy can make a definite diagnosis. We found only two cases reports of TL patients manifesting leukemic cutis [15].

Although TL has a characteristic spontaneous remission, it may also be a preleukemic disorder. Follow-up of 85 patients who were initially diagnosed with TL, showed that 33% developed a subsequent hematologic disorder, most often acute nonlymphocytic leukemia, at 0.5 to 3 years of age with a median of 16 months [2,9]. Because of this, we will follow our case monthly until she is 3 to 5 years old.

Since TL may occur in mosaic trisomy 21 infants who have no stigma of Down syndrome [12], we would like to emphasize the necessity of chromosome analysis in every newborn with a leukemic disorder. It is then possible to predict the natural course and prevent unnecessary chemotherapy. On the other hand, although TL may resolve spontaneously, one series review showed that 11% of patients with TL die within the first few months due to sepsis, congestive heart failure, hyperviscosity syndrome and disseminated intravascular coagulopathy [2]. We still have to be alert to these possible complications.

### References

9. Liang DC, Ma SW, Lu TH, Lin ST. Transient myeloproliferative disorder and acute myeloid leukemia—study of six neonatal cases with long term fol-

### Table The blood series normalized completely at 65 days of life

<table>
<thead>
<tr>
<th>Age</th>
<th>2 days</th>
<th>7 days</th>
<th>14 days</th>
<th>30 days-40 days</th>
<th>65 days</th>
<th>343 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (x10^9/L)</td>
<td>154</td>
<td>81.7</td>
<td>59.3</td>
<td>8.1</td>
<td>4.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Blast cells %</td>
<td>97%</td>
<td>97%</td>
<td>90%</td>
<td>78%</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Hb(g/dL)</td>
<td>9.5</td>
<td>8.7</td>
<td>7.1</td>
<td>9.6</td>
<td>5.7</td>
<td>11.1</td>
</tr>
<tr>
<td>Platelets (x10^9/L)</td>
<td>82</td>
<td>17</td>
<td>40</td>
<td>22</td>
<td>28</td>
<td>357</td>
</tr>
</tbody>
</table>

*Packed red blood cells were transfused at 40 days due to obvious anemia.

**Clinical Neonatology 1998 Vol.5 No.2**


