A Case of Juvenile Chronic Myelogenous Leukemia Presented as Recurrent Erythema Nodosum-like lesions

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We report a case of chronic myelogenous leukemia in a 2-year-old boy which was manifested as recurrent erythema nodosum-like lesions during his illness. He presented with recurrent erythema nodosum-like lesions involving both legs, and some lesions were followed by cellulitis-like swelling. He had 3 episodes of leg swelling accompanied by high fever, and the erythema nodosum- and cellulitis-like lesions subsided with antibiotic therapies, but recurred. After his transfer to the pediatric department, he was initially diagnosed as having tuberculosis and was treated with anti-tuberculosis medication. However, subsequent peripheral blood examination showed an increase of immature granulocytic cells and monocytes, and bone marrow aspiration revealed increased myeloid blasts.


Keywords: Juvenile chronic myelogenous leukemia, Erythema nodosum-like lesions

Juvenile chronic myelogenous leukemia (JCML) is a rare fatal myeloproliferative disorder of childhood. It differs from adult CML due to its fetal red cell characteristics and poor prognosis. It represents about 2% of leukemia in children. It has no specific type of chromosome aberration. Effective regimens of chemotherapy have not been established.

Eczematous rashes, erythematous maculopapules, and indurated lesions are reported as skin lesions of JCML. Xanthomas and neurofibromatosis can also be associated with JCML.

The association of erythema nodosum with leukemia has rarely been reported. We report a case of JCML in a 2-year-old boy which was manifested as recurrent erythema nodosum- and cellulitis-like lesions.

REPORT OF A CASE

In February, 1995, a 2-year-old boy presented with fever and erythematous swelling of the right foot. He had 3 episodes of leg swelling accompanied by high fever, which subsided with antibiotic therapies at other hospitals. The swelling of the right foot was aggravated by acupuncture. He had night sweating, arthralgia, cough, and rhinorrhea. The physical examination on admission showed a temperature of 38.4°C. There was no lymph node swelling. However, his liver was 2-finger-breadth palpable and his spleen was 1cm palpable. He had an ill-defined child palm-sized erythematous swelling with tenderness on his right foot (Fig. 1), and well defined pea-to-bean sized erythematous dermal nodules on his left leg (Fig. 2) and face. His leukocyte count was 22800/mm³ with prominent monocytosis (19%). Platelet count was 167,000/ mm³. The hemoglobin value was 10.5 gm/dl. The C-reactive protein was elevated. Other laboratory data showed normal levels of liver function test, blood urea nitrogen, serum creatinine, electrolyte, immunoglobulin G/A/M, and

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complement. The urinalysis and chest X-ray were within normal limits. A tuberculin mantoux test caused a 11 mm induration in the skin.

He was managed with intravenous antibiotics for 5 days. The erythematous nodules and cellulitis-like lesions resolved with antibiotic therapy. High fever and skin lesions recurred 6 days after he was discharged. An initial peripheral blood smear (PBS) showed no specific abnormalities. In the pediatric department, he was initially treated for tuberculosis. However, a skin biopsy revealed atypical infiltration of monocytes (Fig. 3) stained positively with MAC 387 (Fig. 4), a subsequent peripheral PBS showed an increase of immature granulocytic cells and monocytes, and a bone marrow examination revealed increased myeloid
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blasts (Fig. 5). The leukocyte alkaline phosphatase (LAP) score was decreased and the fetal hemoglobin level was 50.8%. Chromosomal study of the marrow showed a 46 XY karyotype with no Philadelphia chromosome. Following a diagnosis of JCML, he was treated by chemotherapy composed of Ara-C, VP-16, and vincristine.

DISCUSSION

Two types of CML occur in children: juvenile and adult. Although both forms present with an increased number of differentiating myeloid cells in the blood, increased serum vitamin B12 level, and decreased Leukocyte Alkaline Phosphatase (LAP) activity1, many features differentiate the two. In the juvenile form, leukemic cells may have variable chromosomal aneuploidy, but the Ph1 chromosome is never found3.

The patients of JCML usually have a history of an eczematoid rash, lymphadenopathy, and recurrent bacterial infections3. By the time of diagnosis they have usually developed pallor, purpura, and moderate enlargement of both liver and spleen. The consistent laboratory findings are anemia, thrombocytopenia, an increased white blood cell count, and normoblastemia. There may be a striking monocytosis. The bone marrow is usually cellular, with fewer megakaryocytes and erythroid cells than are found in the adult form. The LAP may be either normal or reduced and is not a pathognomonic feature. The proportion of fetal hemoglobin ranges from 30 to 70%, and other characteristics of fetal erythropoiesis occur, such as Hb A2 level. In our patient, the diagnosis of JCML was made by bone marrow examination, increased fetal hemoglobin level4, and a normal cytogenetic pattern.

The neoplastic cells of JCML range from cells with irregular nuclei possessing nuclear grooves to large blastic cells with round to lobulated nuclei and prominent nucleoli. They show positive staining for acid phosphatase and nonspecific esterase. One study reported that the neoplastic cells of JCML exhibit the immunophenotype positive S-100 protein and share features with dendritic cells. Although neoplastic cells stained positively with S-100 protein are not required for diagnosis, JCML was proposed to be a histiocytic malignancy in which S-100 protein is a useful marker5. However, our case showed a positive MAC 387 stain in the skin, while the S-100 stained negative. Therefore, the infiltrated neoplastic cells of our case were monocytic cells rather than dendritic cells.

Erythema nodosum associated with leukemia is rare. Erythema nodosum-like lesions found in various kinds of leukemia are clinically compatible with erythema nodosum, but histologically not consistent with erythema nodosum in some cases. In our case, the histologic findings of dense atypical infiltration of monocytic cells in the dermis was not consistent with erythema nodosum. Why the leukemic cells are present in the erythema nodosum-like lesions is conjectural. One explanation is that the lesions are an expression of an inflammatory reaction rather than a granulocytic sarcoma. The neoplastic cell may be the stimulus or may play an role of the inflammatory cell to some other unknown stimulus. A second explanation is that the erythema nodosum-like lesions are hypersensitive expressions of the skin that are precipitated by the leukemic cell acting as a foreign antigen6. Recurrences of erythema nodosum-like lesions and fever in leukemia have been rarely reported7. Moreover, such recurrences occur spontaneously or following chemotherapies. Our patient presented with fever and recurrent erythema nodosum-like lesions accompanied by cellulitis-like swelling in some lesions which subsided rapidly after antibiotic therapies alone. The reason for the recurrence of the lesions is not well defined. To our knowledge, only three cases of leukemia cutis associated with JCML have been published8, and the combination of erythema nodosum-like lesions and JCML has not been described.

Treatment for JCML is totally unsatisfactory; most children surviving less than 1 year from diagnosis regardless of radiotherapy or chemotherapy9. Median survival is about 6 months. The most encouraging results in both forms of CML have been obtained recently by allogenic bone marrow transplantation, which is the only treatment capable of eradicating the leukemic clone10.

REFERENCES