

A CLINICAL AND ULTRASTRUCTURAL STUDY OF ACUTE EOSINOPHILIC LEUKEMIA

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The present study analyses two cases with acute immature eosinophilic leukemia. The clinical, physical, laboratory and pathologic materials are discussed. There is an abnormal number of immature eosinophilic cells in the blood and bone marrow, usually accompanied by anemia and thrombocytopenia. Especially the ultrastructural features include abnormal granules, asynchronous maturation of the nucleus and cytoplasm, dilated endoplasmic reticulum and more conspicuous nucleoli. Differential count was more precise under electron microscope than under light microscope. These findings may be helpful for differential diagnosis and classification.

Key words: Acute immature eosinophilic leukemia, Ultrastructural feature.

Acute eosinophilic leukemia is rare and it can be classified morphologically into three categories: blastic, immature and mature. Marked eosinophilia with blastic, immature and mature cells above normal in the bone marrow and peripheral blood existed during the course of the illness.^{1,3} In the present paper two cases of acute eosinophilic leukemia are reported. Their clinical and ultrastructural features are discussed.

CLINICAL DATA

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Case I

A 41-year-old man was admitted in February 1986 for low fever, progressive weight loss, lump in the cervical and right lower quadrant, occult pain in the epigastrium for about two months. He was operated on for laparotomy in a local hospital and multiple lymphadenopathies were found in abdomen. Biopsy showed many little abscesses and giant cell hyperplasia. Physical examination showed a temperature of 37.5 °C, enlarged tonsil of degree 2. Cervical, axillary, and inguinal lymph nodes were present with individual node measuring up to 4 cm in diameter. The liver and spleen were palpable 3 and 4 cm below the respective costal margins. A 3×3 cm mass was found in the right lower quadrant. Hemoglobin 90 g/L; platelets 30×10⁹/L; white blood cells 6×10⁹/L with 75%–90% eosinophilic granulocytes. Many of them were mature eosinophils. The bone marrow aspiration showed hypercellularity with decrease in erythroid series and megakaryocytes. Differential count was myeloblasts 5%, myelocytes 35%, eosinophilic granulocytes 57% (promyelocytes 3%, myelocytes and metamyelocytes 24%, bands and segmentocytes 30%), lymphocytes 3%. Under the electron microscope, 100 eosinophilic granulocytes of bone marrow smear were counted, and there were 78% of myelocytes and metamyelocytes. It was 36% more than that found under light microscope. In others, certain morphologic features were described as the characteristics of leukemic eosinophilia. These include mixed baso-eosinophilic granules and vacuoles of the

cytoplasm etc. Biopsy of cervical lymph node revealed infiltration by a number of immature eosinophilic cells.

Therefore, he was diagnosed with acute immature eosinophilic leukemia. The patient was given prednisone 45 mg per day. The condition gradually improved. The temperature was normal and lymph node decreased. After two weeks he soon became progressively ill. Chemotherapy of harringtonine, vincristine, cytarabine and prednisone (HOAP) was not effective. He died of oliguria, renal failure and bloody ascites.

Case II

A 27-year-old man was admitted in May 1993 for dizziness, weakness lasting about one month and recently accompanied by fever, gingival hemorrhage. Bone marrow aspiration was considered acute eosinophilic leukemia in a local hospital. Physical examination revealed that he was acutely ill with a temperature of 39 °C, pallor, skin sporadic petechial hemorrhage, bleeding from gingiva, and sternal tenderness. The liver was not palpable. The spleen was palpable one fingerbreadth at the left costal margin. Eye ground examination revealed hemorrhage. Hemoglobin 40 g/L, platelets $70 \times 10^9/L$, white blood cells $3.3 \times 10^9/L$ with differential count of myeloblasts 30%, eosinophilic granulocytes 16% (promyelocytes 8%, myelocytes 1% bands 1% and segmentocytes 6%), lymphocytes 54%, 1 normoblast/100 white blood cells. The bone marrow aspiration showed hypercellularity with decrease in erythroid series and megakaryocytes. Differential count was myeloblasts 5%, promyelocytes 3.5%, neutrophilic granulocytes 7%, eosinophilic granulocytes 79.5% (myelocytes 33.5%, metamyelocytes 15.5%, bands 17% and segmentocytes 13.5%), lymphocytes 4.5%. Also were found Auer's bodies in myeloblasts, mixed baso-eosinophilic granules and vacuoles in cytoplasm. Erythrocyte sedimentation rate was 174 mm/h. Glutamic pyruvic transaminase was 91U. Serum lactate dehydrogenase was 1181 IU/L. A chromosomal analysis of the bone marrow cells was hypodiploidy. Chest roentgenogram revealed calcification in the bilateral hilar and right upper lobe. Ultrasound examination showed mild hepatomegaly and splenomegaly. EKG was normal. The diagnosis was acute immature eosinophilic leukemia. The patient was given daunorubicin, cytarabine (DA) and BCNU+VP16 regimens but ineffective. After treatment with

aclarubicin he obtained partial remission. Blood differential count was promyelocytes 2%, neutrophilic granulocytes 41%, eosinophilic segmentocytes 1% and lymphocytes 56%. Bone marrow aspiration showed myeloblasts 7%, promyelocytes 4%, neutrophilic granulocytes 5.5%, eosinophilic granulocytes 9.5% (myelocytes and metamyelocytes 6%, segmentocytes 3.5%), lymphocytes 9% and erythroid series 65%. Soon after, he got fever again. Staphylococcus grew in the culture of urine. Chest x-ray revealed larger patchy density in right upper lobe. He became progressively ill and died on 30 October 1993.

RESULTS

The Common Ultrastructural Findings

The granules were abnormal. There were mixed baso-eosinophilic granules in most immature and mature cells. The basophilic granules were primary granules. They were larger than those of neutrophilic primary granules. The eosinophilic granules presented some heterogeneity in size, shape and number of crystalloid internum. About 7–12 crystalloid sticks arranged regularly or disorderly (Figure 1). A few granules revealed vacuolar degeneration. Moreover uneven distribution of granules was present. Some cells depicted sparse granules. For example, only three granules were found in one eosinophilic myelocyte.

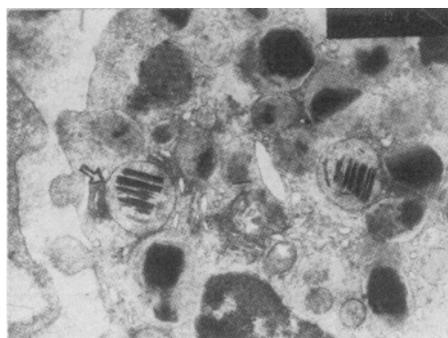


Fig. 1. There were 7–12 crystalloid sticks arranged regularly or disorderly $\times 15000$.

The maturation of the nucleus and cytoplasm became asynchronous. The development of the cyto-

plasm fell behind the nucleus. Although the nucleus of the cell appeared matured, not many of granules had formed crystalloids (Figure 2). In others the development of the fell behind the cytoplasm and the nuclear features resembled those of the promyelocyte, in which nucleus with euchromatine and relatively large nucleolus were present, but there were crystalloid granules already in the cytoplasm (Figure 3).

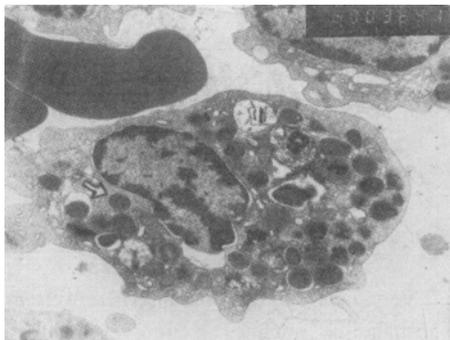


Fig. 2. There were more eosinophilic primary granules in the cytoplasm of eosinophilic metamyelocyte $\times 6000$.

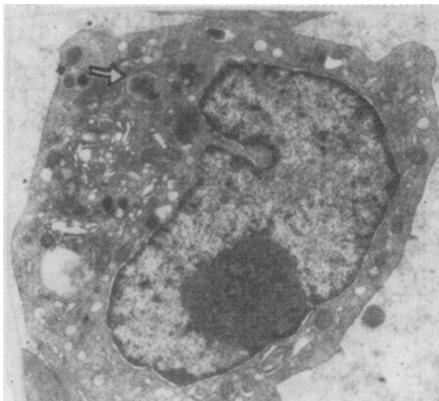


Fig. 3. The nucleus liked eosinophilic promyelocyte. large nucleolus was present. But there were crystalloid granules in the cytoplasm $\times 6000$.

Differential count was more precise under electron microscope than under light microscope. Many immature eosinophils were found under electron microscope in case 1. According to the finding, the

diagnosis of immature type of eosinophilic leukemia was made.

There were various shapes of endoplasmic reticulum. It dilated like cyst, bleb and cistern. Nucleoli presented mostly in eosinophilic myelocytes and metamyelocytes, sometimes were found in segmentocytes. Nuclear hypersegmentation was found in mature cells.

Therefore, it is possible that ultrastructural features showed a particularly helpful adjunct for differential diagnosis of benign or neoplastic eosinophilia and classification of type.

DISCUSSION

In patients with excessive numbers of immature eosinophils and myeloblasts, the diagnosis of leukemia can be made without difficulty. In others, especially in those with predominately mature eosinophils, the differential diagnosis of hypereosinophilic syndrome may be difficult.^{4,5} In our cases, we noted the clinical, morphologic and pathologic features. The patients presented with fever, fatigue, weakness, weightless, lassitude, bleeding and purpura. On physical examination hepato-splenomegaly, lymphadenopathy, bone tenderness, and tumor in the right lower quadrant were found. These were described as marked persistent eosinophilia usually accompanied by anemia and thrombocytopenia. Besides Auer's bodies, abnormal chromosome, eosinophilic infiltration of lymph node were found. Ultrastructural study showed: excessive numbers of immature eosinophils existed. The granules were abnormal; the maturation of nucleus and cytoplasm became asynchronous;^{6,7} hypersegmentation, dilated endoplasmic reticulum and more conspicuous nucleoli presented. The patients were unresponsive to chemotherapy. They died within 6–12 months. These findings suggested the diagnosis of acute immature eosinophilic leukemia. In case 2, the myeloblasts in peripheral blood were more numerous than those in bone marrow. According to the differential count of bone marrow, immature type can be considered. But how to explain such more myeloblasts in peripheral blood? The possibility is that the hemopoietic islands may be of various degree of myeloidosis.

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