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CASE REPORT

A Case of Acute Mixed Cell Leukemia Resembling AML1-ETO Positive Acute Myeloid Leukemia

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SUMMARY

Background: **The aim of the study was to improve the understanding of complex karyotype acute mixed cell leukemia containing pseudo Chediak-Higashi granules.**
Methods: **A case of acute mixed cell leukemia resembling AML1-ETO positive acute myeloid leukemia was reported. The results of morphological, immunophenotypic, and cytogenetic tests were analyzed by reviewing relevant literature.**
Results: **The patient was a young boy with clinical manifestations of recurrent fever. Bone marrow smear: Granulocyte system hyperplasia is obvious, visible at each stage, primitive cells account for 12%. These cells are large in volume, mostly round or class round, with abundant cell mass, stained gray blue, unbalanced development of some nuclear plasma, abnormal cytoplasmic staining, and visible "sunrise red" -like changes. Typical Auer bodies, pseudo Chadiak-Higashi granules and phagocytic erythroid substances were observed. The nuclei are irregular in shape, distorted and depressed, with fine chromatin and prominent large nucleoli. Bone marrow was extracted 3 days later, the bone marrow smear showed 65% primitive cells. The morphology of primitive cells was similar to that of 3 days ago. The results of flow cytometry showed that the primary/naive T cells in the samples possessed nuclear cells. Flow cytometry showed two groups of abnormal cells. One group accounted for 3.87% of nuclear cells and was a primitive/naive T-cell phenotype, mainly expressing: CD34+, CD7+, CD5+, CD2dim+, MPO-, CCD3 + part, CD3-, CD4-, CD8 -, CD117 -, CD13-, CD33-, HLA - DR -, CD10-, CD11b-, CD56-. The other group which accounted for 79.8% of the nuclear cells was monocyte phenotype, mainly expressing: CD34-, CD117-, CD13+ small amount, CD33+, HLA-DR-, CD11b+, CD14+, CD15+, CD36+, CD56+, CD64+, CD4+, CD85J+, CD85K + part. It matched the immunophenotype of acute mixed cell leukemia (T/MMPAL). Immunophenotypic leukemia-related fusion genes were negative, and karyotype analysis results were 45, XY, T (11; 12)(p13; Q13), -12-17, + mar [12]/90 < n > 4, idem x 2 [6]/46, XY. Combined with the above results, acute mixed cell leukemia was diagnosed.**
Conclusions: **The flow cytometry is the gold standard in the diagnosis of acute mixed cell leukemia. The diagnosis of acute mixed cell leukemia requires the combination of clinical manifestations, cellular morphology, immunology, cytogenetics and molecular biology, and the comprehensive diagnosis efficiency is obviously better than that of morphology.**
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KEYWORDS

acute mixed cell leukemia, pseudo Chediak-Higashi granules, complex karyotype

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INTRODUCTION

The pseudo Chadiak-Higashi granules mainly exist in granulocytes and monocytes, which have been reported in acute myeloid leukemia (AML), chronic myeloid leukemia (CML), and myelodysplastic syndrome (MDS), but rarely in acute mixed cell leukemia [1]. This paper reports a case of complex karyotype acute mixed cell leukemia containing pseudo Chediak-Higashi granules admitted to our hospital and reviews relevant literature.

CASE PRESENTATION

A 6-year-old boy came to our hospital due to intermittent fever for 7 days. Since the onset of the disease, the patient's mental diet has been normal, and the body temperature has repeatedly increased, reaching 39.5℃. Hemorrhagic spots and rashes can be seen on the face, and facial erythema is obvious when fever occurs. There is no yellow stain on the skin and mucous membrane and sclera of the whole body. Several swollen lymph nodes can be touched on the neck, right jaw, bilateral axilla and groin. A mass is palpable in the right thigh root which is 3 x 2 cm in size. Ultrasound showed that the liver was slightly larger and the spleen was larger. Blood routine: White blood cell 49.26 x 10^9/L, Red blood cell 2.16 x 10^{12}/L, Hemoglobin 67 g/L, Platelet 26 x 10^9/L, primitive cells account for 7%. Bone marrow smear: Granulocyte system hyperplasia is obvious, visible at each stage, primitive cells account for 12%. These cells are large in volume, mostly round or class round, with abundant cell mass, stained gray blue, unbalanced development of some nuclear plasma, abnormal cytoplasmic staining, and visible "sunrise red" - like changes. Typical Auer bodies, pseudo Chadiak-Higashi granules and phagocytic erythroid substances were observed. The nuclei are irregular in shape, distorted and depressed, with fine chromatin and prominent large nucleoli (Figure 1). Three days later, blood routine: White blood cell 79.09 x 10^9/L, Red blood cell 1.77 x 10^{12}/L, Hemoglobin 54 g/L, Platelet 57 x 10^9/L, primitive cells account for 64%. The bone marrow smear showed 65% primitive cells. The morphology of primitive cells was similar to that of 3 days ago. The results of flow cytometry showed that the primary/naive T cells in the samples possessed nuclear cells. Flow cytometry showed two groups of abnormal cells. One group accounted for 3.87% of nuclear cells and was a primitive/naive T-cell phenotype, mainly expressing: CD34+, CD7+, CD5+, CD2dim+, MPO-, CCD3 + part, CD3-, CD4-, CD8 -, CD117 -, CD13-, CD33-, HLA - DR -, CD10-, CD11b-, CD56-. The other group which accounted for 79.8% of the nuclear cells was monocyte phenotype, mainly expressing: CD34-, CD117-, CD13+ small amount, CD33+, HLA-DR-, CD11b+, CD14+, CD15+, CD36+, CD56+, CD64+, CD4+, CD85J+, CD85K + part. It matched the immunophenotype of acute mixed cell leukemia (T/MMPAL) (Figure 2). Immunophenotypic leukemia-related fusion genes were negative, and karyotype analysis results were 45,XY, T (11; 12)(p13; Q13), -12-17, + mar [12]/90 < n > 4, idemx2 [6]/46, XY. The patient was diagnosed with acute mixed cell leukemia according to WHO classification. The patient received treatment with DAE (daunorubicin + cytarabine + etoposide) protocol after the diagnosis was rendered.

DISCUSSION

Acute mixed cell leukemia is a rare form of leukemia, occurring in 4% of acute leukemia cases. The diagnosis of acute mixed cell leukemia requires the combination of clinical manifestations, cellular morphology, immunology, cytogenetics, and molecular biology. Flow cytometry is the gold standard in the diagnosis of acute mixed cell leukemia. The cytogenetic and molecular biological analyses are important for further prognostic stratification and treatment modalities [2]. In this case, the number of primitive cells detected at admission < 20% is not enough for the diagnosis of leukemia, but the morphology of primitive cells suggests that there may be t(8;21) AML1-ETO positive acute myeloid leukemia. After 3 days, the number of primitive cells in bone marrow and peripheral blood reached more than 60%. Flow cytometry and fusion genes excluded AML with ETO positive. The patient was diagnosed acute mixed cell leukemia with complex karyotype. Complex karyotype refers to the presence of 3 or more additional abnormal karyotype chromosomes. Patients with complex karyotype have a lower CR rate and shorter RFS and OS than patients with non-complex karyotype, and the higher the chromosomal complexity, the lower the CR rate of patients with complex karyotype. Complex karyotypes play an important role in the prognosis and treatment of hematologic diseases [3]. The cytogenetic and molecular biological analyses are important for prognostic stratification and treatment modalities. Acute leukemias with complex karyotypes have a poor prognosis and are associated with morphogenesis [4]. The morphologic diversity of primitive cells in this patient may be related to complex karyotypes. Bone marrow smear: These cells are large in volume, mostly round or class round, with abundant cell mass, stained gray blue, unbalanced development of some nuclear plasma, abnormal cytoplasmic staining, and visible "sunrise red" - like changes. Typical Auer bodies, pseudo Chadiak-Higashi granules and phagocytic erythroid substances were observed. The nuclei are irregular in shape, distorted and depressed, with fine chromatin and prominent large nucleoli. The pseudo Chadiak-Higashi granules mainly exist in granulocytes and monocytes, which have been reported in acute myeloid leukemia (AML), chronic myeloid leukemia (CML), and myelodysplastic syndrome (MDS), but rarely in acute mixed cell leukemia. The pseudo Chadiak-Higashi granules were correlated with the malignant degree and prognosis of pa-

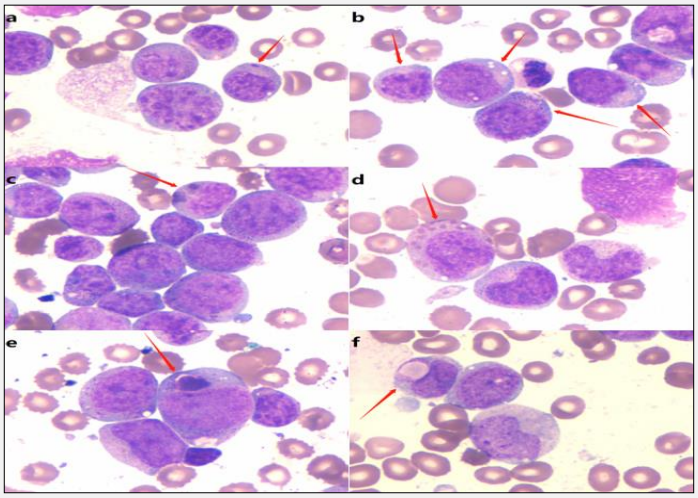

Figure 1. Bone marrow smear: These cells are large in volume, mostly round or class round, with abundant cell mass, unbalanced development of some nuclear plasma, abnormal cytoplasmic staining (b). Typical Auer bodies (a), pseudo Chadiak-Higashi granules (c - e), and phagocytic erythroid substances were observed (f). The nuclei are irregular in shape, distorted and depressed, with fine chromatin and prominent large nucleoli (Wright-Giemsa, 1,000).

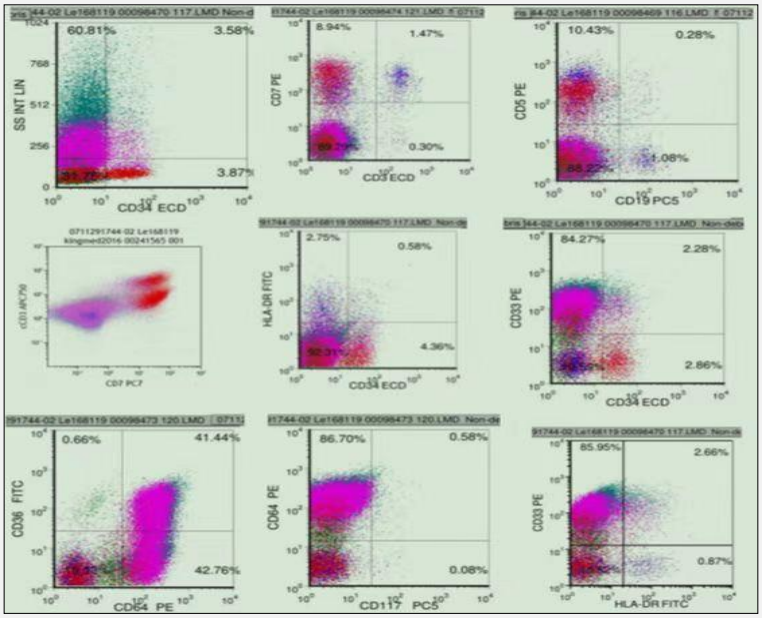

Figure 2. Flow cytometry showed two groups of abnormal cells.

One group accounted for 3.87% of nuclear cells and was a primitive/naive T-cell phenotype, mainly expressing: CD34+, CD7+, CD5+, CD2dim+, MPO-, CCD3 + part, CD3-, CD4-, CD8 -, CD117 -, CD13-, CD33-, HLA - DR -, CD10-, CD11b-, CD56-. The other group which accounted for 79.8% of the nuclear cells was monocyte phenotype, mainly expressing: CD34-, CD117-, CD13+ small amount, CD33+, HLA-DR-, CD11b+, CD14+, CD15+, CD36+, CD56+, CD64+, CD4+, CD85J+, CD85K + part. It matched the immunophenotype of acute mixed cell leukemia (T/MMPAL).

tients [5]. In this case, pseudo Chadiak-Higashi granules were found in the cytoplasm of the protocell, and various morphologies were observed. Further study is needed to determine whether the pseudo Chadiak-Higashi granules particles have an impact on the treatment and prognosis.

Declaration of Interest:

All authors declare:1, No funding was received for this study. All views and data in this paper are supported by references and data. The manuscript has not been published before and is not being considered for publication elsewhere. 2, All authors have contributed to the creation of this manuscript for important intellectual content and read and approved the final manuscript. We declare there is no conflict of interest. 3, This paper is published with the consent of patients, in line with ethical requirements.

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