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CASE REPORT

Clinical Characteristics and Diagnosis of Ph-Positive Mixed Phenotype Acute Leukemia

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SUMMARY

Background: **The goal was to improve the clinical cognition of Ph-positive mixed phenotype acute leukemia and avoid misdiagnosis or delayed diagnosis.**
Methods: **The clinical manifestations and laboratory results (bone marrow cell morphology, multiparameter flow cytometry, and cytogenetics) of a case of Ph-positive mixed phenotype acute leukemia were analyzed, and related literature was reviewed.**
Results: **Blood routine: WBC 386.35 x 10^9/L, HGB 117.00 g/L, PLT 31 x 10^9/L; 80% of the original cells can be seen by artificial classification. Morphological examination of bone marrow cells showed that the proliferation of nucleated cells was obviously active, and the original cells accounted for 76%. The size of the original cells was somewhat uniform, most of the cells had less mass, were stained light grayish blue, the cytoplasm particles were not obvious, the nuclei were mostly round or quasi-round, some of them showed distortion and nuclear notch, and the chromatin was coarse. Some of the cells were rich in mass, small azurin granules were seen, the nuclei were regular, most of them were round, the chromatin was fine, the myeloperoxidase and esterase staining were negative, the eosinophils accounted for 2.5%, and the basophils accounted for 0.5%. Flow cytometry immunotyping: Two groups of abnormal cells were seen in the bone marrow. 1. A group included 12.32% of nuclear cells and showed abnormal myeloid primitive cell phenotype. Main expression: CD117, CD34, CD38, HLA-DR, CD33, CD64, CD123, weak expression: CD13, CD19. 2. The other group included 45.61% of the nuclear cells and had a B-lymphoblastic phenotype. Main expression: CD34, CD38, HLA-DR, CD123, CD19, CD10, CD9, cCD79a, TDT, weak expression of CD13, CD22. Mixed phenotype acute leukemia (M/B) immunophenotype was considered. Chromosome: 46,XY,t(9; 22)(q34;q11.2) [20]. BCR-ABL (P210) fusion gene was positive.**
Conclusions: **Mixed phenotype acute leukemia (MPAL) is a rare type of malignant hematologic disease. Its diagnosis is based on the comprehensive evaluation of bone marrow cell morphology, immunophenotype, molecular and cytogenetic features.**
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KEYWORDS

mixed phenotype acute leukemia (MPAL), BCR-ABL fusion gene, cellular morphological, cytogenetics, immunophenotype

INTRODUCTION

Mixed phenotype acute leukemia (MPAL) is a rare type of malignant blood disease that originates from early hematopoietic stem cells. It is defined as the simulta-

neous expression of more than one lineage antigen by leukemia cells in the bone marrow. The diagnosis is mainly based on the comprehensive evaluation of bone marrow cell morphology, immunophenotype, molecular biology characteristics and cytogenetic features. The incidence of MPAL accounts for about 2 - 5% of the incidence of all leukemia in the same period [1,2]. In recent years, it has been reported that MPAL only accounts for 0.5 - 1% of acute leukemia (AL) [3]. Recently, a rare PH + MPAL patient was admitted to our hospital. The patient's case is reported as follows:

CASE REPORT

The patient, a 63-year-old male, mainly had intermittent left abdominal pain accompanied by poor appetite for 10 days. The patient had a history of hemorrhoid surgery and had post-stool bleeding again in the past half month, which was treated with topical drugs. The patient had left abdominal pain accompanied by poor appetite without obvious causes 10 days ago, no diarrhea, nausea or vomiting, and his body temperature was normal, and the pain could be relieved by itself. Therefore, no special treatment was given. Then, the pain gradually worsened and the duration prolonged, so he came to our hospital for treatment. Abdominal B ultrasonography showed increased echo of liver parenchyma and splenomegaly. Abdomen was flat and soft, no tenderness and rebound pain. The liver was not reached, the 3 fingers below the spleen were reached, and there was no edema in the lower limbs. There were no significant positive signs in the nervous system. Blood routine: WBC 386.35 x 10^9/L, HGB 117.00 g/L, PLT 31 x 10^9/L; 80% of the original cells can be seen by artificial classification. Morphological examination of bone marrow cells showed that the proliferation of nucleated cells was obviously active, and the original cells accounted for 76%. The size of the original cells was somewhat uniform, most of the cells had less mass, were stained light grayish blue, the cytoplasm particles were not obvious, the nuclei were mostly round or quasi-round, some of them showed distortion and nuclear notch, and the chromatin was coarse. Some of the cells were rich in mass, small azurin granules were seen, the nuclei were regular, most of them were round, the chromatin was fine, the myeloperoxidase and esterase staining were negative, the eosinophils accounted for 2.5%, and the basophils accounted for 0.5% (Figure 1). Flow cytometry immunotyping: Two groups of abnormal cells were seen in the bone marrow. 1. A group included 12.32% of nuclear cells and showed abnormal myeloid primitive cell phenotype. Main expression: CD117, CD34, CD38, HLA-DR, CD33, CD64, CD123, weak expression: CD13, CD19. 2. The other group included 45.61% of the nuclear cells and had a B-lymphoblastic phenotype. Main expression: CD34, CD38, HLA-DR, CD123, CD19, CD10, CD9, cCD79a, TDT, weak expression of CD13, CD22. Mixed phenotype acute leukemia (M/B) immunophenotype was considered. Chromosome: 46,XY,t(9; 22)(q34; q11.2) [20] (Figure 2). BCR-ABL (P210) fusion gene was positive. The comprehensive diagnosis was Ph-positive mixed phenotype acute leukemia.

DISCUSSION

In 2008, the World Health Organization (WHO) published the relevant diagnostic criteria for primary acute leukemia with two or more series of immunophenotypes, which cannot be classified as acute myeloid leukemia or acute lymphoblastic leukemia, into a separate type - mixed phenotype acute leukemia (MPAL), which includes: MPAL, B/myeloid, non-specific type (NOS); MPAL,T/myeloid system, NOS; MPAL, rare type, NOS. MPAL with t(9;22) (q34;q11.2)/BCR-ABL fusion gene; MPAL with t(v;vq23)/MLL gene rearrangement. MPAL is accompanied by t(9;22)(q34;q11.2)/BCR-ABL fusion gene, also known as Ph + MPAL, is extremely rare in clinic. The common genetic abnormalities of MPAL were t(9;22)(q34;q11), t(v;vq23) and complex karyotype [4]. Even so, Ph-positive MPAL does not exceed 1% of AL and can occur in both adults and children, with adults predominating, accounting for 2.1% of adult AL and only 0.1% of child AL [5]. The results showed that Ph-positive MPAL was mostly male patients, often accompanied by high white count, most of them had extramedullary infiltrates such as liver, spleen enlargement, and lymph node enlargement, and the immunophenotype was mostly B/M type, which could be accompanied by Ph positive and/or complex karyotype, and could be accompanied by EV11 and BCR-ABL gene positive. Some MPAL patients with BCR-ABL fusion gene positive are primary acute leukemia, while some are rapidly transformed by CML [6]. The pathogenesis of the two is different, but the clinical manifestations, cell morphology and prognosis are very similar. It is generally believed that the recovery of BCR-ABL-positive MPAL to the chronic stage of CML after treatment is a more reliable method to retrospectively diagnose the acute change of CML rather than the primary BCR-ABL-positive MPAL [7]. This case is a newly diagnosed patient with left abdominal pain for 10 days, and he is a middle-aged and elderly male with splenomegaly. Eosinophilic and basophilic granulocytes can be seen in the classification of bone marrow cells, except for CML. In addition to Ph chromosomes, other additional chromosomal abnormalities, BCR-ABL fusion protein types, and related cell series phenotypes involved are also difficult to distinguish. Mixed phenotype acute leukemia (MPAL) is a rare type of malignant hematologic disease. Mixed cell leukemia can be divided into double series and double phenotype mixed cell leukemia. Morphology in the bone marrow smear, when there are more typical primitive lymphocytes and myeloid primitive cells, the morphological characteristics of this case are not prominent. Its diagnosis is based on the comprehensive evaluation of bone marrow cell mor-

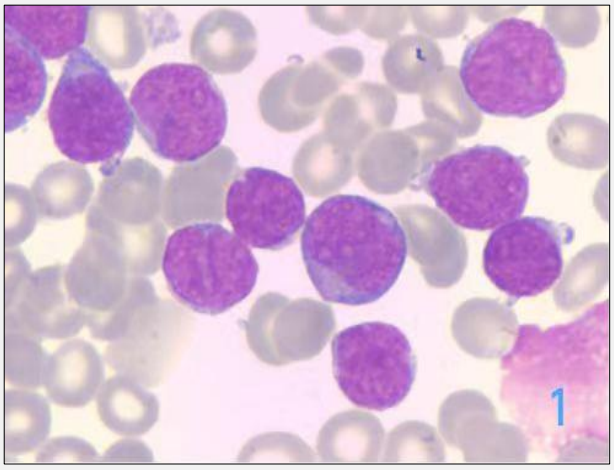

Figure 1. Cell morphology of bone marrow smear in Ph-positive MPAL patients.

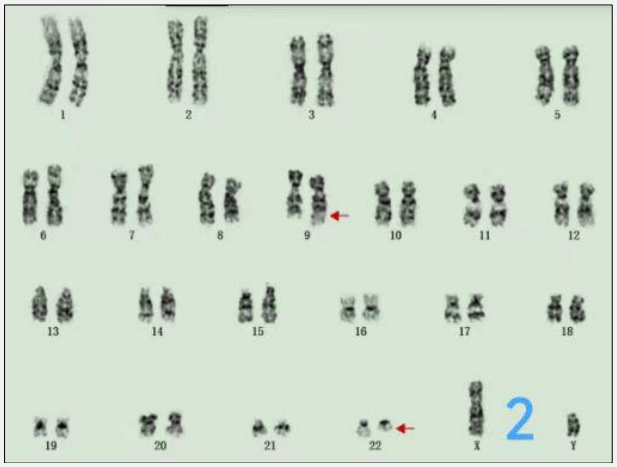

Figure 2. Chromosomal karyotypes of Ph-positive MPAL patients.

phology, immunophenotype, molecular biology characteristics and cytogenetic features.

Declaration of Interest:

All authors declaration: 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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