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CASE REPORT

Clinical Characteristics and Diagnosis of Nonaccelerating MDS/MPN-U Patient with 5q- Karyotype

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SUMMARY

Background: **The aim of the study was to improve the clinical cognition of nonaccelerating myelodysplastic/myeloproliferative neoplasms-unclassifiable (MDS/MPN-U) with 5q- karyotype and to avoid misdiagnosis or delayed diagnosis.**
Methods: **The clinical manifestations and laboratory results of a patient with nonaccelerating MDS/MPN-U with 5q- karyotype were analyzed, and related literature was reviewed.**
Results: **The patient was admitted to hospital mainly due to chest tightness and shortness of breath, aggravated for 4 days. After admission, combined with clinical manifestations, bone marrow cell morphology, immunology, multiparameter flow cytometry, cytogenetics and molecular biology, etc., the final diagnosis was MDS-MPN-U.**
Conclusions: **Research on the correlation between MPN-U and MDS with 5q deletion is still needed. Clinically, MPN-U combined with MDS is prone to misdiagnosis. In diagnosing MPN-U patients, it is essential to not only complete routine and immunological tests but also consider clinical manifestations and laboratory results. It is crucial to be vigilant about the possibility of concurrent diseases, especially cancer, and to choose targeted examinations in a timely manner to avoid missed or incorrect diagnoses.**
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KEYWORDS

MDS/MPN-U, 5q- karyotype, myelodysplastic syndrome, MDS

INTRODUCTION

MDS/MPN is a group of rare hematological malignancies characterized by both myelodysplastic syndromes (MDS) and myeloproliferative neoplasms (MPN) that are at risk of transformation into acute myeloid leukemia (AML) [1]. Long arm deletion of chromosome 5 (5q-) is one of the common cytogenetic abnormalities of MDS and can be seen in all subtypes of MDS. 5q- syndrome is narrowly defined as a primary MDS-RA with a separate cytogenetic abnormality involving the q21 - q32 zone of chromosome 5 [2,3]. Recently, a rare MDS/MPN-U with 5q- karyotype patient was admitted to our hospital. The patient's case is reported as follows:

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CASE REPORT

The patient was admitted to hospital mainly due to chest tightness and shortness of breath, aggravated for 4 days. With a history of chronic bronchitis and emphysema for more than 50 years and type 2 diabetes for 4 - 5 years, metformin was used to control blood sugar, and normal fasting blood sugar was controlled between 8 - 9 mmol/L. No hypertension, coronary heart disease, or cerebrovascular history was found. The aim of the study was to improve the clinical cognition of nonaccelerating myelodysplastic/myeloproliferative neoplasms-unclassifiable (MDS/MPN-U) with 5q- karyotype and to avoid misdiagnosis or delayed diagnosis.

Methods

The clinical manifestations and laboratory results (bone marrow cell morphology, multiparameter flow cytometry, and cytogenetics) of a patient with nonaccelerating MDS/MPN-U with 5q- karyotype were analyzed, and related literature was reviewed.

Results

Blood routine: white blood cell 18.86 x 10^9/L, red blood cell 3.85 x 10^{12}/L, hemoglobin 94.00 g/L, platelet 48 x 10^9/L. Blood clotting test: thrombin time 13.90 seconds, activated partial thromboplastin time 58.80 seconds, fibrinogen 3.15 g/L, D-dimer 1.17 mg/L, international normalized ratio 1.50, prothrombin time 16.60 seconds. Patients suffers from coagulation dysfunction, hypoproteinemia, electrolyte disturbance, hyponatremia, and hypochloremia. Blood smears showed granulocytosis and cells at various stages, including 10% primitive granulocytes, 29% eosinophils, and 14% basophilic granulocytes. Bone marrow smears showed hyperactive myelodysplasia (95% granulocytes), with 9% primitive granulocytes, 30.5% eosinophils, 8.5% basophilic granulocytes, and binucleocytes. Polylobulated granulocytes also can be seen (Figure 1). Considering the high possibility of CML, it is recommended to combine the fusion gene and other related tests to confirm the diagnosis. Bone marrow biopsy showed hyperactive hyperplasia with an increased proportion of myeloid original cells with eosinophilia and fibrous tissue hyperplasia. Flow cytometry showed that the proportion of myeloid original cells increased (7.78%), the aggregation expression of CD34, CD56, and CD33 was enhanced, the expression of CD13 was weakened, the expression of CD117 and CD38 was absent, accompanied by partial expression of CD7 T lymphocytes CD3+CD4+/CD3+CD8+ = 6.53, the ratio increased. Gene test showed BCR/ABL, JAK2/V617F, CARL, and MPL gene mutations were negative. The chromosome shows deletion of the long arm segment of chromosome 5 (5q-),46,XY,del(5)(q15q31),t(9; 19)(q34; q13.1) (Figure 2). Bone marrow primitive granulocyte was 9%, peripheral blood primitive granulocyte was 10%, bone marrow biopsy indicated hyperactive hyperplasia, MDS/MPN was considered to be a high possibility, and chromosome showed deletion of long arm fragment of chromosome 5 (5q-). According to the diagnostic criteria of MDS/MPN-U in WHO Classification of Hematopoietic and Lymphoid Tissue Tumors in 2016 [4], the patient had the chromosomal karyotype characteristics of MDS-5q- and significantly increased white blood cells, which was considered as myelodysplastic syndrome/myelodysplastic tumor. However, it does not meet the diagnostic conditions of chronic granulomonocytic leukemia (CMML), juvenile granulomonocytic leukemia (JMML) or atypical chronic myeloid leukemia (aCML). Bone marrow iron staining did not show ringed sideroblasts, and the final diagnosis was MDS-MPN-U.

DISCUSSION

The detection rate of chromosome karyotype abnormalities in patients first diagnosed with myelodysplastic syndrome (MDS) is about 50%, and the long arm deletion of chromosome 5 (5q-) is one of the most common chromosome karyotype abnormalities in MDS. The detection rate of 5q- chromosome abnormalities in patients first diagnosed MDS is 10% - 20% [5,6]. In 2016, the World Health Organization revised the cytogenetic criteria for 5q syndrome, proposing that those with a second cytogenetic abnormality (in addition to -7/del7q), accompanied by other chromosomal changes, are called MDS containing 5q complex karyotype. In the diagnosis of 5q syndrome, the bone marrow cell morphology of megakaryocytes with undivided lobes, oligolobia, and chromosome karyotype analysis have characteristic abnormalities, which are helpful for clinical diagnosis [7]. MDS-5q- is a subtype of MDS accompanied by refractory macrocytic anemia, erythroid hyperplasia, increased PLT, abnormal proliferation of megakaryocytes, and poor karyomerism. The number of bone marrow primitive cells is < 5%, and the number of peripheral blood primitive cells is < 1%. In this medical case, both bone marrow and peripheral blood primitive cells are > 5% [1,2,8]. 5q- syndrome generally does not have Auer bodies, is refractory macrocellular anemia, the degree of anemia is relatively severe, the number of platelets is generally normal or increased. However, in this case, thrombocytopenia was observed. Bone marrow hyperplasia is active, the number of megakaryocytes is generally normal or increased, and the megakaryocyte nuclear karyomerism is reduced. In this medical case, there are few megakaryocytes, and a total of 1 megakaryocyte is seen in the whole film. In this medical case, in addition to 5q-, the patient also had translocation of chromosomes 9 and 19, belonging to MDS with complex karyotype 5q. Simple 5q- syndrome generally has a good prognosis and a low conversion rate to leukemia. However, this case is MDS with complex 5q- karyotype, MPN features, and increased primitive cells. The patient has poor mental condition, severe anemia, multiple ecchymosis and flaky rash on the skin of the whole body, large liver and spleen, and obvious edema

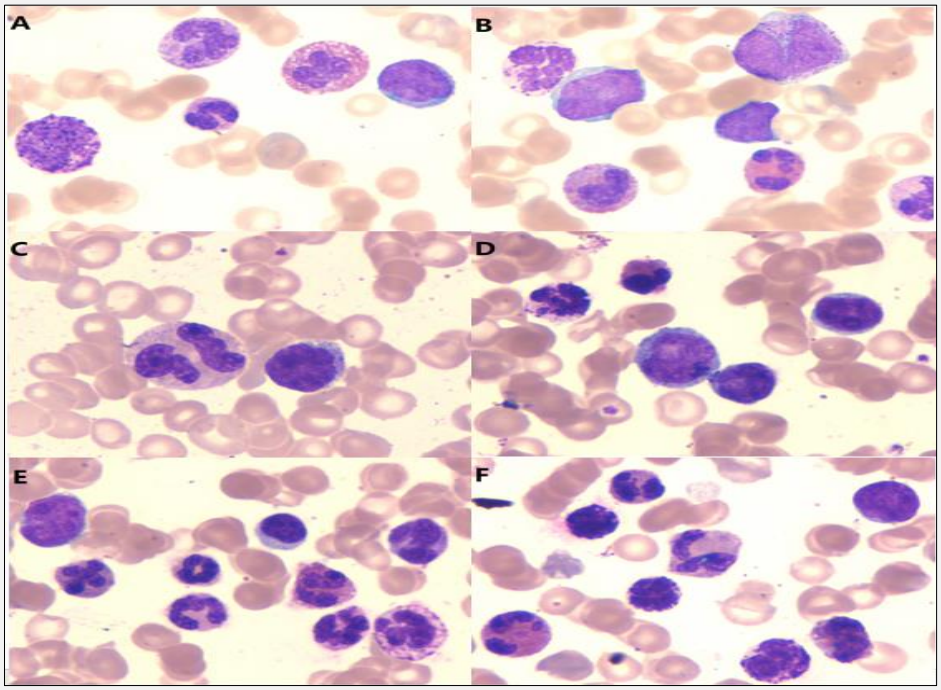

Figure 1. Blood smears image (Giemsa stain 10*100), (A, B). Bone marrow image (Giemsa stain 10*100), (C - F).

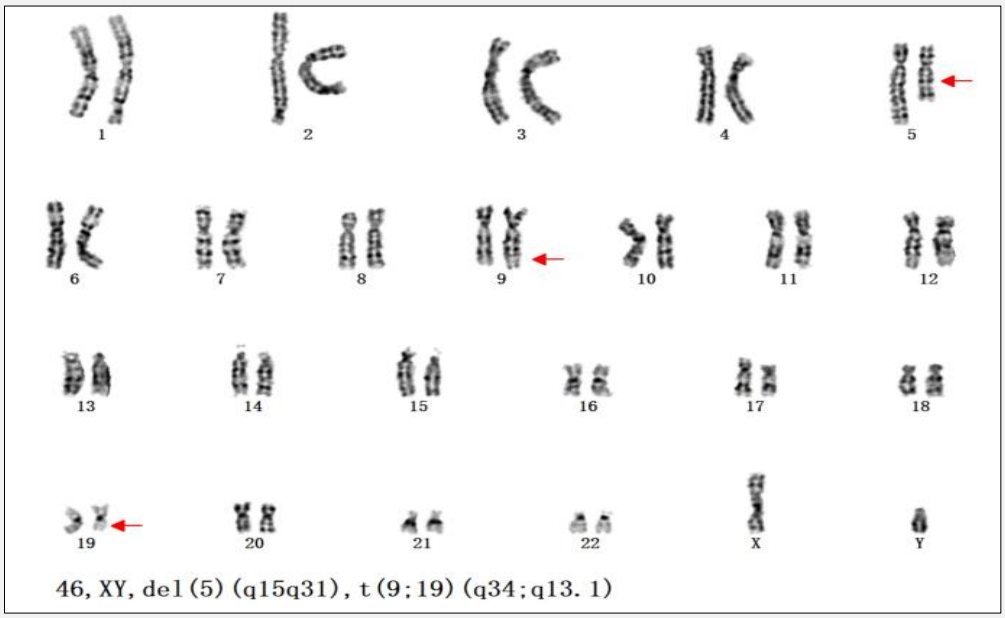

Figure 2. Chromosomal karyotypes of MDS/MPN-U with 5q- karyotype patients.

of both lower limbs, and is expected to have a poor prognosis. It is easy to miss diagnosis of MDS/MPN-U with 5q- karyotype clinically. The diagnosis should be combined with clinical manifestations and laboratory tests. Consideration should also be given to the possibility of combining other diseases. In particular, the clinician should be vigilant about complicated tumors and should timely select targeted tests to avoid missed diagnosis and misdiagnosis.

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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