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CASE REPORT

Clinical Characteristics and Diagnosis of Nonaccelerating MDS/MPN-U Patient with Granulocyte Dysplasia

Nana Jin [1], Shang Li [2]

[1] *Department of Clinical Laboratory, Handan People's Hospital, Handan, Hebei Province, China*
[2] *Department of Gastroenterology, The Third Hospital of Hebei Medical University, Shijiazhuang, Hebei Province, China*

SUMMARY

Background: **The goal was to improve the clinical cognition of nonaccelerating myelodysplastic/myeloproliferative neoplasms-unclassifiable (MDS/MPN-U) and avoid misdiagnosis or delayed diagnosis.**
Methods: **The clinical manifestations, laboratory indicators, histopathology, and therapeutic effects of a patient with nonaccelerating MDS/MPN-U were analyzed and the relevant literature was reviewed.**
Results: **Blood routine: white blood cell 98.48 x 10^9/L, red blood cell 3.20 x 10^{12}/L, basophils 0.42 x 10^9/L, eosinophils 1.31 x 10^9/L, hemoglobin 112 g/L, and platelet 113 x 10^9/L. Blood smears showed granulocytosis and cells at various stages, polylobular granulocytes also can be seen. Bone marrow images show granulocytosis and dysplastic neutrophils, such as binuclear granulocyte, cyclic nuclear granulocyte, nuclear punch, cytoplasm vacuoles, polylobular granulocytes and so on. Bone marrow biopsy: Bone marrow proliferation tumor, combined with cell morphology and molecular biochemistry is recommended. Gene test showed Jak-2 positive, BCR/ABL and MPL negative. Chromosome examination indicated the presence of 46, XY, add (2)(p25), del (12) (p11.2p13)[16]/46, XY.**
Conclusions: **MDS/MPN-U with granulocytosis and dysplastic neutrophils is rare, mostly in the elderly, and the diagnosis should be made except for other myeloid tumors. Currently, there is no uniform treatment guideline or expert consensus. The treatment options are limited and need to be further confirmed by more studies. MDS/MPN-U with granulocytosis and dysplastic neutrophils has adverse prognostic factors such as advanced age, increase of bone marrow original cells and related gene mutations. Whether the adverse prognosis is related to specific gene mutations and cytogenetic variation remains to be clarified by more research data.**
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Correspondence:
Shang Li
Department of Gastroenterology
The Third Hospital of
Hebei Medical University
Shijiazhuang, Hebei Province
China
E-mail: laopoaini777@sina.com

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KEYWORDS

MDS/MPN-U, myelodysplastic syndrome, myeloproliferative neoplasms

INTRODUCTION

MDS/MPN is a kind of myeloid diseases in which the bone marrow has the main pathological features of both myelodysplastic syndrome (MDS) and myeloproliferative neoplasms (MPN), but does not conform to the diagnosis of MDS or MPN [1]. MDS/MPN-U patients are rare and the incidence is unclear, accounting for 2% - 5% of all malignant myeloid tumors, and it is even rarer to be accompanied by granulocytosis and dysplastic neutrophils of bone marrow [2,3]. In this study, the clin-

ical diagnosis and treatment of one case of MDS/MPN-U was reported. The related literature was reviewed to improve the clinician's understanding of this disease. The research results are reported as follows.

CASE REPORT

The patient, a 65-year-old male, had abdominal distension symptoms without obvious inducement 5 years ago. He was diagnosed with primary myelofibrosis (PMF) by bone marrow puncture biopsy in other hospitals and was given 0.5 g/d treatment with hydroxyurea. Blood routine: white blood cell 6.4 x 10^9/L, red blood cell 5.01 x 10^{12}/L, hemoglobin 137 g/L and platelet 222 x 10^9/L. Ten days prior to admission, the patient appeared to have swelling of both upper limbs and both lower limbs without obvious cause. Both lower limbs were obvious, which was concave edema of finger. So, he came to our hospital for further treatment. Admission for physical examination: The body temperature was normal, no ecchymosis was observed in the skin and mucous membranes of the whole body, no swelling of superficial lymph nodes, no tenderness in the sternal bone, clear respiratory sounds in both lungs, no obvious dry and wet rales were heard, heart rate was 83 beats/minute, rhythm was smooth, no obvious pathological murmurs were heard in the auditory areas of each valve. The abdomen was soft, no tenderness or rebound pain, liver subcostal not reached and the spleen was palpable 2 cm below the umbilicus. Both lower limbs had pitting edema, and no obvious abnormalities in the nervous system. Blood routine: white blood cell 98.48 x 10^9/L, red blood cell 3.20 x 10^{12}/L, basophils 0.42 x 10^9/L, eosinophils 1.31 x 10^9/L, hemoglobin 112 g/L, and platelet 113 x 10^9/L. Blood smears showed granulocytosis and cells at various stages, polylobular granulocytes also can be seen (Figure A - B). Bone marrow images show granulocytosis and dysplastic neutrophils, such as binuclear granulocyte, cyclic nuclear granulocyte, nuclear punch, cytoplasm vacuoles, polylobular granulocytes, and so on (Figure C - F). Bone marrow biopsy: Bone marrow proliferation tumor, combined with cell morphology and molecular biochemistry is recommended. Gene test showed JAK-2 positive, BCR/ABL and MPL negative. Chromosome examination indicated the presence of 46, XY, add (2)(p25), del (12) (p11.2p13) [16]/46, XY. The diagnosis was MDS/MPN-U.

DISCUSSION

In 2016, WHO diagnostic criteria for MDS/MPN-U were as follows: Patients had clinical, laboratory and bone marrow cell morphological characteristics of certain subtypes of MDS; The proportion of bone marrow and peripheral blood original cells is less than 20%; The clinical and morphological characteristics of bone marrow cells were prominent myeloproliferative, such as platelet count ≥ 450 x 10^9/L, with megakaryocytosis, or WBC ≥ 13 x 10^9/L, with or without significant splenomegaly. No history of MPN or MDS before onset, no recent history of receiving cytotoxic drugs or growth factors that can cause MDS/MPN characteristics; No BCR/ABL1 fusion gene, no PDGFRA, PDGFRB, or FGFR1 rearrangement, no PCM1/JAK2 fusion gene, no t(3; 3)(q21; q26) and inv(3)(q21q26) or 5q-, or the patient has a primary disease with mixed manifestations of myelodysplasia and dysplasia and cannot be classified as either MDS, MPN, or MDS/MPN subtype. This patient met the above diagnostic criteria and was accompanied by granulocytosis and dysplastic neutrophils of bone marrow [4]. MPN includes PMF, polycythemia vermiculata (PV), and essential thrombocythemia (ET), which are malignant clonal hematopoietic stem cell diseases. An important cause of MPN is the mutation of JAK2V617F gene. Compared with negative JAK2V-617F gene mutation, mutation-positive patients had higher white blood cell count at first diagnosis. This patient was positive for JAK2 gene, but had no significant increase in white blood cell count at first diagnosis of MPN-PMF 5 years ago. Recently, it was found that the number of white blood cells increased significantly, and the excessive proliferation of granulocytes caused the increase of peripheral blood granulocytes. The chromosome is a complex karyotype, and P190, P210, and P230 are negative, which is consistent with the characteristics of MPN. Abnormal granulocytosis was observed in bone marrow and peripheral blood, and abnormal hematopoiesis was observed in granulocyte series and erythrocyte series, which was consistent with the pathological characteristics of myelodysplastic tumors (MDS). The above results suggested that the patient was diagnosed with MDS/MPN because of the coexistence of abnormal cell development and excessive proliferation, hypergranulocytosis in peripheral blood, and both pathological features of MDS and MPN. However, it does not meet the diagnostic conditions of chronic myelomonocytic leukemia (CMML), juvenile myelomonocytic leukemia (JMML) or atypical chronic myeloid leukemia (aCML). Bone marrow iron staining did not show ring sideroblasts, and was finally considered as MDS-MPN-U. MDS/MPN-U usually involves peripheral blood, bone marrow, spleen, liver and other extramedullary tissues. MDS-MPN-U usually has hepatosplenomegaly, in this medical case only the spleen is enlarged. Most patients with MDS-MPN-U were newly diagnosed patients. In this medical case, the conversion from MPN-PMF to MDS-MPN-U was not reported [5-7]. MDS/MPN-U with granulocytosis and dysplastic neutrophils is rare, mostly in the elderly, and the diagnosis should be made except for other myeloid tumors. Currently, there is no uniform treatment guideline and expert consensus. The treatment options are limited and need to be further confirmed by more studies. MDS/MPN-U with granulocytosis and dysplastic neutrophils has adverse prognostic factors such as advanced age, increase of bone marrow original cells, and related gene

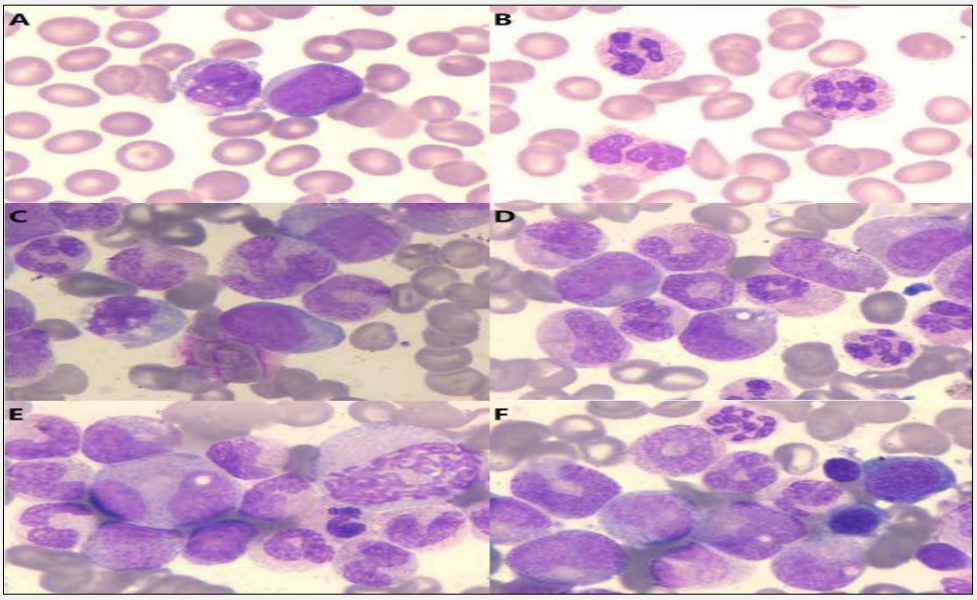

Figure A - B. Blood smears showed granulocytosis: cells at various stages and polylobular granulocytes (Giemsa stain 10*100). Figure C - F. Bone marrow smears revealed granulocytosis and dysplastic neutrophils: binuclear granulocyte, cyclic nuclear granulocyte, nuclear punch, cytoplasm vacuoles, polylobular granulocytes. (Giemsa stain 10*100).

mutations. Whether the adverse prognosis is related to specific gene mutations and cytogenetic variation remains to be clarified by more research data.

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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