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Case Report

Myelodysplastic Syndrome Mimicking Thrombotic Thrombocytopenic Purpura Treated with Allogeneic Bone Marrow Transplantation

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Abstract

Myelodysplastic syndrome(s) (MDS) are a group of hemopoietic stem-cell disorders characterized by ineffective hematopoiesis and dysplasia. The clinical presentation is not specific in MDS and initial symptoms are generally related to the underlying cytopenias. Thrombotic thrombocytopenic purpura (TTP) is a life threatening condition with thrombocytopenia and hemolytic anemia in which immediate initiation of treatment is critically important. Fragmented erythrocytes (schistocytes) are classically observed in TTP and are rarely a sign for MDS. Herein, we aim to report a 41 year-old woman having thrombotic microangiopathy in admittance and then eventually diagnosed with MDS.

Keywords: Myelodysplastic Syndrome; Thrombotic Microangiopathy; Transplantation

Introduction

Myelodysplastic syndromes (MDS) compass a group of hematologic malignancies characterized by clonal hematopoiesis, one or more cytopenias (anemia and/or neutropenia and/or thrombocytopenia) and dysplasia. MDS commonly occurs in older adults with a peak incidence between 60 and 75 years and there is a male predominance [1]. Clinical presentation is variable and onset of the disease is generally smouldering being the initial symptoms often related to cytopenias [2]. As MDS has a wide range of disease phenotypes, it has several microscopic characteristics of the dysplastic cells in bone marrow and peripheral blood as well. However schistocytes are characteristic for microangiopathic hemolytic anemias and are rare findings for MDS [3].

Thrombotic thrombocytopenic purpura (TTP) is a life threatening primary thrombotic microangiopathy (TMA) caused by ADAMTS13 deficiency. The test for ADAMTS13 activity is a requirement for diagnosis of TTP, however it takes several days for the result [4]. Diagnosing TTP and initiating plasmapheresis is urgent. TTP predominantly affects previously healthy women with a peak incidence between the ages 30 and 40 [1]. Not all patients are critically ill; they may have minor symptoms of weakness, dizziness or gastrointestinal complaints. Neurologic, cardiac, renal abnormalities are not always present. Presumptive diagnosis of TTP based on clinical features, complete blood count and review of the peripheral blood smear, serum chemistry and creatinine, tests showing hemolysis, and a negative coombs test, is an indication to initiate plasmapheresis as it is potentially life-saving and should not be delayed till the results of the confirmatory tests come.

In this report, we present the case of a 41 year-old woman with MDS which was initially difficult to distinguish from TTP.

Case

A 41-year-old woman was referred to our hematology department because of pancytopenia. Earlier the patient had been admitted to a local hospital with complaints of fatigue and dizziness worsening during the last three days. She had no constitutional symptoms, arthralgia, arthritis, cough, diarrhea or bleeding. There was no sign of recent infection, no recent history of drug exposure. She didn't have significant personal or family history. She looked pale but showed no remarkable findings, no palpable organomegaly or lymphadenopathy upon her physical examination. Complete blood count on presentation showed pancytopenia (hemoglobin: 6.9 g/dl, platelets: $26x10^9$ and leucocytes: $2.47x10^9$, neutrophils: $1.66x10^9$). Fragmented erytrocytes (schistocytes), anisocytosis, poikilocytosis were observed on peripheric smear (Picture 1). Her coagulation workup, direct and indirect coombs tests were negative. Lactate Dehydrogenase (LDH) level was 304 U/L (Normal range: 150-220 U/L), and reticulocyte absolute count was $92x10^9$. Based on these results, the patient initially was accepted as TMA, and as such, she was started on daily plasmapheresis (PEX) and steroids, while further testing was ordered for secondary causes for TMA, acute leukemia, solid organ malignancies, lymphoproliferatif diseases. ADAMST13 antigen-antibody- activity tests were sent before PEX. Neck, chest and abdominal tomography studies were normal. She underwent to bone marrow (BM) aspiration and biopsy which showed markedly hypercellular marrow, significant dysplasia in erythroid elements with budding, karyorrhexis, occasional binucleate-trinucleate forms and giant erythroblasts, dysplastic megacaryocytes, single nucleate with typical pawn ball megacaryocytes (Picture 2, 3). This revealed myelodysplastic syndrome (MDS) in the first place, and cytogenetic, FISH panel for MDS was added to the workup. Because bone marrow findings indicated MDS with no other possible pathology responsible for dysplasia and not responding to PEX, steroids and plasmapheresis was stopped 5 days after starting. ADAMST13 antigen-antibody-activities were normal, therefore TTP was excluded. Cytogenetic analysis on bone marrow cells showed a normal karyotype of all of 20 analyzed metaphases. FISH analysis, for myelodysplastic syndrome, including 5q, del 7, trisomy 8, del17p, and 20q were also found to be normal. The IPSS-R score was 3.5 and the IPSS-R category was Intermediate. Due to her young age and the severe cytopenias the patient referred to the transplantation center and had allogeneic bone marrow transplantation from matched sibling donor. After 4 months from transplantation, the patient had no immunological and non-immunological complication, and being followed-up regularly at outpatient clinic.

Picture 1: Multiple fragmented erytrocytes on peripheral blood smear.

Picture 2: Dysplastic (anbormal shape and size) nucleated red blood cell precursors on bone marrow aspiration.

Picture 3: Abnormal megakaryocytes, disconnected multiple small lobes (pawn ball changes).

Discussion and Conclusion

We described a 41 year-old woman with acute onset MDS who presented with schistocytosis, a rare manifestation of MDS. Her symptoms and laboratory findings mimicked TTP. To the best of our knowledge there are only five cases reporting the association between TTP and MDS [1,2,4-6]. MDS can clinically present like TTP as in our case, and life saving treatment such as plasmapheresis in this setting should not be delayed until further testing to clarify the diagnosis is in process.

Schistocytes refer to fragmented erythrocytes has also been reported in other malignant hematologic disorders as well as malignant hypertension, disseminated intravasculary coagulation, metastatic cancers but are commonly associated with microangiopathic hemolytic anemias and they are unusual manifestation of MDS. Diagnosis of MDS relies on the morphological assessment of bone marrow aspiration and biopsy as well as cytogenetic analysis [4,5,7]. In our case, we excluded all of the possible causes of the TMA and diagnosed MDS based on the morphological assessment.

There have been five more cases with TTP associated with MDS as far as we know. As in our case most of the previously reported cases showed thrombocytopenia, anemia and high LDH levels in serum, schistocytosis detected in all of the cases. The first case reported was published in 1992; a 20 year-old girl with hemolytic anemia and thrombocytopenia diagnosed of hemolytic anemia with thrombotic microangiopathy and MDS (RA) progressed into acute myeloid leukemia in about 6 months [2].

Sasaki N., *et al*. presented their case in 2008, a 21 year old non -pregnant woman presented with pancytopenia and diagnosed as MDS. A month later she was first admitted neuropsychological symptoms appeared with a decrease in ADAMST13 activity and increase in the autoantibody for ADAMST13 and she was diagnosed as having TTP. PEX and steroid treatment was started, but a while after, because this treatment was failing, cyclosporine-A was added to the treatment. CsA treatment improved both the blood cell count and BM dysplasia. And relationship of TTP and MDS was suggested to be that MDS could be an underlying disorder for TTP [1].

Okabe., *et al*. and Moscoso Martiez., *et al*. reported another two cases [4,5]. Both cases were clinically presented as TTP with the ''classic TTP pentad'' (MAHA, thrombocytopenia, fever, neurologic disturbances and renal renal involvement) and finally diagnosed as MDS. For both of the patients PEX and steroid treatment was started firstly while the results of further investigations were on process. Our patient didn't have fever, neurologic or renal involvement but anemia with schistocytes on peripheral blood smear and thrombocytopenia were presumptive for TTP and PEX was initiated immediately as well during other examinations result in. The first mentioned patient by Okabe M., *et al*. was recommended to go under allogeneic stem cell transplantation after diagnosing of MDS but he refused treatment and died a month after because of infection.

Our presented patient demonstrated anemia with schistocytes on peripheral blood smear, thrombocytopenia and negative coombs tests which are presumptive for TMA, which is a life threatening medical emergency and prompt diagnosis and initiating treatment are critical. Because her findings were suggestive for TMA, PEX was initiated and was performed until bone marrow aspiration showed signs of MDS and because the patient was unresponsive to plasmapheresis it was ceased at this time. Then our patient went through successfull allogeneic bone marrow transplantation from matched sibling donor and she is free from complications now after 4 months from transplantation.

In summary we presented a case of MDS which was initially difficult to distinguish from TTP. In this clinical aspect MDS is a diagnosis of exclusion and life threatening conditions such as TTP needs to be assessed first with appropriate evaluation and initiation of adequate treatment until this medical emergency is being ruled out. Even though MDS presented with TMA is very rare, MDS should be considered in differential diagnosis in such cases.

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