



Myelodysplastic Syndrome Type Refractory Anemia with Ringed Sideroblasts According to the WHO Classification: A Case Report and Literature Review

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Abstract

Introduction: The myelodysplastic syndromes integrate a group of clonal disorders characterized by progressive cytopenias and dishematopoiesis causing a disruption in the normal function of the three hematopoietic lines. There are two types of myelodysplastic syndrome (MDS), the primary one which is idiopathic and the secondary type or acquired commonly associated with antineoplastic drugs. Diagnosis can be clinically suspected or found out in control routine blood studies. However, it is a matter of necessity to know the clinical manifestations, treatment options and prognosis of patients who suffer from these syndromes.

Methods: Retrospective, observational study in which we present the case of a 73-year-old woman who presented idiopathic myelodysplastic syndrome, we obtained and analyzed information with the clinical chart of the patient, not only do we evaluate the clinical history but also her risk factors, clinical manifestations, treatment, and final outcomes. A bone marrow sample corroborated a refractory anemia with ringed sideroblasts type of MDS in this patient. Added to this case report we made a short literature review of myelodysplastic syndromes.

Results: In spite of all medical and therapeutical efforts, after a long-time treatment, multiple blood transfusions and clinical progressive deterioration with recurrent low hemoglobin ranges and chronic anemia, the patient deceased six months after MDS diagnosis.

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Conclusions: Myelodysplastic syndromes are most common in the elderly population; patients with chronic diseases have a higher risk for presenting MDS, the chronic cytopenias due to these syndromes predispose to a high mortality risk and decrease in life quality becoming an important public health problem.

Keywords:

Anemia; Cytopenia; Hemoglobin; Hematopoiesis; Myelodysplastic Syndrome; Ringed Sideroblasts; WHO.

Introduction

The term "myelodysplastic syndrome" (MDS) was introduced in 1975, according to the National Institute of Cancer in México the average presentation age is 70 years old and the pediatric and young adult presentation is rare [1]. The myelodysplastic syndrome integrates a group of clonal disorders characterized by progressive cytopenias and dishematopoiesis [1-2] disrupting the normal function of the three hematopoietic lines [1-17].

The accompanying alterations of the MDS include immunologic and molecular adjustments [18]. Elderly people must be considered as risk population mostly male patients [1, 12].

There are two types of MDS, the primary one which is idiopathic (the cause is unknown), and the secondary type commonly associated to antineoplastic drugs, alkylating agents, chronic contact with chemical products, benzene exposure, ionizing radiations, etc. Mexican

Table-1: MDS classification according to the WHO (2008)

MDS Subclass	Peripherally Blood	Bone Marrow
Refractory cytopenia with unilineage dysplasia (RCUD) Refractory anemia (RA) Refractory neutropenia (NT) Refractory thrombocytopenia (TR)	Anemia <1% blasts	Uni-linear erythroid dysplasia (in ≥ 10% of cells) <5% blasts
	Neutropenia <1% blasts	Uni-linear granulocytic dysplasia. <5% blasts.
	Thrombocytopenia <1% blasts	Megakaryocytic dysplasia <5% blasts
Refractory anemia with ringed sideroblasts (ARSA)	Anemia; <1% blasts	Erythroid dysplasia (of erythrocytes); <5% blasts, ≥15% ring sideroblasts
Refractory cytopenia with multilineage dysplasia (CRDM)	Cytopenia; <1% blasts; without Auer sticks	Multiline dysplasia ± ring sideroblasts <5% blasts, without Auer sticks
Refractory anemia with excess blasts type-1 AREB-1	Cytopenia; <5% blasts; Without Auer sticks.	Mono- or multi-lineage dysplasia 5-9% blasts; without sticks of Auer
Refractory anemia with excess blasts type 2 AREB-2	Cytopenia (s) 5% -19% blasts ± Auer canes	Uni or multilineage dysplasia 10% -19% blasts ± Auer sticks
MDS associated with isolated deletion 5q Del (5q)	Anemia; <1% blasts; Normal or augmented platelets	Isolated deletion 5q, Anemia, hypolobated megakaryocytes, <5% blasts
Unclassified MDS-U	Cytopenias; ≤ 1% blasts	It does not clearly fit other categories of dysplasia <5% blasts; if there isn't dysplasia or karyotype associated with MDS

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guidelines mention that tobacco use increases the risk of MDS [2]. The classifications and taxonomies are by nature mental constructions imposed on a reality often complex and ambiguous. Despite this, classifying diseases is of utmost importance since it allows us to standardize nomenclatures, facilitate communication between specialists and researchers. In 1999 the world health organization (WHO) modified the classification of the group FAB (1982) for MDS and in 2008 conducted a review and proposed a new classification [1-3]. This WHO MDS classification is summarized in table 1 (See table 1).

Methods and Case Presentation

This is a retrospective observational study in which with analysis of the clinical file of a patient with chronic anemia, we present a case of a 73-years-old female from Zacatlán, Puebla that attended to the hemodialysis unit for renal substitutive treatment secondary to end-stage chronic kidney disease (CKD). Her medical record high lightened a long-term hypertension treated with Losartan, Diabetes Mellitus type 2 treated with Metphormine and Insulin, also end-stage chronic kidney disease receiving hemodialysis treatment and chronic anemia supposedly secondary to renal chronic disease, this last one treated with human recombinant erythropoietin 8000 UI 3 times a week, though, over time and in spite of erythropoietin treatment and multiple blood transfusions secondary to persisted low hemoglobin ranges it was decided to perform extension studies to rule out occult hemorrhage. No genetic studies were performed. Occult blood in stool resulted positive reason why a panendoscopy and colonoscopy were performed concluding the presence of two active bleeding ulcers in gastric antrum, therapy based on sucralfate and esomeprazole was established, a follow-up panendoscopy was made two weeks after demonstrating decrease in mucosal disruption and bleeding absence, however, this pharmacological therapy remained for three months. Blood control studies showed that the three hematopoietic lines persisted low, and hemoglobin levels remain in low ranges

increasing our patient mortality risk, reason why she was referred to the hematologist. The Oncologic disease was discarded.

A bone marrow aspirate was carried out reporting myelodysplasia. Results of the bone marrow biopsy showed hypercellularity and alteration of the three hematopoietic lines with blasts presence, iron stain demonstrated ringed sideroblasts. Hematologic treatment was initiated with continuous Cyclophosphamide weekly application.

The diagnosis of MDS type refractory anemia with ringed sideroblasts according to the WHO classification for MDS was established.

Results

In spite of all medical and therapeutical efforts, patient deceased 6 months after diagnosis. At every hemodialysis treatment, the patient received subcutaneous human recombinant erythropoietin 3 times a week along with hematologic prescription based in a weekly dose of Cyclophosphamide for a 6 months period. On the other hand diabetes and high blood pressure remained controlled, bleeding from the digestive tract remitted, still, after a long-time treatment and multiple blood transfusions performed trying to increase hemoglobin levels which persisted in low ranges, our patient presented clinical worseness, progressive deterioration, chronic anemia with low hemoglobin ranges in spite of therapeutic medical management of the MDS. Hematologic alternative treatment was proposed with Lenalidomide and stimulants of colony forming units as well as an hematopoietic cell transplantation was suggested, nevertheless, patient and her relatives decided to interrupt any type of treatment for economic reasons, then patient deceased 6 months after MDS diagnosis for cardiac arrest, no reanimation measures were performed.

Discussion

In México we don't have statistical information about MDS because of the lack of epidemiological studies, whereby the estimates

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are similar to the reported in other countries [1-2]. As mentioned before the main etiology of primary MDS is unknown [13-15]. Our patient presented an idiopathic MDS since she did not have risk factors except for the age to develop chronic anemia and present this syndrome in its primary form. Her medical history reported neither treatment with antineoplastic drugs nor family history of blood dyscrasias, also she didn't have a tobacco use history. So, the only explicable cause was the age, which is over 70-years-old.

It was necessary to find causal associations between her comorbidities and the manifestation of the disease, however, the clinical record wasn't complete. As Mexican guidelines mention, the MDS diagnosis is based in the exclusion of other diseases that by laboratory manifest as cytopenias and dyspoiesis that are caused by infectious agents such as virus (HIV, hepatitis, and parvovirus), antineoplastic drugs, immunosuppressive therapy, B12 deficiency or alcohol usage [1-3]. The diagnosis requires a complete blood study, peripheral blood smears, bone marrow aspiration and biopsy with iron stain, basal erythropoietin, iron and ferritin studies, all of which we performed in our patient corroborating the diagnosis of MDS type refractory anemia with ringed sideroblasts, she presented dyspoiesis of >10% in the three hematopoietic lines.

Our patient was not a candidate for support treatment taking into account that she required transfusion support as in early stages of the chronic anemia diagnosis as with the MDS diagnosis in multiple occasions; she received more than 27 blood and platelet transfusions. Call our attention she didn't present any kind of infection regarded to the alteration of the white cell line.

It is known that the gold standard treatment for MDS is the hematopoietic cell transplant, though, as already mentioned patient and her relatives rejected this possibility. Hematopoietic cell transplant is the only curative treatment nowadays.

It is important to be aware of these syndromes in order to suspect them and perform an adequate protocol study in order to increase our patient's quality of life and establish a prompt treatment in order to diminish complications. As in our patient, chronic diseases contribute to the increased mortality, because of that, we must identify the risk population that could present MDS and take the necessary measures into action plans.

Conclusions

Myelodysplastic syndromes are most common in the elderly population; patients with chronic diseases have a higher risk for presenting MDS, the chronic cytopenias due to these syndromes predispose to a high mortality risk and decrease in life quality becoming an important public health problem. It's our obligation as researchers and physicians to promote and stick to the national and international guidelines regarded to MDS to contribute in the decrease of fatal cases and improve in the soon diagnosis and early treatment of these syndromes.

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Conflict of Interests

None of the authors have conflicts of interest or something to disclose.

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