Clinical case
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The clinical application of Della-Porta et al score in a Mexican patient with myelodysplastic syndrome.

Aplicación clínica de la puntuación Della-Porta y colaboradores en un paciente mexicano con síndrome mielodisplásico

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Abstract

BACKGROUND: The myelodysplastic syndromes are one of the most studied diseases in hematology in recent years. By definition and according to the World Health Organization Classification of Tumours of hematopoietic and Lymphoid Tissues 2017, myelodysplastic syndromes are a group of clonal hematopoietic stem cell diseases characterized by cytopenia, dysplasia in one or more of the major myeloid lineages, ineffective hematopoiesis, recurrent genetic abnormalities and increased risk of developing acute myeloid leukemia (AML). To identify in a quick way this disease, we designed a worksheet based on the article of Matteo Della-Porta et al to developed a systematic approach to assess the morphological features in the bone marrow smears of three cell lineages in patients with myelodysplastic syndromes and provide the basis to validate flow cytometric and immunohistochemistry data.

CLINICAL CASE: A 47-year-old male patient in whom we applied a worksheet that we designed based on Della-Porta score criteria to each cellularity lineage in the bone marrow smears and we obtained significant results according to the bone marrow biopsy final report.

CONCLUSIONS: If we apply the worksheet that we designed base on Della-Porta score in the bone marrow smears myelograms, we can identify in early stages myelodysplastic syndromes processes.

KEYWORDS: Myelodysplastic syndrome; Bone marrow.

Resumen

ANTECEDENTES: Los síndromes mielodisplásicos son unas de las enfermedades más estudiadas en hematología en los últimos años. Por definición y según la clasificación de tumores de tejidos hematopoyéticos y linfoides de la Organización Mundial de la Salud (WHO) 2017, los síndromes mielodisplásicos son un grupo de enfermedades de las células madre hematopoyéticas clonales que se distinguen por citopenias, displasia en uno o más de los principales linajes mieloides, hematopoyesis ineficaz, anormalidades genéticas recurrentes y mayor riesgo de desarrollar leucemia mieloide aguda. Para identificar de manera rápida esta enfermedad, diseñamos una hoja de trabajo basada en el artículo de Matteo Della-Porta y colaboradores para desarrollar un enfoque sistemático para evaluar las características morfológicas en los frotis de médula ósea en tres líneas celulares en los pacientes con síndromes mielodisplásicos y proporcionar la base para validar datos de citometría de flujo e inmunohistoquímica.

CASO CLÍNICO: Paciente masculino de 47 años de edad en quien aplicamos una hoja de cálculo diseñada con base en los criterios del índice de Della-Porta para cada linaje celular en frotis de médula ósea y obtuvimos resultados significativos de acuerdo con el reporte final de la biopsia de médula ósea.

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CONCLUSIONES: Si aplicamos la hoja de cálculo que diseñamos con base en el índice de Della-Porta en mielogramas de frotis de médula ósea, podemos identificar procesos de síndromes mielodisplásicos en etapas tempranas.

PALABRAS CLAVE: Síndrome mielodisplásico; médula ósea.

CASE REPORT

A 47-year-old male patient was presented in the Hematology and Internal Medicine Center (CHMI) in Puebla, Puebla, Mexico, with the main complaints of fatigue, myalgia, lightheadedness, palpitations, arthralgia and dyspnea of 2-weeks evolution with recent hemorrhoidal bleeding. Complete blood count (CBC) showed hemoglobin of 4.9 g/dL, hematocrit of 15.8%, MCV of 87.8 fL, MCH of 27.2 pg, MCHC of 31.01%, RDW of 21.9%, leucocytes of 2.7 x 10^9/L, neutrophils 57%, lymphocytes 36.2%, monocytes 5.8%, eosinophils 0.6%, basophils 0.4%, total platelets of 132 x 10^9/L, erythrocytes sedimentation rate (ESR) of 36 mm/h. Serum chemistry studies revealed a functional fibrinogen of 441.7 mg/dL.

The peripheral blood (PB) smear showed poikilocytosis (+/+++), ovalocytes (+/+++), anisocytosis (+/+++), anisochromia (+/+++), without circulating blasts. Bone marrow (BM) aspirate smear showed decreased cellularity, normoblasts 38% (**Figure 1**), myeloid erythroid ratio 1:1.6, myeloid precursors 15.6%, myeloid mature 33.4%, blasts 1.4% with Aüer-rods (**Figure 2**) and lymphocytes 10.8%. Monolobar megakaryocytes, mycromegakaryocytes and binucleated megakaryocytes have been observed in more than 5% of total (**Figure 3**). Flow cytometry immunophenotype (FCI) studies did not show abnormal expression of B and T cell markers. The BM biopsy was a hypercellular marrow with erythroid hyperplasia, dyserythropoiesis and dysmegakaryopoiesis compatible with Myelodysplastic Syndrome (MDS). Additional immunohistochemical (IHQ) staining with TRAP was negative, CD138 (+) in plasma cells 8%, CD34 + (1%). We applied a worksheet that we designed based on Della-Porta score criteria (**Table 1**) to each cellularity lineage in the BM smears and we obtained significant results according to the bone marrow biopsy final report.

INTRODUCTION

Myelodysplastic syndromes (MDS) are one of the most studied pathologies in hematology in recent years. By definition and according to the World Health Organization (WHO) Classification of Tumours of hematopoietic and Lymphoid Tissues 2017, MDS are a group of clonal hematopoietic stem cell diseases characterized by cytopenia, dysplasia in one or more of the major myeloid lineages, ineffective hematopoiesis, recurrent genetic abnormalities and increases risk of developing acute myeloid leukemia (AML).[1] These diseases are extremely heterogeneous disorders, which range from indolent disease with near-normal life expectancy for patients, to forms similar to AML. This clinical heterogenecity possibly results from the different somatic mutations that caused the original clonal proliferation

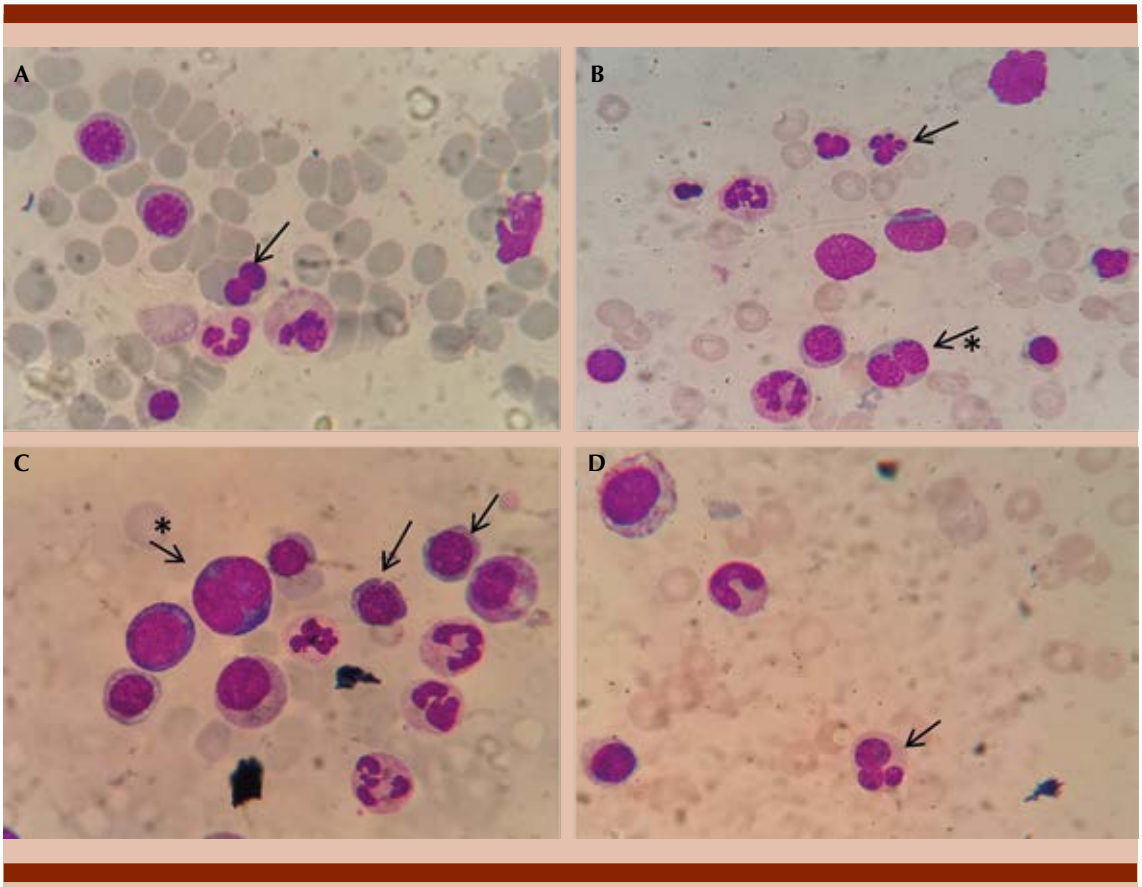

Figure 1. Patient with erythroid lineage changes. **A.** Double nucleated erythroid precursor. **B.** Erythroid dysplasia. * Double nucleated erythroid precursor. **C.** Cytoplasmatic fraying. * Double nucleated erythroid precursor. **D.** Erythroid dysplasia.

of myelodysplastic stem cells.[2] If we are going to consider MDS as a possible diagnosis, first of all, the patient most have cytopenias in multiple lineages.[3]

Diagnosis of myelodysplastic syndromes

Currently, there are different subtypes of MDS. Many international societies classify MDS subtypes by different factors; two of the most important and better known systems to classify MDS are the French American British (FAB) Classification System and the WHO Classification System, the latter being the most current and the most updated.[4] The WHO classification proposed an alternative that incorporated molecular and cytogenetic factors; since then, this classification has been updated twice, once in 2008 and then again in 2016.

FAB Classification

The FAB Classification divided the MDS into five subtypes based on the percentage of blasts in the BM and the PB, the number of ring sideroblasts (RS) and the degree of monocytosis (elevated number of white blood cells) as follows:[4]

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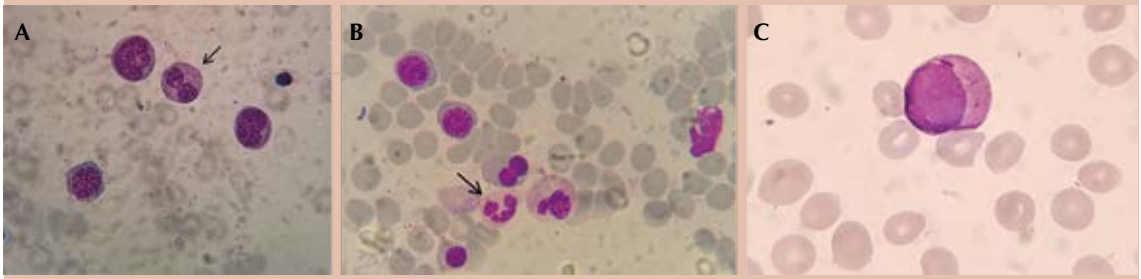

Figure 2. Patient with granulocytic lineage changes. **A.** Pseudo Pelger-Hüet anomaly. **B.** Neutrophil hypogranulation. **C.** Aüer Rods.

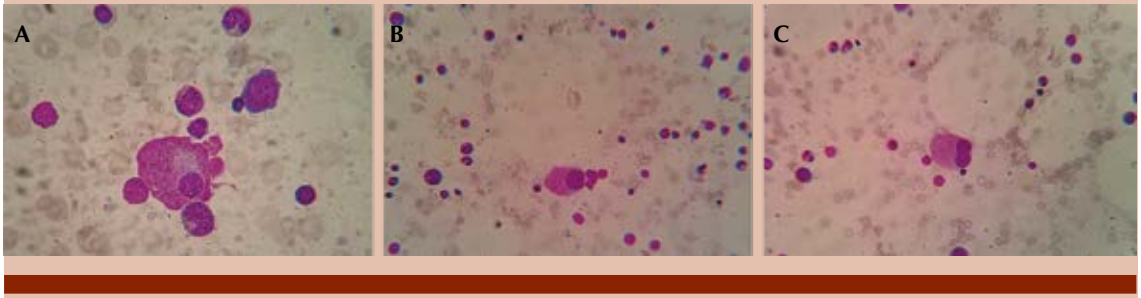

Figure 3. Patient megakaryocytic lineage changes. **A.** Monolobar megakaryocyte. **B.** Micromegakayiocyte. **C.** Small binucleated megakaryocyte.

- Refractory anemia (RA)
- Refractory anemia with ringed sideroblasts (RARS)
- Refractory anemia with excess blasts (RAEB)
- Refractory anemia with excess blasts in transformation (RAEB-T)
- Chronic myelomonocytic leukemia (CMML)

WHO Classification

The current WHO guidelines identify six subtypes of MDS based on the results of PB and BM test; and the number of dysplastic lineages is relevant for distinguishing between the types of MDS and may be important of predicting disease behavour.[1,4,5] They are classified in 6 subtypes:

- MDS with single lineage dysplasia (MDS-SLD)
  - Refractory anemia (RA)
  - Refractory neutropenia (RN)
  - Refractory thrombocytopenia (RT)
- MDS with ring sideroblasts (MDS-RS)
  - Single lineage dysplasia (MDS-RS-SLD)
  - Multilineage dysplasia (MDS-RS-MLD)

Table 1. Morphological criteria and scoring for myelodysplastic syndromes in bone marrow*

Definition of cell lineage dysplasia	Cells with abnormality (%)	Interobserver agreement	Score	Px. score	Pos (≥ 3)/ Neg (< 3)
Erythroid lineage					
Megaloblastoid changes	> 5	0.83	2	-	
Bi-or multinuclearity	> 3	0.87	1	-	
	> 5		2	**2**	
Nuclear lobulation or irregular contours	> 3	0.84	1	**1**	
Pyknosis	> 5	0.81	1	-	**Positive**
Cytoplasmatic fraying	> 7	0.82	1	**1**	
Ring sideroblasts	> 5	0.95	2	-	
	> 15		3	-	
Ferritin sideroblasts	> 30	0.92	1	-	
			Final score:	**4**	
Granulocytic lineage					
Myeloblasts	> 3	0.92	1	**1**	
	> 5		3	-	
Aüer rods	> 1	0.9	3	**3**	
Pseudo Pelger-Hüet anomaly	> 3	0.87	1	**1**	
	> 5		2	-	**Positive**
Abnormal nuclear shape	> 7	0.86	1	-	
Neutrophil hypogranulation	> 3	0.81	1	**1**	
	> 5		2	-	
			Final score:	**6**	
Megakaryocytic lineage					
Micromegacaryocytes	> 5	0.88	3	**3**	
Small binucleated megakaryocytes	> 5	0.81	1	**1**	
Megakaryocytes with multiple separated nuclei	> 5	0.84	2	-	**Positive**
Hypolobated or monolobar megakaryocytes	> 5	0.86	2	**2**	
			Final score:	6	
Suggestive morphological diagnosis:			Pb. Myelodysplastic syndrome		

* Della Porta MG. Leukemia 2015.
Step A: Standardized definition of morphological abnormalities and representative pictures.
Step B: Percentage of hematopoietic cells carrying the specific morphological abnormality.
Step C: Inter-observer agreement between two morphologist expert panels was evaluated in bone marrow samples.
Step D: Erythroid dysplasia was defined in the presence of a score value X3 (a minimum of 10% of dysplastic erythroid cells is required to reach a score value X3).
Granulocytic dysplasia was defined in the presence of a score value X3 (a minimum of 10% of dysplastic granulocytic cells is required to reach a score value X3, with the exception of cases with 45% blasts or with the presence of Auer rods). Megakaryocytic dysplasia was defined in the presence of a score value X3; (a minimum of 10% of dysplastic megakaryocytes is required to reach a score value X3, with the exception of cases with 45% micromegakaryocytes).

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- MDS with multilineage dysplasia (MDS-MLD)
- MDS with excess blasts (MDS-EB)
  - MDS with excess blasts-1 (MDS-EB-1)
  - MDS with excess blasts-2 (MDS-EB-2)
- MDS with isolated del(5q)
- MDS unclassifiable
  - With 1% blood blasts
  - With SLD and pancytopenia
  - Based on defining cytogenetic abnormality

Also, we can use other tools to diagnose MDS, one of them is the International Prognostic Scoring System (IPSS) and in this classification, we have three main different subtypes systems: The IPSS, IPSS Revised (IPSS-R) and the WHO classification-based Prognostic Scoring System (WPSS).

IPSS

The IPSS score is the most commonly used to staging the prognosis of MDS patients.[6] IPSS (**Table 2**) uses three prognostic indicator to predict the course of the patient's disease:[6]

- The percentage of leukemic blast cells in the marrow
- The type of chromosomal changes, if any, in the marrow cells (cytogenetics)
- The presence of one or more low cell counts (cytopenias)

The score have been divided in three factors; the first one is, if the patient have blast cells in the BM less than 5%, the score is 0; if they have 5% to 10% of blasts, the score is 0.5 points; if they have 11 to 20% of blasts, the score is 1.5 points; and if they have 21 to 30% of blasts, the score is 2.0 points.

The second one is about cytogenetics or chromosomic changes and if there is no evidence of the del(5q) or del(20q), the score is 0 points; if there are 3 or more abnormalities, or abnormal chromosome 7, the score is 1.0 points; and if there are other abnormalities, the score is 0.5 points.

The third and last factor is about the cytopenias; if we found 0 or only 1 cytopenia, like anemia, neutropenia or thrombocytopenia, the score is 0; but if there are 2 or 3 cytopenias, the score is 0.5 points.

If we add the calculated score of our patient according to the previous points, we can categorize into risk groups based on a total risk score: low, if the patient have a total IPSS risk score equal to 0; intermediate – 1, if the total IPSS risk score is equal to 0.5 to 1 point; intermediate – 2, if the total IPSS risk score is equal to 1.5 to 2.0 points and high, if the total IPSS risk score is equal or greater to 2.5 points.[6]

IPSS-R

This is a revised IPSS score and it is also known as the IPSS-R score, which covers the same disease factors as the IPSS, but the factors are identified in a more detailed way.[6] The IPSS-R (**Table 3**) shows five disease factors:

- Percentage of blasts in BM
- Chromosomic changes (cytogenetics)
- Cytopenias
  - Hemoglobin levels
  - Absolute neutrophil count
  - Platelet count

Table 2. The International Prognostic Scoring system (IPSS) Score for risk stratification of myelodysplastic syndrome

Factors	Prognostic factors scored	Criterion	Score
Blast cells in bone marrow	Less than 5%	Present	0
	5% to 10%	Present	0.5
	21% to 30%	Present	1.5
	Greater than 10%	Present	2
Cytogenetics (chromosome changes)	None, del(5q), del(20q)	Present	0
	3 or more abnormalities, abnormal chromosome 7	Present	1
	Other abnormalities	Present	0.5
Cytopenias	Number of cytopenias (anemia, neutropenia or thrombocytopenia)		-
	None or 1	Present	0
	2 or 3	Present	0.5

Anemia: Men < 14.5 g/dL; women < 12.5 g/dL. Neutropenia: < 40%. Thrombocytopenia: < 150 x 10^3/µL.

IPSS Risk Groups Based on Total Risk Score	
Risk Group	**Total score**
Low	0
Intermediate -1	0.5 to 1
Intermediate -2	1.5 to 2
High	2.5 or higher

The score have been divided in 5 different factors; the first one is if the patient have blast cells in the BM less or equal to 2%, the score is 0; if they have greater than 2% or less than 5% of blasts, the score is 1 point; if they have 5% to 10% of blasts, the score is 2 points; and if they have greater than 10% of blasts, the score is 3 points.

The second one is about cytogenetics or chromosomic changes and if they have –Y or del(11q), the score is equal to 0; if they have normal cytogenetics changes, del(5q), del(12p), del(20q) or a double cytogenetic change including del(5q), the score is equal to 1 point; if they have del(7q) or del(20q), gain of chromosome +8, gain of chromosome +19, isochromosome(17q) and any other single or double independent clone, the score is equal to 2 points; if they have monosomy 7, inv(3)/+(3q)/del(3q), double including -7/del(7q), or a complex of 3 abnormalities, the score is equal to 3 points and if the patient have greater than 3 abnormalities, the score is equal to 4 points.

The third and the last factor is about the cytopenias, and it is divided in three sections, the first section is about hemoglobin levels (g/dL); if we found an hemoglobin level equal to or greater than 10, the score is 0, if we found 8 g/dL or less than 10 g/dL, the score is 1, and if we found less than 8 g/dL, the score is 1.5. The second section is about platelet's count (x 10^9/L of blood); if we found a count equal to or greater than 100 x 10^9/L, the score is 0, if we found a count of platelets 50 x 10^9/L or less than 100 x 10^9/L, the score is 0.5 and if the count of platelets is less than 50 x 10^9/L, the

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Table 3. The Revised International Prognostic Scoring system (IPSS-R) Score

Factors	Prognostic factors scored	Criterion	Score
Blast cells in bone marrow	Less than or equal to 2%	Present	0
	Greater than 2% to less than 5%	Present	1
	5% to 10%	Present	2
	Greater than 10%	Present	3
Cytogenetics (chromosome changes)	-Y, del(11q)	Present	0
	Normal, del(5q), del(12p), del(20q), double including del(5q)	Present	1
	del(7q), +8, +19, i(17q), any other single or double independant clone	Present	2
	-7, inv(3)/(3q)/del(3q), double including -7/ del(7q), complex: 3 abnormalities	Present	3
	Greater than 3 abnormalities	Present	4
Cytopenias	Hemoglobin level (g/dL)		-
	Equal to or greater than 10	Present	0
	- 8 to less than 10	Present	1
	- Less than 8	Present	1.5
	* Platelet count (x 10^9/L of blood)		-
	Equal to or greater than 100	Present	0
	50 to less than 100	Present	0.5
	Less than 50	Present	1
	Neutrophil count [(ANC) x 10 9/L of blood]		-
	Equal to or greater than 0.8	Present	0
	Less than 0.8	Present	0.5

IPSS-R Risk Groups Based on Total Risk Score	
Risk group	**Total score**
Very low	1.5 or lower
Low	2 to 3
Intermediate	3.5 to 4.5
High	5 to 6
Very high	6.5 or higher

score is 1. The third and last section is about neutrophil count (ANC x 10^9/L of blood); if we found a neutrophil count equal to or greater than 0.8 x 10^9/L, the score is 0 and if we found less than 0.8 x 10^9/L the score is 0.5.

Now, if we add the calculated score of our patient according to the previous points, we can categorize into risk groups based on a total risk score: very low, if the patient has a total IPSS-R risk score of 1.5 points or lower; low if the total IPSS-R risk score is 2 to 3 points; intermediate, if the total IPSS-R risk score is 3.5 to 4.5 points; high, if the total IPSS-R risk score is 5 to 6 points and very high if total IPSS-R risk score is to 6.5 points or higher.[6]

WPSS

The World Health Organization Prognostic Scoring System, better known as the WPSS score (**Table 4**), it is not used as often as the IPSS and IPSS-R. It differs from the other two systems in that it includes the MDS subtype as a prognostic factor. It also assigns a score based on the presence or absence of severe anemia.[6]

The score have been divided in three factors; the first one is to categorized MDS as one of the different subtypes described in the WHO classification; if the patient has been diagnosed with MDS-SLD, MDS-RS and MDS with isolated del(5q), the score is 0; if the patient is diagnosed with MDS-MLD the score is 1 point; if the patient is diagnosed with MDS-EB type 1 (Blasts 5%-9% in BM or 2%- 4% in PB without Aüer rods), the score is 2 points and if the patient is diagnosed with MDS-EB type 2 (Blasts 10%-19% in BM or 5%-19% in PB with presence of Aüer rods), the score is 3 points.[1,6]

The second one is about cytogenetics or chromosomic changes, it is considered a good prognostic factor when there is no evidence of chromosomic changes, if there is –Y alone, del(5q) alone, or del(20q) alone, the score is 0; then, it is considered as an intermediate prognostic factor when there are other abnormalities, in these case the score is 1 point; and it is considered as a poor prognostic factor when the patient have three or more abnormalities, such as abnormalities on the chromosome 7, the score is 2 points.

Table 4. World Health Organization Prognostic Scoring System (WPSS) score for myelodysplastic syndrome

Factors	Prognostic factors scored	Criterion	Score
Myelodysplastic syndrome classification	MDS-SLD, MDS-RS, MDS with isolated del(5q)	Present	0
	MDS-MLD	Present	1
	MDS-EB-1	Present	2
	MDS-EB-2	Present	3
Cytogenetic abnormalities	Normal, -Y alone, Del(5q) alone, Del(20q)	Good	0
	Other abnormalities	Intermediate	1
	≥ 3 abnormalities; abn ch 7	Poor	2
Anemia	Hemoglobin < 9 g/dL in men; < 8 g/dL in women	Absent	0
		Present	1

MDS: myelodysplastic syndrome; MDS-SLD: MDS with single lineage dysplasia; MDS-RS: MDS with ring sideroblasts; MDS-MLD: MDS with multilineage dysplasia; MDS-EB-1: MDS with excess blasts 1; MDS-EB-2: MDS with excess blasts 2.

WSPP risk groups based on total risk score	
Risk group	**Total score**
Very low	0
Low	1
Low-intermediate	2
High	3-4
Very high	5-6

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The third and the last factor it is about Anemia; if the patient has severe anemia in a cut-off of hemoglobin less than 9 g/dL in men and less than 8 g/dL in women, the score is 1 point.

Now, if we add the calculated score of our patient according to the previous points, we can categorize in risk groups based on a total risk score: very low, if the patient has a total WPSS risk score of 0; low if the total WPSS risk score is equal to 1 point; intermediate, if the total WPSS risk score is 2 points; high, if the total WPSS risk score is 3 to 4 points and very high total WPSS risk score if is 5 points to 6 points.[6]

Risk groups

Before initiating a treatment, we have to make groups of patients according to the condition in two different risk categories: The first one is the lower risk-MDS and the second is the higher risk-MDS. Each category includes certain risk groups from each of the scoring systems.

The **Table 5** shows how the risk groups are divided into these two main categories. It is important to note that prognostic systems and risk groups do not predict how MDS will respond to treatment but instead how MDS is likely to behave over time without treatment.

Lower risk-MDS patients tend to grow and progress slowly. It may not cause many or even severe symptoms for a long time. Hence, less intensive treatment is frequently used. In contrast, higher-risk MDS is likely to progress more quickly or become acute myeloid leukemia (AML) more quickly without treatment. It may cause more symptoms and health complications in a short amount of time. Thus, more intensive treatment is often required.

Table 5. Equivalence between different systems to estimate Risk of progression in MDS

	Lower-risk MDS	Higher-risk MDS
IPSS	Low and intermediate 1	Intermediate 2 and high
IPSS-R	Very low, low, intermediate	Intermediate, high, very high
WPSS	Very low, low, intermediate	High, very high

Immunophenotypic assessment of myelodysplastic syndromes by flow cytometry

In this disease, to make a good flow diagnostic utility is necessary to do a gating strategy on $CD34^+$ blasts with aberrant expression of certain antigens or abnormally high or low expression of normal antigens. The abnormal expression levels of CD13, CD33, CD34, CD117 and CD123 can be seen in this disease, but a decreased expression of CD38 is also useful indicator of MDS. Aberrant expression of CD2, CD5, CD7, CD10, CD19, or CD56 also supports the diagnosis of MDS. Furthermore, absent or markedly increased CD15, CD64 or CD65 expression is an additional sign of other abnormalities. Another important strategy is to check hematogones and plasmacytoid dendritic cells precursors, if there is a decrease number or absence of these cells, is also sign of MDS. It is important to mention that one abnormality by itself it is not sufficient to support the diagnosis of MDS using flow cytometry, but the combination of different aberrations usually ≥ 3 can provide sufficient support for the diagnosis.[3]

Abnormal patterns seen on maturing myeloid cells are also of substantial diagnostic utility. Myeloid hypogranulation can be evidenced by side scatter and is a sign of MDS. A decreased expression of CD10, CD15, CD33, CD38, CD64 and CD65 and increased HLA-DR (human leukocyte antigen D related) are also signs of MDS. Similar to the $CD34^+$ blasts, aberrant expression of CD2, CD5, CD7 and CD56 is also a useful finding.[3]

Abnormalities in monocytes gating, can also provide further MDS diagnostic information. Hidalgo et al[3] used a decreased expression of CD45, which can result in blending of the monocyte and granulocyte windows. Increased CD56+ expression (> 25%) is also atypical for monocytes. Additional abnormalities include decreased CD11b, CD13 or CD14.[3]

A consensus statement emphasized the importance of certain findings in supporting a diagnosis of MDS. These, include an increased frequency of $CD34^{+}$, an increased frequency of $CD19^{-}$ (> 2%), or an increased proportion of $CD38^{dim}$ and $CD34^{+}$ cells; abnormal expression of CD5, CD7, or CD56 on progenitor myeloid cells, neutrophils or monocytes; and an aberrant patterns of CD11b/CD16 and CD13/CD16 on granulocytes (the last one, is better known when it's normal as nike pattern). Consequently many authors such as Porwit et al[7] recommended the integration of flow cytometry data findings with the findings from other diagnostic tools in the diagnostic evaluation of MDS.[3]

A worksheet to identify in a quick way patients with MDS according to the morphological critera of Della-Porta score

In the Hematology Laboratory of the Clinical Laboratories of Puebla, we designed a worksheet based on the article of Della Porta et al[8] to developed a systematic approach to assess the morphological features of three cell lineages in patients with MDS involving BM and provide the basis to validate flow cytometric data and immunohistochemistry to discuss briefly (**Table 1**).

To start filling out the worksheet, first of all we have to standardize the definition of morphological abnormalities and representative pictures, then we have to start to count the BM smear in the microscope and define the percentage of hematopoietic cells carrying the specific morphological abnormality. To continue with this method, there have to be an inter-observer agreement between two morphologist experts that have evaluated the BM smears samples. Once this is done, the final step is to punctuate the morphological abnormalities found in the BM smear and start to categorize the dysplasia. For the erythroid dysplasia (**Figures 1 and 4**), this is defined by the presence of a score value of more than 3 points (X3) (a minimum of 10% of dysplastic erythroid cells is required to reach a score value X3), for the granulocytic dysplasia (**Figures 2 and 5**), is defined by the presence of a score value X3 (a minimum of 10% of dysplastic granulocytic cells is required to reach a score value X3, with the exception of cases with 45% blasts or with the presence of Auer rods) and finally, the megakaryocytic dysplasia (**Figures 3 and 6**), is defined by the presence of a score value X3; (a minimum of 10% of dysplastic megakaryocytes is required to reach a score value of 3 points, with the exception of cases with 45% micromegakaryocytes).

Differential diagnosis of myelodysplastic syndrome

Not all cases of cytopenias or dysplasia should be determined as MDS. There are other determinants that contribute to the definitive diagnosis of this disease, therefore, it is very important to make a differential diagnosis with other illness that present similar abnormalities described in MDS.[9]

Vitamin B12 or folic acid deficiency, congenital dyserythropoietic anemia, viral infections, post-transplant immunosuppressive agents or treatments with granulocyte colony stimulating factors may have some abnormal complications in those described in the MDS should therefore be discarded prior to the definitive diagnosis.[10]

http://doi.org/10.24245/rev_hematol.v21i3.4004

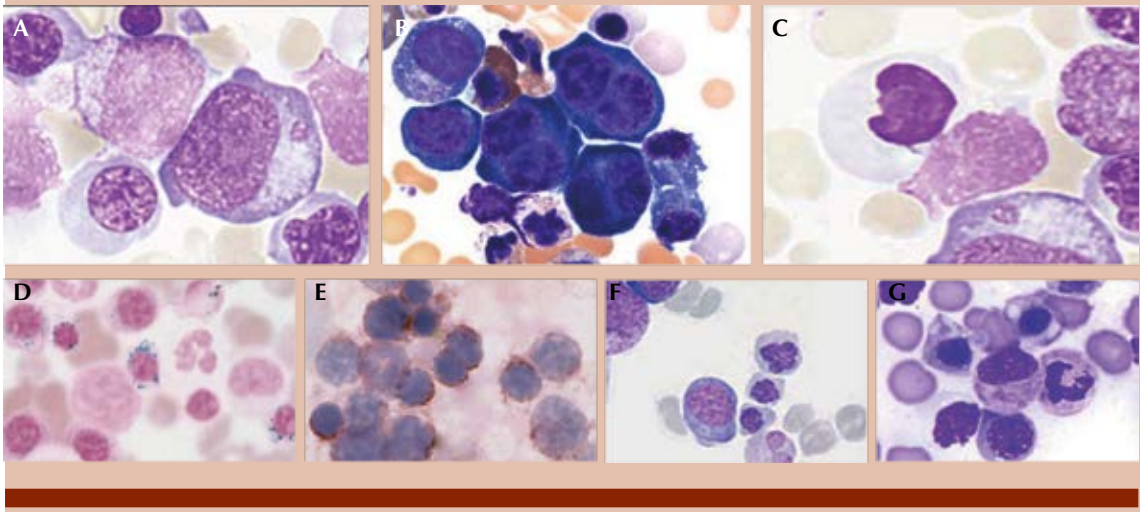

Figure 4. Others examples pictures of erythroid lineage changes. **A.** Megaloblastoid changes. **B.** Bi- or multi-nuclearity. **C.** Pyknosis. **D.** Ring sideroblasts. **E.** Ferritin sideroblasts. **F.** Nuclear lobulation or irregular contours. **G.** Cytoplasmatic fraying.
Courtesy of Bueso-Ramos CE. UTMDACC.

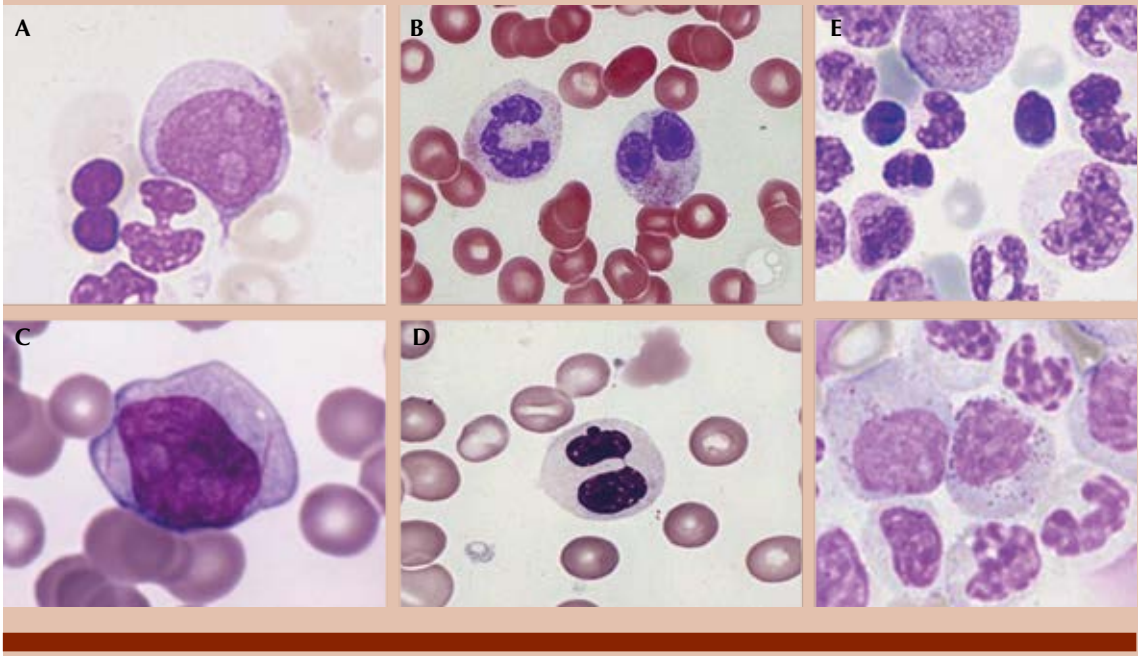

Figure 5. Other examples pictures of granulocyte lineage changes. **A.** Myeloblasts. **B.** Pseudo Pelger-Hüet anomaly. **C.** Aüer rods. **D.** Neutrophil hypogranulation. **E.** Abnormal nuclear shape.
Courtesy of Bueso-Ramos CE. UTMDACC.

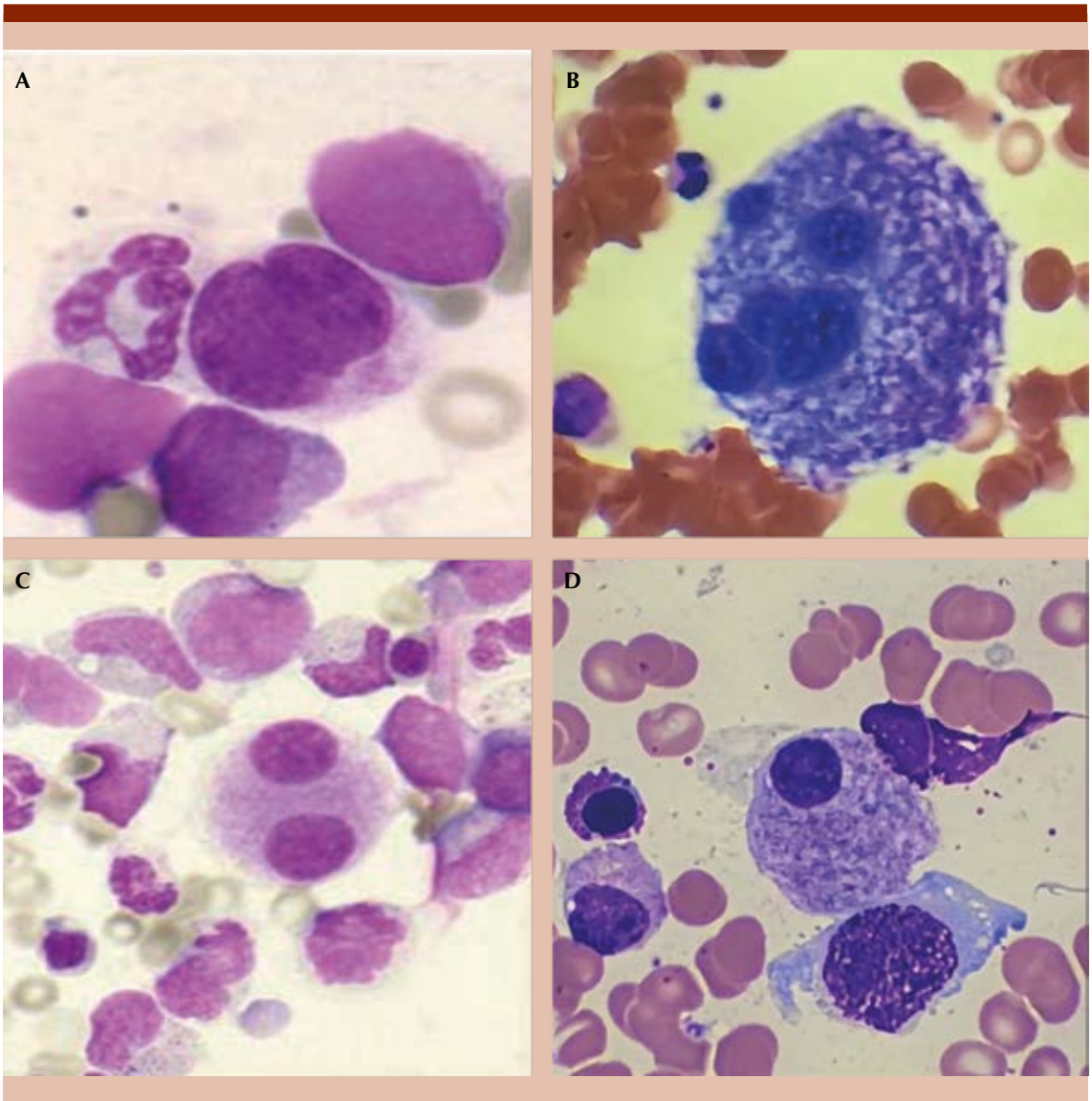

Figure 6. Other examples pictures of megakaryocyte changes. **A.** Micromegacaryocytes. **B.** Megakaryocytes with multiple separated nuclei. **C.** Small binucleated megakaryocytes. **D.** Hypolobated or monolobar megakaryocytes. Courtesy of Bueso-Ramos CE. UTMDACC.

The presence of viral infectious complicates the diagnosis of MDS, an example is reflected in HIV-positive patients; cytopenias and cell morphology are compatible, making MDS as a differential diagnosis, therefore, it is necessary to request starting serological determination.[9,11]

On the other hand, erythroid alterations such as giant precursors, multinucleated, nuclear fragmentation, carriorrexis or increase BM sideroblasts, are not specific for dysplasia and are shared with some types of anemias. The identification of an increase percentage of sid-

http://doi.org/10.24245/rev_hematol.v21i3.4004

eroblasts by Perls-Staining may be suggestive of other pathologies, such as hemolytic anemias, megaloblastic anemias or hemosiderosis.[9]

The presence of small megakaryocytes, unilobed with a halo of platelets around it, is considered as one of the elements of the MDS. In patients with 5q deletion, these types of characteristics are frequently observed, which guide the differential diagnosis of MDS with other pathologies.[1,9]

CONCLUSIONS

Mexico does not have many places with all the resources to make the complete diagnosis for a patient with the probable diagnosis of MDS, due to the non-integrated system of clinical and anatomic pathology laboratories, giving a delay of approximately 7 days between the BM smear and the BM biopsy report. If we apply the worksheet that we designed base on Della-Porta score[8] in the BM smears myelograms, we can identify in early stages the detection of a MDS process.[12]

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