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Bone Marrow Puncture (BMP): The Initial Step in the Management of Myelodysplastic Syndromes (MDS)

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ABSTRACT

Myelodysplastic Syndromes (MDS) encompass a variety of bone marrow disorders characterized by insufficient production of healthy blood cells. Myelodysplastic Syndromes (MDS) represent a cluster of bone marrow conditions where there's a deficiency in generating a sufficient quantity of healthy blood cells. Patients with MDS often exhibit an asymptomatic nature. The clinical manifestations of MDS vary widely depending on the cellular line involved. Infections, bleeding, and anemia are common features of the MDS, while unusual findings include hepatomegaly, splenomegaly and lymphadenopathy. However, the situation changes when the patient progresses to acute myeloid leukemia (AML), leading to a transformation into thrombocytosis. During the process of improving the general condition, on the third day of treatment, the patient experienced a deterioration and unfortunately passed away. The lack of medical and healthcare personnel in Indonesia and the unequal distribution of them are the reasons why patients with rare cases are still far from obtaining their health rights. An important challenge in clinical practice involves distinguishing between primary myelofibrosis and other conditions, as misidentification can delay treatment, potentially leading to patients not receiving necessary healthcare and possibly resulting in fatalities.

KEYWORDS: Bone Marrow Puncture, Myelodysplastic Syndromes

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I. INTRODUCTION

Myelodysplastic Syndromes (MDS) encompass various bone marrow conditions where there is a deficiency in generating sufficient healthy blood cells, often termed as a disorder of bone marrow failure.[1] Malfunctioning blood cells progressively dominate the bone marrow, resulting in a reduction in the number of normal blood cells (including Red blood cells carry out the function of transporting oxygen, white blood cells are crucial in the fight against infections, and platelets play an essential role in blood clotting) circulating in the bloodstream.[2]

Patients with MDS often exhibit an asymptomatic nature.[3] The clinical manifestations of MDS vary widely depending on the cellular line involved. Infections, bleeding, and anemia are common features of MDS, while unusual findings include hepatomegaly, splenomegaly, and lymphadenopathy.[4] However, the situation changes when the patient progresses to acute myeloid leukemia (AML), leading to a transformation into thrombocytosis.[5]

The diagnosis of MDS is determined through analysis of blood cell characteristics, examination of peripheral blood cell structure, and inspection of bone marrow that show cytopenia in one or more hematopoietic lines or dysplasia on blood smears. In the case of most pediatric patients, pancytopenia is more commonly encountered than just

anemia (hypocellular bone marrow). Further examinations include cytogenetic analysis and immunophenotyping.[6] However, not all healthcare facilities in Indonesia have supporting tests like bone marrow puncture. This is what contributes to the suboptimal fulfillment of the rights to health for the entire Indonesian population.

II. DISCUSSION

The initial laboratory findings indicate a reduction in count of red blood cells, levels of hemoglobin, levels of hematocrit, average volume of red blood cells (MCV), average amount of hemoglobin per red blood cell (MCH), and average concentration of hemoglobin in red blood cells (MCHC), and lymphocyte count in the patient. Meanwhile, there is a drastic increase in the number of leukocytes and platelets. The decrease in the number of blood cells that occurs in patients is called cytopenia and is a hallmark of MDS.[7]

MDS is also responsible for symptoms such as infection, anemia, and spontaneous bleeding.[7] Signs of infection can be observed from the elevated leukocyte count (43.6 10^3/ul) in the patient, while anemia is indicated by a decreased hemoglobin level (4.4 g/dl), and signs of bleeding are evident from a drastic decrease in platelet count (2618 10^3/ul).

However, blood test results alone are not sufficient to establish a diagnosis of MDS because many conditions resemble MDS, especially when viewed from their blood test results. These conditions include exposure to toxins, such as arsenic or benzene, which can cause bone marrow damage. Side effects of chemotherapy, leading to a decrease in bone marrow function. Malignancies like multiple myeloma, leukemia, Hodgkin's lymphoma, or non-Hodgkin's lymphoma. Suffering from aplastic anemia. Working in places vulnerable to exposure to chemicals or toxins, such as agricultural fields using pesticides. Having hereditary diseases, such as Fanconi anemia or Diamond-Blackfan anemia, or a family history of bone marrow disorders. Suffering from autoimmune diseases, such as lupus. Having tumors or cancers that have spread to the bone marrow. Taking certain medications, such as long-term use of anticonvulsant drugs. Suffering from infectious diseases, such as HIV/AIDS or mononucleosis.[8]

During blood tests, referred to as a complete blood count (CBC), a sample of blood is sent to the lab for analysis. People with MDS generally exhibit reduced counts of red blood cells and platelets, while their white blood cell counts typically show abnormalities.[2] However, in this case, something different occurred, namely an increase in the number of platelets.

Therefore, another examination in the form of a bone marrow puncture is needed. If blood tests suggest the presence of MDS, a bone marrow biopsy can validate the diagnosis. This procedure entails extracting a bone marrow sample, typically from the hip bone, to further assess the condition.[2]

In the BMP, more detailed information about the occurring abnormalities can be observed. Further clarification is needed to determine the precise clinical significance of bone marrow fibrosis in patients with MDS. Presently, the classification of MDS relies on assessing bone marrow dysplasia through morphological evaluation and doesn't consider histological characteristics. However, histological information complements the morphological data derived from a marrow aspirate, and diagnostic guidelines recommend performing a biopsy in all suspected cases of MDS where bone marrow examination is deemed necessary.[9]

Bone Marrow Puncture (BMP) is utilized for various purposes, including investigating unexplained anemia, abnormal red cell indices, cytopenia, or cytosis. It is also utilized to analyze abnormal morphology seen in peripheral blood smears, which can suggest bone marrow issues, as well as to diagnose, stage, and monitor various malignant blood disorders such as acute and chronic leukemia, myelodysplastic syndromes, chronic myeloproliferative disorders, lymphoma, plasma cell myeloma, amyloidosis, and mastocytosis. Additionally, BMP is utilized to explore potential bone marrow metastases, clarify focal bone lesions that are unclear on radiological imaging, investigate unexplained organ enlargement or the existence of mass lesions that cannot be biopsied, and perform microbiological cultures to investigate unexplained fever or specific infections such as disseminated tuberculosis, leishmaniasis, and malaria. It is also employed for evaluating iron stores, exploring lipid/glycogen storage disorders, and excluding hematological diseases in potential allogeneic stem cell transplant donors.[10]

Histological factors have the potential to improve the accuracy of diagnosis and prognosis within the WHO classification system. Specifically, the detection of abnormal localization of immature myeloid precursors (ALIP) and the presence of CD34+ cell aggregates have been associated with an increased risk of leukemia development in MDS.

(Figure 1)

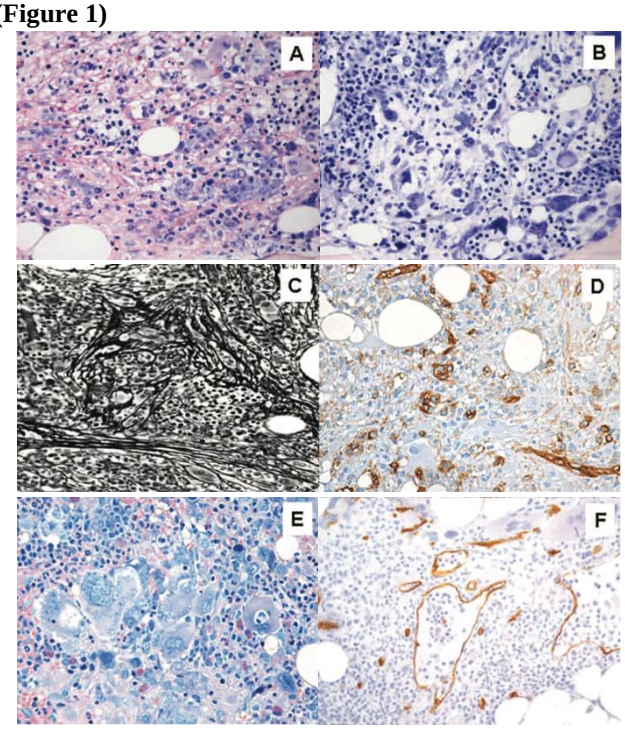


Figure 1. Demonstrates common histological findings in myelodysplastic syndrome with bone marrow fibrosis (MDS-F).

In addition to histological analysis in bone marrow puncture, cytology examination with myeloperoxidase stain, esterase stain, and staining for iron can also be performed to determine the presence of dysplasia and the percentage of blast cells. Cytogenetic testing can also be conducted to identify chromosomal abnormalities.[11] For example **(Figure 1)** we can see to many differential result from histological (A) Increased bone marrow cell density with overgrowth of erythroid cells, (B) Abnormal megakaryocytes, including those with underdeveloped lobes, occasionally forming noticeable clusters, (C) Bone marrow fibrosis detected using Gomori's silver staining technique, and (D) Clusters of CD34+ cell aggregates. A notable clinical challenge involves differentiating between MDS-F and primary myelofibrosis. MDS-F is strongly linked with elevated bone marrow cell density, heightened presence of CD34+ cells in the bone marrow, and dysplasia across multiple blood cell lineages. Primary myelofibrosis, on the other hand, exhibits distinctive features such as (E) Increased megakaryocyte production with clusters and nuclei resembling clouds or balloons, and (F) Expansion of marrow sinuses with hematopoietic activity within the sinusoidal spaces (Courtesy of Emanuela Boveri).[12]

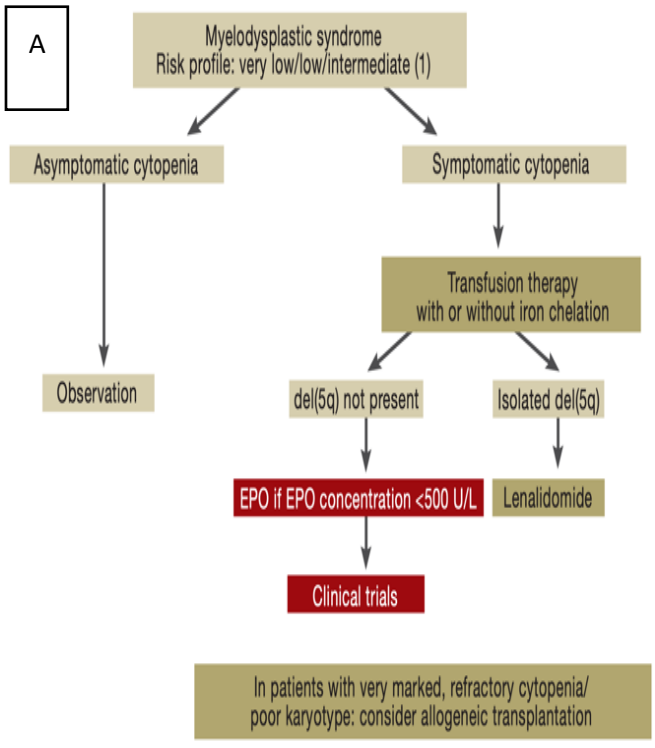
Further investigations that can assist in confirming the diagnosis of MDS involve peripheral blood or bone marrow analyses. These assessments include mutation analysis, such as bcr-abl, pdgfr-α/β (to differentiate between CMML/CML/aCML), and tet2, runx1, asxl1, sf3b1, srsf2, tp53, u2af1, dnmt3a, zrsr2, ezh2, nras, kras (if deemed necessary for confirming the diagnosis and predicting prognosis).[11]

Table 1. Differential diagnoses in myelodysplastic syndrome and suitable diagnostic assessments for identifying MDS

Differential Diagnoses	Diagnostic Test
Pure red cell aplasia (PRCA), aplastic anemia.	Cytology, histology, parvovirus B19
Toxic bone marrow injury (NSAR, lead, alcohol, etc.)	History, lab tests
Bone marrow alterations due to reactive conditions (sepsis, HIV, chronic infections, tuberculosis, autoimmune diseases, etc.), as well as copper deficiency	Cytology, history, lab tests
Monocytosis of other etiology	Molecular genetic testing, history, lab tests
Paroxysmal nocturnal hemoglobinuria (PNH)	Immunophenotyping
Immune thrombocytopenia	History, course
Megaloblastic anemia	Vitamin B12/folic acid concentration
Hypersplenic syndromes	History/clinical features (splenomegaly)
Acute leukemia (especially erythroleukemia, FAB-M6)	Cytology, genetic and molecular genetic testing
Myeloproliferative disorders, particularly aCML and PMF	Cytogenetic, histology, and molecular genetic testing
Hairy cell leukemia, LGL	Cytology, immunophenotyping, molecular genetic testing (braf, stat3), T-cell receptor
Congenital dyserythropoietic anemia (rare)	Molecular genetic (sec23b und cdan-1)

To many differential diagnoses in myelodysplastic syndrome **(Table 1)** was the point of urgency of bone marrow puncture in healthcare facilities can lead to misdiagnosis, delayed patient treatment, and may result in patients passing away without receiving the rightful access to healthcare. This risk can occur due to the numerous diseases that resemble MDS.

Errors or delays in establishing the diagnosis of MDS due to the absence of BMP in the healthcare facility can have fatal consequences for patients with an MDS diagnosis. The management of MDS can be categorized as follows:
(Figure 2)



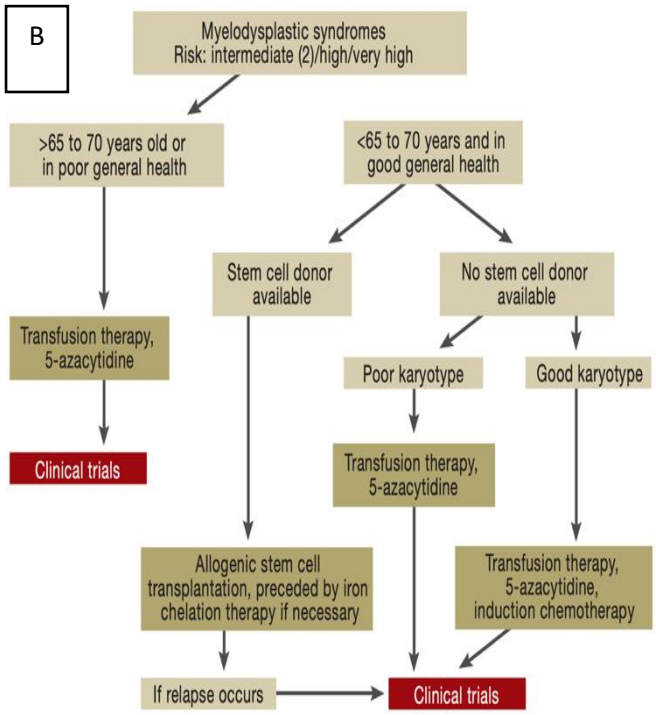


Figure 2. Treatment plan for myelodysplastic syndrome: (A) People classified as having very low, low, or intermediate risk levels; (B) People with intermediate, high, or very highrisk levels.

This is the problem in Indonesia. Not all healthcare facilities can conduct bone marrow puncture examinations, especially in the era of healthcare through the Social Security Organizing Agency for Health (BPJS-Kesehatan), a diagnosis must be established by a specialist doctor according to their specialization. If this does not align, BPJS will not reimburse the treatment costs to healthcare facilities because it does not comply with Indonesia Case-Based Groups (INA-CBG's).[13] For example, the diagnosis of MDS must be established by a specialist doctor in internal medicine with consultation in medical hematology oncology (Sp.PD K-HOM). However, the number of specialist doctors in internal medicine with consultation in medical hematology oncology is only 139 doctors and is only distributed in 17 provinces.[14] The shortage of medical and healthcare personnel in Indonesia and the unequal distribution of them are the reasons why patients with rare cases are still far from obtaining their health rights.

III. CONCLUTION

Myelodysplastic Syndromes (MDS) is a group of bone marrow disorders where the bone marrow fails to produce enough healthy blood cells. Patients with MDS often exhibit asymptomatic symptoms, with common features including infections, bleeding, and anemia. However, the situation changes when the patient progresses to acute myeloid leukemia (AML), leading to thrombocytosis. The diagnosis of MDS is based on hematologic examination, peripheral blood cell morphology, and bone marrow examination, which show cytopenia in one or more hematopoietic lines or dysplasia on blood smears. Further examinations include cytogenetic analysis and immunophenotyping. In Indonesia, not all healthcare facilities are equipped with essential tests such as bone marrow puncture, which hampers the adequate fulfillment of the right to health for the entire population.

REFERENCES

I. Center for Clinical Haematology. What Are Myelodysplastic Syndrome (MDS)? *Center for Clinical Haematology* https://cfch.com.sg/myelodysplastic-syndromes-mds/.

II. Parkway Cancer Center. Myelodysplastic Syndrome (MDS). *Parkway Cancer Center* https://www.parkwaycancercentre.com/id/idn/learn-about-cancer/types-of-cancer/cancer-details/myelodysplastic-syndromes-(mds).

III. Wijaya, I. G. H. A. Myelodysplastic Syndromes: Laporan Kasus. *Intisari Sains Medis* **13**, 613–617 (2022).

IV. Nalluru, S. S., Jindal, V., Piranavan, P., Kate, Y. & Siddiqui, A. D. Splenic Infarction Secondary to Myelodysplastic Syndrome: Unravelling More Etiologies. *AME Case Rep.* **3**, 1–4 (2019).

V. Tim Promkes RSST. Akut Myeloid Leukemia. *Kemeterian Kesehatan Direktorat Pelayanan Kesehatan* https://yankes.kemkes.go.id/view_artikel/2185/akut-myeloid-leukemia (2023).

VI. Agustin, B. N. & Maani, H. Gambaran Hematologi Pasien Myelodysplastic Syndrome di RSUP Dr. M. Djamil Padang. *J. Kesehat. Andalas* **8**, (2019).

VII. MDS Foundation. What is MDS? *MDS Foundation* https://www.mds-foundation.org/what-is-mds/.

VIII. Tim Promkes RSST. Pansitopenia. *Kemeterian Kesehatan Direktorat Pelayanan Kesehatan* https://yankes.kemkes.go.id/view_artikel/2169/pansitopenia (2023).

IX. Bowen, D. *et al.* Guidelines for the Diagnosis and Therapy of Adult Myelodysplastic Syndromes. *Br. J. Haematol.* **120**, 187–200 (2003).

X. Arthamin, M. Z. Evalution Blood Smear and Bone Marrow Aspiration. in *Buku Rumpun Patologi Klinik: Enhance The Role of Laboatory Medicine in Evidance-Based-Planning and Dicision Making to SUpport Health Transformation in Indonesia* (PDS PatKlin, Pekanbaru, 2023).

XI. Germing, U., Kobbe, G., Haas, R. & Gattermann, N. Myelodysplastic Syndromes: Diagnosis, Prognosis, and Treatment. *Dtsch. Ärztebl. Int.* **110**, 783–790 (2013).

XII. Della Porta, M. G. & Malcovati, L. Myelodysplastic Syndromes with Bone Marrow Fibrosis. *Haematologica* **96**, 180–183 (2011).

XIII. Roesbiantoro, A. *et al.* Description of Characteristics, Diagnosis And Financing Of BPJS Patients In ENT Poly

Health Service Facility Level 2. *Med. Technol. Public Health J.* **6**, 169–176 (2022).

XIV. Arlita, D. Dokter Spesialis Onkologi Tidak Merata, Jejaring Para Ahli Dioptimalkan. *Kompas.com* https://www.kompas.id/baca/ilmu-pengetahuan-teknologi/2021/11/02/dokter-spesialis-onkologi-tidak-merata-jejaring-para-ahli-dioptimalkan (2021).