Health Sciences

UM6SS EDITIONS

Volume 1 | Issue 1 Article 16

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Recommended Citation

Bendari, Mounia; Bouanani, Nouama; Khalfaoui, Mohamed Amine; Ahnach, Maryam; Laaraj, Aziza; and Doghmi, Kamal (2020) "Renal Infarction and Pulmonary Embolism in Patient with Myelodysplastic/Myeloproliferative Neoplasm Unclassifiable," *Health Sciences*: Vol. 1: Iss. 1, Article 16.
Available at: https://doi.org/10.15342/hs.1.182

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Health Sciences
2020, Volume 1, ID 182
DOI: 10.15342/hs.1.182

CASE REPORT

Renal Infarction and Pulmonary Embolism in Patient with Myelodysplastic/Myeloproliferative Neoplasm Unclassifiable

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ABSTRACT
The myelodysplastic syndrome-myeloproliferative neoplasms (MDS/MPNs) are defined by a group of heterogeneous hematological malignancies resulting from stem cell−driven clonal growth of pathological hematopoietic progenitors and ineffective hematopoiesis, they are characterized concomitant myelodysplastic and myeloproliferative signs. Myelodysplastic/myeloproliferative disorders have been considered to have a higher risk of thrombus formation.
We report a rare case about a 64 years old Moroccan woman, experienced renal infarction (RI) associated with pulmonary embolism as a complication of a myelodysplastic/myeloproliferative disorder.
The patient complained of acute-onset severe left flank pain, a contrast-enhanced computed tomography (CT) of the chest and abdomen revealed RI by a large wedge-shaped defect in the right kidney with pulmonary embolism.
The biological exam showed deep anemia, the bone marrow aspiration found myelodysplasia. the bone biopsy showed signs of myeloproliferative disease. The karyotype was normal, BCR-ABL, JAK2, CALR mutations were absent, and MPL mutation was positive. The International Prognostic Scoring System (IPSS-R) was 0, and the patient was included in the low risk group.
Anticoagulation therapy was initiated with heparin to treat RI and pulmonary embolism. Three months later, pulmonary embolism had resolved without the appearance of additional peripheral infarction.
This case emphasizes the need to consider myelodysplastic/myeloproliferative disorders as a cause of infraction renal and pulmonary embolism.
KEYWORDS: Myelodysplastic Syndrome, Myeloproliferative Neoplasms, Pulmonary Embolism, Renal Infarction.

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INTRODUCTION

The myelodysplastic syndrome-myeloproliferative neoplasms (MDS/MPNs) are defined by a group of heterogeneous hematological malignancies resulting from stem cell−driven clonal growth of pathological hematopoietic progenitors and ineffective hematopoiesis. (1) They are characterized by bone marrow dysplasia and cytopenia. They are also characterized by an increased risk of development of secondary acute myeloid leukemia. (2)

The last revision of the WHO classification of myeloid neoplasms and acute leukemia updated the MDS/MPN category, on the new version (2016), MDS/MPN syndromes include chronic myelomonocytic leukemia (CMML), atypical chronic myelogenous leukemia (aCML), juvenile myelomonocytic leukemia (JMML), MDS/MPN with ringed sideroblasts and thrombocytosis (MDS/MPN-RS-T), as well as unclassifiable forms of

mixed myelodysplastic/myeloproliferative disorders (MDS/MPN-U). (3)

Treatment is not proposed systematically for all patients, asymptomatic patients are not treated initially, treatment is reserved for symptomatic patients, such as those requiring frequent blood transfusions. Prognosis and overall survival depend upon multiple factors such as the severity of cytopenias, the percentage of blasts in the peripheral blood and bone marrow, and karyotype.

The International Prognostic Scoring System (IPSS-R) is utilized to define life expectancy and leukemic progression [4,5]. Transformation to acute myeloid leukemia (AML) occurs in approximately 10% and 70% of lower- and higher-risk (HR) patients, respectively. (6)

Myelodysplastic/myeloproliferative disorders have been considered to have a higher risk of thrombus formation. In this manuscript, we report the case of a 64-year-old Moroccan woman suffering from myelodysplasic/myeloproliferative disorder with deep thrombosis consisting on pulmonary embolism and renal infarction.

CASE REPORT

We report a rare case about a 64 years old postmenopausal Moroccan woman, without medical history, was admitted to the emergency department with acute-onset severe left flank pain with dyspnea which started a week before admission.

The initial examination found a patient in good general condition, Performance Status was at 2, a blood pressure of 140/64 mmHg, and a heart rate of 85 beats per minute. She was afebrile, with normal saturation. She had diffuse abdominal tenderness, with splenomegaly (17cm).

Laboratory testing revealed anemia at 6.8g/dl, white blood count at 8.9×10^3/L, absolute neutrophil count at 7.2×10^3/L, absolute monocyte counts at 0.5×10^3/L eosinophile count at 0.07×10^3/L, and lymphocytes count at 1.03×10^3/L. Platelet count at 416×10^3/L and lactate dehydrogenase at 145 IU / L.

Electrolytes, renal function, and liver function were normal, albumin was 43 (32–45) g/L and urine analysis was sterile.

CT scan of the chest and abdomen showed no signs of pancreatitis or stones neither, evidence of ischemic bowel or perforation was noted. It showed a focal area of infarction in the right kidney with pulmonary embolism. At first, we suspected the diagnosis of nephrolithiasis and pyelonephritis, but the patient was afebrile and urine analysis was normal, then the diagnosis of renal infarction was retained, the Ultrasound for lower extremity deep venous was normal.

The bone marrow aspiration showed normocellular marrow and found a multiline dysplasia (more than 33% of red cell precursors have signs of dysplasia, granulocytic precursors have hyposegmentation and hypersegmentation on 20% of cell) with blasts at 2%, no ring sideroblasts by iron stains were found, Relevant immunostains were performed including myeloperoxidase (MPO), CD34, CD117, CD61 for megakaryocytes, CD68 for monocytes, CD20, and CD19 for B-cell lineage and CD3 for T-cell lineage. The CD34, is an antigen expressed on progenitor and early precursor cells, which is a marker for blasts, it showed the absence of blasts. New Generation Sequencing (NGS) was not performed.

The bone marrow biopsy showed a myeloproliferative syndrome type essential thrombocytemia. The karyotype was normal, molecular biology showed the absence of BCR-ABL rearrangement and JAK2 V617F (exon12) and CALR mutations. The mutation in the MPL gene (exon10) was positive.

According to WHO criteria, this patient was classified in the category SMD / SMP unclassifiable. The International Prognostic Scoring System (IPSS-R) was 0, and the patient was included in the low risk group. No treatment was indicated for the hematological disease.

The patient received anticoagulation therapy was initiated with heparin to treat RI and pulmonary embolism. Three months later, pulmonary embolism had resolved without the appearance of additional peripheral infarction.

The patient was not overweight, she had no past medical history of diabetes or high blood pressure, neither hypercholesterolemia, she doesn't smoke, the MDS/MNP was considered as the unique origin of deep thrombosis

To date, the patient received a preventive dose of 10 mg of Rivaroxaban per day continuously after six months of treatment with heparin.

DISCUSSION

Myelodysplastic/ Myeloproliferative neoplasms are a rare and heterogeneous hematologic neoplasm, the annual incidence of MDS is more than 20 per 100,000 people. (7) The median age of diagnosis is 71 to 76 years (2). Patients suffering from MDS/MPN neoplasms can be clinically asymptomatic for years and may have incidental findings of cytopenias on routine labs. Others may have complained about signs and symptoms related to bone marrow failures such as fatigue, bleeding, or infections. (8) the particularity of this entity is the association between MDS signs and MPN features: MDS-like features consist of cytopenias and dysplasia of various cell lines while MPN-like features can be traduced by constitutional symptoms (e.g. night sweats and/or weight loss), elevated blood counts as well as extramedullary infiltration.

The underlying pathogenesis responsible for this group of neoplasms remains unclear as does the molecular convergence point that biologically defines the MDS/MPN category.

Transformation to acute myeloid leukemia (AML) occurs in approximately 10% and 70% of lower- and higher-risk (HR) patients, respectively. (6)

The last revision of the WHO classification of myeloid neoplasms and acute leukemia updated the MDS/MPN category, on the new version (2016), MDS/MPN syndromes include chronic myelomonocytic leukemia (CMML), atypical chronic myelogenous leukemia BCR/ABL-negative (aCML), juvenile myelomonocytic leukemia (JMML), MDS/MPN with ringed sideroblasts and thrombocytosis (MDS/MPN-RS-T), as well as

unclassifiable forms of mixed myelodysplastic/myeloproliferative disorders (MDS/MPN-U). (3)

The prognosis for patients with MDS/MPN disorder is heterogeneous; depending on the number of cytopenia, presence of blasts, severity, and type of cytogenetic defect. Karyotype with a good prognosis includes normal karyotype, -Y, deletion 5q, deletion 20q. Poor risk karyotypes include complex cytogenetics (greater than three abnormalities), or chromosome 7 abnormalities. All other karyotypes are categorized as intermediate risk. Based on these findings, a score is calculated to determine a risk score of either low, intermediate-1 or intermediate-2, or high risk. (9)

The International Prognostic Scoring System (IPSS-R) is utilized to define life expectancy and leukemic progression. [4,5] It includes the degree of pancytopenia, cytogenetic abnormalities, and some blasts. The early stage, also known as very low-risk and low-risk MDS, is characterized by low IPSS-R scores. Intermediate-, high-, and very high-risk MDS patients have high IPSS-R scores with profound pancytopenia, unfavorable cytogenetic abnormalities, and increased blast count.

More than 100 genes have been identified to be recurrently mutated in MDS, and these encode spliceosome components, chromatin remodeling factors, epigenetic pattern modulators, and transcription factors among others. (10) The identification of the major genetic pathways implicated in their pathogenesis not only will help in their diagnosis, but also will enable the development of targeted molecular therapy as well as prognostic markers.

MDS/MPN disorders are considered as a high risk factor of thrombosis. Arterial or venous thrombosis can appear at the beginning of the disease and thus constitute a telltale sign or occur later and become a complication of the disease

Renal infarction (RI) results of sudden disruption of blood flow in the renal arteries, and rapid diagnosis and treatment are critical to prevent permanent loss of renal function. (11) RI is an underdiagnosed and underreported phenomenon, it is often mistaken for renal colic. The differential diagnoses are nephrolithiasis and pyelonephritis, the presence of hematuria and elevated lactate dehydrogenase should raise the suspicion of this diagnosis.

For our patient, elevated lactate dehydrogenase was elevated, but the diagnosis was initially suspected because of the concomitant presence of pulmonary embolism.

To the best of our knowledge, and according to the literature, the risk factors of thromboembolic RI, other than atrial fibrillation, include valvular or ischemic heart disease, endocarditis, hypercoagulation disorders, and hematological diseases. (11)

Clinical manifestations of RI are not specific. Patients with acute renal infarction typically complain of acute onset of flank pain, frequently accompanied by fever, nausea, and vomiting. Oliguria is less common. (12-14)

Our patient was admitted with sudden onset of abdominal pain radiating to the back we suspected at the first time nephrolithiasis and pyelonephritis, but a radiological exam confirms the concomitant presence of pulmonary embolism and renal infarction.

The investigation confirmed the origin of deep thrombosis, and the diagnosis of myelodysplastic/myeloproliferative neoplasm, unclassifiable was retained. The majority of treatment recommendations are extrapolated from clinical trials focused on MDS or MPN patients and thus include very few overlap syndrome patients. Current treatment options for patients with MDS include conventional chemotherapy regimens, chemotherapy with hypomethylating agents, and allogeneic hematopoietic stem cell transplantation (HSCT). The therapeutic strategy depends on many factors: age, IPSS-R score, number of blasts, karyotype, and comorbidities. (15)

Prognosis and overall survival depend upon multiple factors such as the severity of cytopenias, the percentage of blasts in the peripheral blood and bone marrow, and karyotype. The IPSS-R score of the patient was at 0, and she was included to low risk group. On the other hand, the treatment of RI must be treated because of the risk of complete loss of renal function. Our patient received a curative dose of heparin. Two months later, pulmonary embolism had resolved without the appearance of additional peripheral infarction.

CONCLUSION

Myelodysplastic/myeloproliferative neoplasm, unclassifiable represents a heterogeneous group of rare myeloid neoplasia with myeloproliferative and myelodysplastic characteristics which requires vigilance from the hematologist, their diagnostic and therapeutic management is complicated.

We report an unusual case of renal infraction with pulmonary embolism secondary of Myelodysplastic/myeloproliferative neoplasm, unclassifiable. This case emphasizes the need to consider Myelodysplastic/myeloproliferative neoplasm, unclassifiable as a cause of RI, pulmonary embolism and remind that the RI is an easily missed disease due to its nonspecific presentation, and insist that early diagnosis and early curative anticoagulation are the key to rapid recovery but also preventive with long-term antithrombotic prophylaxis.

AUTHORS' CONTRIBUTIONS

The participation of each author corresponds to the criteria of authorship and contributorship emphasized in the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals of the International Committee of Medical Journal Editors. Indeed, all the authors have actively participated in the redaction, the revision of the manuscript, and provided approval for this final revised version.

COMPETING INTERESTS

The author declares no competing interests with this case.

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