Case Report

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Myelodysplastic Syndrome/Myeloproliferative Neoplasm with Simultaneous Cutaneous Involvement

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ABSTRACT

Myelodysplastic syndrome (MDS) and myeloproliferative neoplasm (MPN) are considered to be a group of heterogeneous hematopoietic neoplasms with overlapping myelodysplastic and myeloproliferative features. They occur mostly in the elderly and have an inherent tendency to transform into acute myeloid leukemia. The etiology of MDS/MPN remains uncertain at the present time. Our report describes a patient with MDS/MPN who also had cutaneous involvement (cutaneous carcinoma) several years prior to developing MDS/MPN raising the possibility that his cutaneous involvement may have played a role in the development of MDS/MPN.

Keywords: Myelodysplastic Syndromes (MDS); Myeloproliferative Neoplasm (MPN); Cutaneous Carcinoma

Abbreviations: MDS: Myelodysplastic Syndrome; MPN: Myeloproliferative Neoplasm; ER: Emergency Room; BNP: B-Type Natriuretic Peptide; NGS: Next Generation Sequencing

Introduction

MDS/MPN is considered to be a hybrid group of chronic myeloid neoplasms combining features of both MDS and MPN. The Word Health Organization classification coined this group designation in 2008 to include chronic myelomonocytic leukemia, atypical chronic myeloid leukemia, juvenile myelomonocytic leukemia, refractory anemia with ring sideroblasts, and idiopathic thrombocytosis as a provisional entity, and MDS/MPN unclassified [1]. It primarily affects older individuals with a high risk of progression to acute myeloid leukemia [2-4]. The etiologic factors that lead to the development of MDS/MPN remain unclear. However, whether other disease conditions such as cutaneous carcinoma may predispose a patient to develop MDS/MPN is not known. We describe a patient who developed MDS/MPN following long-term exposure to sun and cutaneous changes that mimicked squamous cell carcinoma/basal cell carcinoma. We speculate that his epithelial cell carcinoma may have played a role in the development of MDS/MPN.

Case Report

The patient was a 76-year-old white male with a past medical history significant for nicotine dependence, COPD, hypertension alcohol dependence, and many years of sun exposure. He presented to the emergency room (ER) with complaints of bilateral lower extremity swelling and shortness of breath that had been progressively worsening over the previous three months. The patient also reported shortness of breath but without abdominal or chest pain the day before he presented to ER. His clinical appearance and laboratory findings have been described [5]. On initial evaluation, the patient was noted to be severely anemic with shortness of breath, but he was not in acute distress. He had bilateral lower extremity edema. His abdomen was soft and mostly non-tender. Bowel sounds were heard. The liver, spleen, and kidneys were not palpable. There was no palpable lymphadenopathy. Heart sounds S1 and S2 were identifiable, along with a soft ejection systolic murmur. His chest was clear to auscultation and vital signs were stable. The blood pressure was 125/70 mm Hg; pulse 72 pm; respiration 18 pm; temperature 97.6 ◦ F. The patient's B-Type Na-

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triuretic Peptide (BNP) was elevated, and his chest x-ray showed vascular congestion without opacification. Laboratory studies revealed WBC 23.1 x 109/L; hemoglobin of 4.8 g/dL; normal MCV 93.7 fl; normal MCH (30.2 pg); and platelet count of 49 x 109/L. The patient denied the passage of black stools. He was transfused and admitted for further evaluation, diagnosis and management. During physical examination marked skin changes (keratitis) were noted particularly in his forearm (Figure 1) and a couple of raised, dry scaley lesions that appeared to be cutaneous carcinoma (Figure 2). A biopsy was not performed because of the possibility of hemorrhage as the patient was thrombocytopenic.

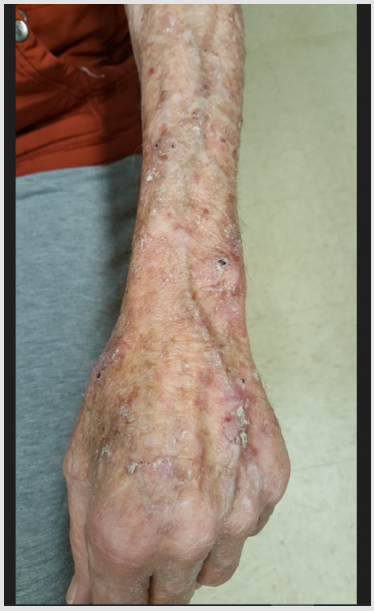

Figure 1: Shows keratotic skin changes in the left forearm.

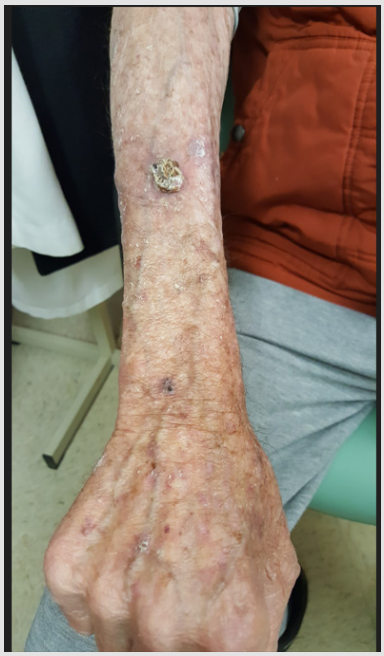

Figure 2: Shows a lesion in the right forearm what appears to be a cutaneous cancer.

Further work-up with a manual differential count of his peripheral blood smear revealed neutrophils 60%; lymphocytes 18%; monocytes and monocytoid cells 15%; absolute monocyte count 4.3 x 109/L (normal <=1.0); neutrophil myelocytes 1%; metamyelocytes 2%; eosinophils 2%; basophils 1%; neutrophil bands 1%; and blast cells 2%. There was 1 nucleated RBC per 100 WBC. The peripheral blood smear revealed hypo granularity and hypolobation (pseudo-Pelger-Huet anomaly) of neutrophils, multinuclear and bizarre nuclear forms. Red cells showed marked anisocytosis, a dimorphic blood picture, presence of ovalocytes and macro-ovalocytes. The peripheral blood smear also displayed platelet clumps, platelet anisocytosis, and giant platelets. His serum iron level was raised, at 348µg/dL (normal range 30-125). The total iron-binding capacity was normal at 336µg (normal range 250-450) and the percent saturation was slightly high at 100% (normal range 20-55). His ferritin level was raised to 927 ng/mL (normal 30-400). Vit B12 was raised at 1309 pg/mL (normal 200-950) and folate level was normal at 39.5 ng/mL (normal >=3.0). His reticulocyte count was normal at 1.8%, and the absolute reticulocyte count was normal at 31 (normal range 20-150). His erythropoietin level was markedly raised at 2636 mU/mL (normal range 2.6-18.5 mU/mL). His complete metabolic profile was mostly normal except for the glucose level, which was slightly increased at 130 mg/dL (normal range 60-100 mg/dL). His JAK2 mutation was negative. The stool occult blood test X3 was negative and routine urine analysis was normal.

Because of leucocytosis, markedly low hemoglobin, moderately low platelet count, and abnormal cytologic findings in the peripheral blood smear, including monocytosis and markedly raised erythropoietin level, hematological malignancy was suspected, and the patient underwent a bone marrow examination. It revealed a markedly hypercellular (>90%) marrow for age (Figure 1) with myeloid hyperplasia, mildly increased frequency of blast cells (3-5%) and, dysplastic changes in all three (erythroid, leucocytic, and megakaryocytic) cell lineages. The erythroid lineage was markedly reduced and displayed megaloblastoid change, binucleated erythroid precursors, inter-cytoplasmic bridging, altered nuclear-cytoplasmic ratios, nuclear cytoplasmic-maturation asynchrony, and nuclear budding. Myeloid changes included hypogranularity and hypolobation (pseudo-Pelger-Huet anomaly), multinuclear and bizarre nuclear forms. Megakaryocytes were decreased with some atypical forms including small hypolobated forms and rare forms with widely spaced nuclei. No ring sideroblasts were seen. Cytogenetic studies of the bone marrow showed a normal male karyotype and the absence of BCR/ABL1 gene rearrangement.

Flow cytometry studies of the bone marrow aspirate sample revealed a CD34 positive blast population, comprising 2% of total events, also positive for dim CD45, CD117, HLA-DR, CD33, and CD38 while negative for CD19, CD20, CD10, CD2, CD3, CD7, CD56, CD15, CD14, CD64, CD16, and CD11b. The granulocyte gate contained 83% of the total events. The monocyte gate contained 4% of total events and consisted phenotypically of mature appearing monocytes (CD13, CD33, CD14, and HLA-DR) with partial CD56 expression. No evidence was seen of MLL (KMT2A) rearrangement, and no abnormalities were detected in the following genes: FLT3, IDH1, IDH2, and NPM1. But next generation sequencing (NGS) myeloid disorders profile revealed that he was positive for ASXL1, ETV6, EZH2, and SMC1A. Smears of peripheral blood and bone marrow aspirate were reviewed in the context of the molecular studies - ASXL1 mutations, found in 37% of chronic myelomonocytic leukemia - and all together a diagnosis of CMML (MDS/MPN) was made.

Because of the patient's age (76 years) and a diagnosis of CMML-MDS/MPN with the presence of circulating and bone marrow blasts (3-5%), presence of ASXL1 mutation, and the degree of anemia (transfusion-dependent), thrombocytopenia, and rapidly increasing WBC count, the patient was considered at higher risk (IPSS-R score 3) [6] and was referred to hospice care. However, the patient's family declined this option and requested a treatment that did not involve chemotherapy. At this point, the patient was started on hydroxyurea 500 mg orally three times daily, low-dose prednisone 20 mg orally daily, and epoetin (Procrit) 30,000 units subcutaneously once a week. The patient did not receive any other cytokines or chemotherapy. However, as his WBC count continued to rise, the dose of hydroxyurea was increased to 1 gm per oral three times daily to which he had a modest response, and his WBC count started to decline. Despite receiving epoetin 30,000 units subcutaneously once a week he remained blood transfusion dependent when lenalidomide (15 mg by mouth daily) was started. However, lenalidomide did not seem to have any significant effect on his blood transfusion requirement. With continued blood transfusions approximately every two weeks, his hemoglobin concentration and platelet count remained low - Hb ~8 g/dL, platelet ~ 40-60,000/µL - but stable, and did not require any platelet transfusion. The peripheral blood smear continued to show a small number (2-4%) of blast and blast-like cells but no overt signs of leukemic transformation. However, despite a high dose of hydroxyurea, his WBC count started to increase, rising to over 80,000 with 50% monocytes. He was then started with AZA 75 mg/m2 intravenously daily for 7 days with allopurinol cover. On the first-day of treatment, his WBC count was 104,000; on the second-day treatment his WBC count was 239,000; on the third-day treatment his WBC count was 384,000; on the fourth-day treatment his WBC count was 473,000. At this point it was evident that the patient was not responding to AZA and the treatment was stopped. No further treatment was given and the patient was referred to hospice care where he died peacefully three days later.

Discussion

Cutaneous manifestations are uncommon but not rare in myelodysplastic syndrome [7]. Various skin manifestations may develop during the course of MDS. They are usually classified as either specif-

ic or non-specific lesions. Non-specific lesions correspond to neutrophilic dermatoses and vasculitis [8]. Specific lesions characterized by a dermal infiltrate of malignant hematopoietic cells seem to be rare and the exact prevalence is unknown [6]. The development of specific skin lesions containing malignant cells can be the first indication of the transformation of the MDS into a malignant phase with shortened survival [5]. The patient under discussion had many years of exposure to the sun and developed what appeared to be cutaneous carcinoma. A biopsy of the lesion was not performed because of the fragile nature of his skin and the fear of hemorrhage as the patient was markedly thrombocytopenic. The association between cutaneous carcinoma and MDS/MPN may be fortuitous or biologically relevant. MDS can be associated with a wide spectrum of skin lesions. When the latter precedes the diagnosis of MDS or appears during the follow-up may suggest these two conditions may be intertwined. The concurrent association of cutaneous carcinoma predating the development of MDS/MPN by several years in this case indicates a potential association between the two. We postulate that the bone marrow and peripheral blood changes akin to MDS/MPN observed, in this case, might be a reflection of underlying disease - cutaneous carcinoma.

References

1. Vardiman JW, Thiele J, Arber DA, Richard D Brunning, Michael J Borowitz, et al. (2009) The 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia: rationale and important changes. Blood 114(5): 937-951.
2. Ma X (2012) Epidemiology of myelodysplastic syndromes. Am J Med 125(7): S2-S5.
3. Sekeres MA (2010) The epidemiology of myelodysplastic syndromes. Hematol Oncol Clin North Am 24(2): 287-294.
4. Clara JA, Sallman DA, Padron E (2016) Clinical management of myelodysplastic syndrome/myeloproliferative neoplasm overlap syndromes. Cancer Biol Med 13(3): 360-372.
5. Islam A (2023) An Unusual Response to 5-Azacitidine by a Patient with Chronic myelomonocytic Leukemia. Clinical Case Reports.
6. Carsuzza F, Pierre C, Jaubert D, et al. (1990) Les manifestations cutanees des syndromes myelodysplastique. A propos de deux observations, Revue de la literature. Sem Hop Paris 66: 77-83.
7. Avivi I, Rosenbaum H, Levy Y, J Rowe (1999) Myelodysplastic syndrome and associated skin lesions: a review of the literature. Leuk Res 23(4): 323-330.
8. Modiano P, Reichert S, Barbaud A, P Bernard, M Weber, et al. (2008) Bullous pemphigoid in association with cutaneous lesions specific to a myelodysplastic syndrome. Br J Derm 136(3): 402-405.

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