The 11th World Congress on CONTROVERSIES IN MULTIPLE MYELOMA (COMy)

MULTIPLE MYELOMA DIAGNOSED IN A PATIENT WITH POLYCYTHEMIA VERA – A RARE CASE

Nina Petkova[1], Liliya Grahlyova[2]

1. *Hematology Clinic – Military Medical Academy-Sofia, Bulgaria; 2. Cytogenetic and Molecular Biology Laboratory – Military Medical Academy-Sofia, Bulgaria*

INTRODUCTION

Polycythemia vera (PV) is a Philadelphia chromosome-negative clonal myeloproliferative neoplasm (MPN) derived from pluripotent hematopoietic stem cells. It is characterized by increased erythroid production independent of the normal regulation mechanism of erythropoiesis, hypercellular bone marrow, and increased hematocrit. Over 95% of the patients are carriers of an acquired somatic Janus kinase 2 (JAK2) V617F mutation or another JAK2 functionally similar mutation.

Multiple myeloma (MM) is a hematologic neoplasm of lymphoid origin that is characterized by monoclonal proliferation of plasma cells in the bone marrow, which have differentiated from lymphoid B cells, monoclonal protein in the serum and/or urine, and associated organ damage.

Since different cell lines give rise to these two malignant hematological diseases – PV and MM, their occurrence in the same patient simultaneously or sequentially is extremely rare, with a small number of cases described in the scientific literature.

We describe a rare case of a patient with PV and subsequent MM diagnosed and treated in our Clinic. Data was collected form medical history and clinical charts. Relevant literature was reviewed.

CLINICAL CASE

We present a female patient diagnosed with PV at the age of 68 years due to elevated hemoglobin and splenomegaly. Laboratory data at diagnosis revealed:

- Hemoglobin (Hb) of 170g/l, red blood cells (RBC) 6.2x109/l, hematocrit (Hct) 55%, mean corpuscular volume (MCV) 79fl; white blood cell count (WBC) was raised at 16.6 x109/l, with blood smear showing: J 1%; St 17%; Sg 69%; Ba 2%; Mo 5%; Ly 6%; ErBl 1%; Platelet count (Plt) was also raised at 529x109/l. Serum erythropoietin level was low 1.6 IU/l, uric acid was elevated and serum iron was decreased.
- Abdominal sonography measured splenomegaly 182mm/55mm.
- The JAK2V617F mutation assay was positive; M-BCR/ABL1 and m-BCR/ABL1 were negative.
- Bone marrow (BM) histology revealed hypercellular BM with a normal number of blast cells and morphology of MPN, most likely PV.

These findings met the WHO diagnostic criteria for PV.

The patient had therapy for arterial hypertension, a history of thrombophlebitis of the lower extremities and PTE a year before the diagnosis of PV. A high thrombogenic risk was calculated and, in addition to therapeutic phlebotomies, she was undergoing cytoreductive therapy with hydroxycarbamide and anticoagulant therapy. In the last 2 years, she did not have the opportunity to be regularly monitored by a hematologist due to the pandemic situation of the COVID-19 and did not take her cytoreductive therapy systematically.

Nine years after the diagnosis of myeloproliferative disease, at the age of 77, the patient had pain in the lumbar region, making it difficult to move. The outpatient MRI examination of the spine showed fractures of the vertebrae Th6, Th11, Th12, a vertebral formation at the level of Th11 – 38/22mm, suspected of plasmacytoma and referred by a neurosurgeon to the clinic. During hospitalization, tests were carried out with the following results:

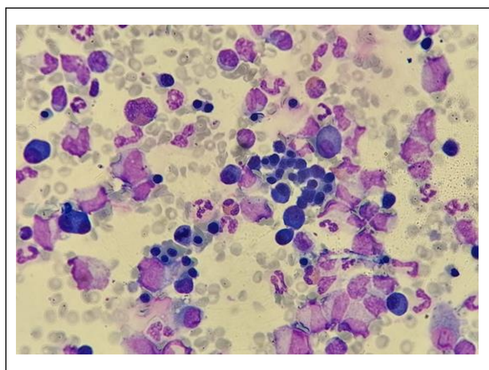

Fig.1 Bone marrow smear with plasma cells by May–Giemsa staining

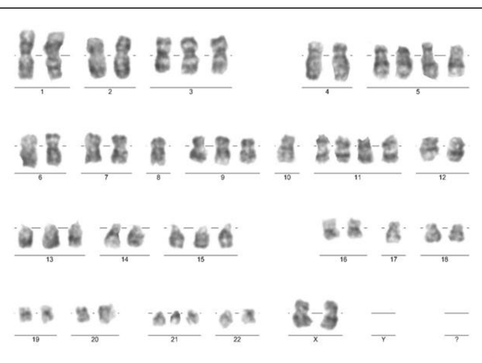

Fig.2 Hyperdiploid karyotype showing trisomies of the odd chromosomes

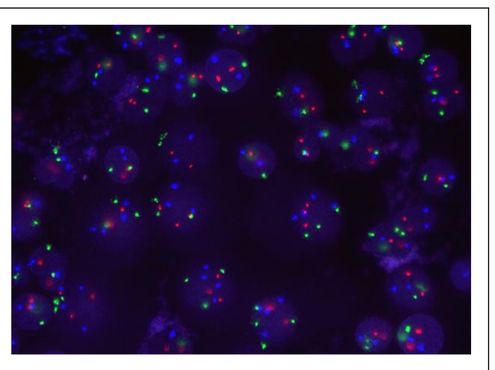

Fig.3 Interphase FISH using MetaSystems XL5p16/9q22/15q22 triple color FISH probe

- Laboratory tests: WBC 22.62x10^9/l (J 1%; Sg 89%; Mo 5%; Ly 5%; erythrocytes grouped in “rouleaux”), Hb 149g/l; RBC 6.41x10^9/l, Hct 48%, MCV 75.7fl, Plt 419x10^9/l; serum protein 89.9g/l, β2-microglobulin 7.67mg/l, LDH 461U/l; serum creatinine, calcium and albumin were within normal ranges; IgG 5.18g/l, IgA 19.69g/l, IgM 0.33g/l.
- Serum immunofixation and electrophoresis: monoclonal protein of IgA kappa subtype 32.18g/l, increased free kappa light chains 101.56mg/l and altered kappa/lambda light chain ratio of 10.28. Urine immunofixation and electrophoresis were negative.
- Bone marrow aspiration biopsy: normal to hypercellular, micronormoblastic erythropoiesis, normal myeloid maturation and megakaryopoiesis; plasma cell infiltration of 14% of the nucleated cells with atypical incl. binucleated cells (Fig.1). FCM confirmed an abnormal plasma-cell population CD45-/ CD19-/ CD38+/ CD138+/ CD20-/ CD27-/ CD28-/ CD56+/ CD81-/ CD117+/ kappa+.
- Cytogenetic analysis of BM: presence of a hyperdiploid myeloma clone (Fig.2), confirmed by FISH analysis with triple-colored 5p15/9q22/15q22 for hyperdiploidity FISH probe showing 17% of nuclei with more than 2 copy numbers of chromosomes 5, 9 and 15 (Fig.3). Negative for 1p deletion and gain 1q using XL 1p36/1q25 del, negative for IGH locus rearrangement using 14q32 Break-apart probe.
- X-ray of the skull, thoracic and lumbar vertebrae and ribs: osteolytic lesions and altered Th11, Th12, Th6, L1 vertebral bodies due to microfractures. Persistent splenomegaly 200mm/45mm during ultrasound examination.

The patient was diagnosed with IgA kappa MM, Durie-Salmon stage IIIA, revised international scoring system stage III, in addition to PV. Because of nerve root compression and myelin displacement she was referred for radiotherapy of the formation first, with clinical effect and reduction of serum paraprotein. HU administration for PV was discontinued upon the diagnosis of MM. Chemotherapy with bortezomib based regimen was started (Kimura H. et al.2022).

CONCLUSION

PV, as a part of MPN, and MM are characterized by different pathogenetic mechanisms and clinical course. The clonality of these two diseases when concomitant remains unclear; as described in literature MM and MPN clones may differ across cases. MPN are often associated with immune system hyperactivation, an example of this altered immune milieu is the presence of monoclonal gammopathy in some patients with MPN. When MM develops, management is focused more on treating the myeloma and MPN is monitored.

REFERENCES

Bochtler T, Hegenbart U, Heiss C, et al. Hyperdiploidy is less frequent in AL amyloidosis compared with monoclonal gammopathy of undetermined significance and inversely associated with translocation t(11;14). Blood. 2011;117(14):3809-15.

Kimura H, Furukawa M, Mori H et al. Development of multiple myeloma after 15 years of treatment for polycythemia vera and successful treatment using bortezomib: A case report. Clin Case Rep. 2022;10:e06614.

Le Clech L, Sakka M, Meskar A et al. The presence of monoclonal gammopathy in Ph-negative myeloproliferative neoplasms is associated with a detrimental effect on outcomes. Leuk Lymphoma. 2017; 58(11): 1–6.

Malhotra J, Kremyanskaya M, Schorr E et al. Coexistence of myeloproliferative neoplasm and plasma-cell dyscrasia. Clin Lymphoma Myeloma Leuk. 2014 Feb;14(1):31-6.

Wuilleme S, Robillard N, Lodé L, et al; Intergroupe Francophone de Myélome. Ploidy, as detected by fluorescence in situ hybridization, defines different subgroups in multiple myeloma. Leukemia. 2005;19(2):275-8.

CONTACT: Dr. N.Petkova , MD, PhD, Military Medical Academy-Sofia, Hematology Clinic, 3, St.Georgy Sofijski str., Sofia, Bulgaria