COEXISTENCE OF MULTIPLE MYELOMA AND MYELOFIBROSIS: IS THERE A CORRELATION?

COMy

The 12th World Congress on CONTROVERSIES IN MULTIPLE MYELOMA (COMy)

Rim Frikha and Yousra Fakhfakh

Faculty of Medicine and university hospital of Sfax/TUNISIA

INTRODUCTION

Multiple Myeloma (MM) is a hematological malignancy that has characteristic abnormal clonal plasma cells present in the bone marrow. The co-occurrence of bone marrow fibrosis with plasma cell dyscrasias in the same patient is an extremely rare incident that has been reported in several cases; and the etiology of the simultaneous manifestation of Multiple Myeloma (MM) and myelofibrosis (MF) remains unclear.

CASE PRESENTATION

The present study reports the case of a 56-year-old male who presented with anemia and thrombocytosis with a clinical suspicion of primary myelofibrosis (PMF). Genetic testing revealed JAK2V617F mutation, but no mutations in MPL, and CALR.

DISCUSSION

The association of MM with PMF raised a few issues that are especially important in theory, but also clinically:

Firstly, although few cases of concomitant MM and PMF have been reported worldwide **(1–4),** there is a significant increase incidence of plasma cell dyscrasia among patients with PMF in comparison with patients with other myeloproliferative diseases **(4)**.

Secondly, several speculations on the possible physiopathology mechanisms linking these two entities have been presented. The interrelation between plasma cell dyscrasia and myelofibrosis supposed different hypotheses **(5-7):**

- Pluripotent hematopoietic stem cells can differentiate into myeloid and lymphoid lineages, and both diseases may have a common origin.
- The treatment of one malignancy may lead to the development of a second malignancy

Then, In these situations, an accurate diagnosis requires molecular testing. Since no research has conclusively shown that the JAK2V617F mutation is present in MM, it is assumed that the JAK2 mutation in our patient originated from persistent MPN rather than myeloma. The role of Janus kinase-signal transducers and activators of transcription (JAK-STAT) signaling in myeloma cell survival and proliferation has been demonstrated, and STAT3 signaling in MM is associated with survival and drug resistance**(7-9)**.

Finally, there are no standard treatment options for MM co-occurring with MPN, and the combined presence of two hematologic tumors makes treatment challenging.

CONCLUSION

Although the reasons for the occurrence of both diseases in one patient may be multi-factorial, the present case highlights the potential clinical and prognosis significance of (JAK/STAT) pathways in pathophysiology of unexpected association. Therefore, further investigation of the mechanism and clinical characteristics of these cases is mandatory.

REFERENCES

1.Kasimis, B. S., Yen-Lin, R. & Neiman, R. S. Multiple Myeloma Associated with Myelofibrosis. *Oncology* **38**, 369–372 (1981).

2.Pulsoni, A. *et al.* Coexistent Multiple Myeloma and Myelofibrosis. *Leuk. Lymphoma* **10**, 401–403 (1993).

3.Schmidt, U., Ruwe, M. & Leder, L. D. Multiple myeloma with bone marrow biopsy features simulating concomitant chronic idiopathic myelofibrosis. *Nouv. Rev. Fr. Hematol.* **37**, 159–163 (1995).

4.Xiang, Q. *et al.* Coexistence of myeloproliferative neoplasms with multiple myeloma. *Cancer Pathog. Ther.* **2**, 212–214 (2024).

5.Subramanian, R., Basu, D. & Dutta, T. K. Significance of bone marrow fibrosis in multiple myeloma. *Pathology (Phila.)* **39**, 512–515 (2007).

6.Coughlin, C., Greenwald, E. S., Schraft, W. C. & Grossman, S. Myelofibrosis associated with multiple myeloma. *Arch. Intern. Med.* **138**, 590–592 (1978).

7.Kawauchi, K., Mori, H., Sugiyama, H., Oshimi, K. & Hirayama, A. Multiple Myeloma with Coexistent Myelofibrosis: Improvement of Myelofibrosis Following Recovery from Multiple Myeloma after Treatment with Melphalan and Prednisolone. *Jpn. J. Med.* **30**, 483–486 (1991).

8.Ravi, S., Sundaresan, D., Pai, S. & Kalashetty, M. MPL-mutated Primary Myelofibrosis and Multiple myeloma – A Rare Coexistence. *Indian J. Hematol. Blood Transfus.* https://doi.org/10.1007/s12288-025-02219-0 (2025) doi:10.1007/s12288-025-02219-0.

9.Leone, G., Scuderi, F., Carlesimo, M. & Crivelli, F. Myelofibrosis Associated with IgG Myeloma. *Acta Haematol.* **67**, 139–140 (1982).

Pr. Rim FRIKHA MD/PhD- E_mail: frikha_rim@yahoo.fr; University hospital of sfax & Faculty of Medicine –SFAX/TUNISIA