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EXTRAMEDULLARY LOCALIZATION IN YOUNG PATIENTS WITH MULTIPLE MYELOMA ELIGIBLE FOR AUTOLOGOUS STEM CELL TRANSPLANTATION: A MULTICENTER TUNISIAN STUDY FROM THE NATIONAL TUNISIAN MULTIPLE MYELOMA STUDY GROUP

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INTRODUCTION

Multiple myeloma (MM) is a hematologic malignancy characterized by the clonal proliferation of plasma cells. Extramedullary localization (EML) represent a rare and aggressive complication of MM, and their clinical and prognostic implications are not fully understood, especially in younger patients. This study aims to compare the clinical features, prognosis, treatment response, and survival between young MM patients with and without extramedullary localization, all of whom are eligible for autologous stem cell transplantation (ASCT).

MATERIALS AND METHODS

This multicenter study was conducted by the National Tunisian Multiple Myeloma Study Group. A total of 357 patients under the age of 65, diagnosed with MM and eligible for ASCT, were included. Treatment followed the National Protocol for Multiple Myeloma Treatment (2016), which stratifies patients into two risk groups: high-risk and standard-risk. The high-risk group includes patients with renal insufficiency, extramedullary localization, or high-risk cytogenetic abnormalities, while the standard-risk group consists of those without these factors. The high-risk group was treated with bortezomib, dexamethasone, and thalidomide (VDT), while the standard-risk group received cyclophosphamide, dexamethasone, and thalidomide (CDT). Patients were divided into two groups for analysis: those with extramedullary involvement (group 1) and those without (group 2). Data collected included demographic information, clinical features, treatment regimens, and survival outcomes. The comparison between both groups focused on clinical presentation, treatment response, overall survival (OS) and Progression free survival (PFS). The median follow-up period was 49 months

RESULTS

A total of 85 patients (24%) had extramedullary involvement, while 272 patients (75%) had no such localization. The axial skeleton location was the most frequent (24 cases). ED was statistically more frequent in male patients (66% vs 48%, p =0.006) and younger patients (sex ratio M/F 1.93 vs 0.91; p=0.011). The patients with extramedullary disease had a significantly lower proportion of ISS stage >1 (p<0.05) and renal insufficiency (p<0.05) compared to the group without extramedullary disease. There were no significant differences between the two groups in terms of anemia (p=0.45) or hypercalcemia (p=0.39). The majority of patients with extramedullary involvement were treated with bortezomib as part of their induction therapy (p<0.05). No significant differences were observed between the two groups in terms of response to therapy overall survival rates were comparable between the two groups. PFS seemed better in MM without LEM but not statistically significant. A table summarizing the results is annexed.

Table 1 : MM with and without extramedullary localization characteristics

	LEM pure	MM without LEM	P=
Population number	85 (24%)	272(76%)	
Sex M	56(66%)	130(48%)	0.05
Aged<40	8(9%)	5(2%)	0.049
ISS > 1	47(55%)	199(73%)	<0.001
Hypercalcemia	18(21%)	70(26%)	0.221
Renal impairement	11(13%)	103(38%)	<0.001
Protocole ttt(VTD)	73(86%)	192(71%)	0.043
Therapeutic response VGPR post induction	68.8%	59.1%	0.17
VGPR post autologous SCT	78.5%	75.2%	0.6
OS	79.4%	79.1%	0.86
PFS	55.6%	65.9%	0.17

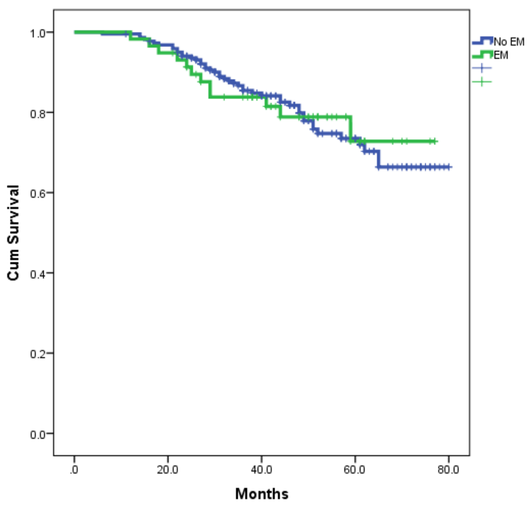

Fig1 : Overall survival

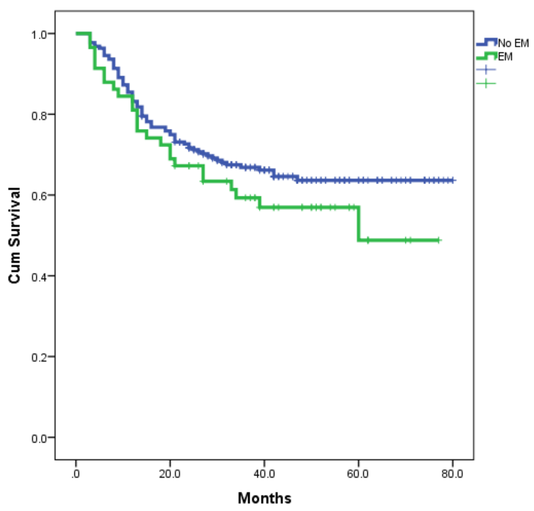

Fig2: Progression Free survival

CONCLUSION

In this multicenter Tunisian study, patients with EML multiple myeloma showed comparable clinical outcomes to those without EML, despite previous reports in the literature suggesting worse prognosis for the former group. The use of proteasome inhibitors in induction therapy may explain these findings, as these therapies may offer additional therapeutic benefits in controlling extramedullary disease. Furthermore, the heterogeneous nature of extramedullary involvement, including both pure and paramedullary lesions, may contribute to the observed outcomes.

In the literature, patients with EML have shown varied response rates, typically ranging from 50% to 70% for overall response (ORR) to treatment (Kumar et al., 2017), with a global survival rate of approximately 60% at 3 years (Palumbo et al., 2014). Progression-free survival (PFS) for patients with extramedullary disease has been reported to range from 18 to 24 months (Zhou et al., 2018), which is notably shorter than those without extramedullary involvement. These findings, however, may not apply in the context of our study, where similar responses and survival outcomes were observed across both groups, likely due to the combination of proteasome inhibitors and daratumumab. This study emphasizes the need for further research to explore the impact of novel therapies on extramedullary disease in multiple myeloma.

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