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CORRESPONDENCE

Clinical characteristics and treatment outcomes in IgE multiple myeloma: A case-control study

To the Editor:

Although the clinical features of IgE multiple myeloma (MM) are generally believed to be similar to other MM isotypes, this assumption is based primarily on single case reports and a few small case series, usually published before the novel agent era.[1] The characteristics of IgE MM patients have not been formally compared with other MM isotypes.

We analyzed the clinical features and outcomes of patients with IgE MM and age-, sex-, and center-matched controls with IgG MM. The retrospective chart review included data from 9 clinical centers in Hungary, Italy, Israel, Poland and the United States. In total 18 patients diagnosed with IgE MM in 1982-2016 were compared with 54 age-, sex- and center-matched IgG MM controls diagnosed during the same period.

The clinical and laboratory features are presented using descriptive statistics. Response was assessed using the International Myeloma Working Group consensus criteria, either current,[2] or older versions depending on the date the patients were diagnosed. Between-group comparisons were performed using chi-square, Fisher exact and Mann-Whitney U-tests, when appropriate. Overall survival (OS) was estimated using the Kaplan-Maier method and compared with log-rank test. All reported *P*-values are 2-sided and were considered significant if < .05. Calculations and graphics were obtained using the STATA (StataCorp, College Station, TX, USA).

Median age of patients with IgE MM was 60 years, and male to female ratio for this group was 1.25:1. No statistically significant differences were detected in laboratory and clinical characteristics of patients with IgE MM and IgG MM at the time of the diagnosis (Table 1). The study groups were also similar in terms of the cytogenetic abnormality profiles; however, these parameters were not subjected to statistical analysis because of a low proportion of patients with available data.

The indication for treatment in the IgE MM group included MM-related bone disease (12/14, 86%), constitutional symptoms (5/14, 36%), anemia (3/14, 21%), renal failure (1/12, 7%), and/or paresthesia (1/12, 7%). Patients with IgG MM were qualified to treatment due to bone disease (21/26, 81%), anemia (8/26, 38%), and/or constitutional symptoms (7/26, 27%).

16/18 (89%) patients with IgE MM and 51 (94%) with IgG MM received a first line treatment. Immunomodulatory drugs (IMIDs) were administered to 37.5% vs 61%, proteasome inhibitors (PIs) to 62.5% vs 45%, and conventional chemotherapy to 69% vs 47% of individuals with IgE MM and IgG MM, respectively. In 7/16 (44%) patients with IgE MM and in 36/51 (47%) with IgG MM, the first line treatment was followed by autologous stem cell transplantation (ASCT).

Responses to the first line treatment were evaluable in 10/16 (62.5%) patients with IgE MM and in 34/51 (67%) with IgG MM. These included complete response (CR) in 40% vs 26%, very good partial response in 30% vs 35%, and partial response (PR) in 30% vs 26%, for IgE and IgG MM, respectively. The overall response rate (ORR) in the evaluable IgE MM and IgG MM patients were 100% (10/10) and 88% (30/34), respectively.

The median follow-up for IgE MM and IgG MM groups was 8.1 years (95% CI 3.7-9.9) and 7 years (95% CI 5.2-11.7), respectively. A total of 7/18 (39%) patients with IgE MM and 20/54 (37%) with IgG MM died during the follow-up period. Cause of death was reported in 3/7 (43%) patients with IgE MM (disease progression, amyloidosis and secondary plasma cell leukemia—PCL), and unknown in the remaining 4 cases. Median OS was not reached in either IgE MM or IgG MM group. 5-year OS rates for patients with IgE MM and IgG MM were 63% (95% CI 35%-82%) and 74% (95% CI 59%-84%), respectively, and 10-year OS rates were 54% (95% CI 26%-76%) and 45% (95% CI 26%-62%), respectively (Log-rank $P = .630$; Figure 1).

Our findings suggest that the clinical characteristics and outcomes in IgE MM were similar as in the more common IgG MM. This observation is consistent with the data from previously published individual case reports and small case series. According to Macro et al.,[3] who reviewed data from 29 case reports on IgE MM published between 1967 and 1992, this condition was diagnosed at a mean age of 62 years, and there was a slight preponderance of male patients (male to female ratio 1.23:1); both these values were similar as documented in our series. Although anemia, osteolytic lesions, hepatomegaly and/or splenomegaly, and PCL were frequently reported in IgE MM, none of those manifestations seem to constitute a characteristic feature of this condition.[1,3,4]

Prognosis for IgE MM was postulated to be worse than for other MM types, with a median survival of 12.5 months,[3] even after ASCT.[5] However, those data originate from the preIMID and prePI era. The evidence from more recently published case reports suggests that the outcomes in IgE MM patients treated with novel agents, such as bortezomib, lenalidomide, or thalidomide, are markedly better.[6] Our

TABLE 1 Clinical and laboratory characteristics of 18 patients with IgE MM and 54 controls with IgG MM

	IgE MM (*n* = 18)		IgG MM (*n* = 54)		
Parameter	**Valid (*n*)**	**Result**	**Valid (*n*)**	**Result**	***P*-value**
Age (years)	18	60 (35-77)	54	60 (38-86)	.780
Men (*n*)	18	10 (56%)	54	30 (56%)	1.000
ISS stage (*n*)					
ISS I	11	8 (73%)	36	13 (36%)	.090
ISS II	11	2 (18%)	36	11 (31%)	
ISS III	11	1 (9%)	36	12 (33%)	
R-ISS stage (*n*)					
I	8	5 (63%)	14	5 (36%)	.550
II	8	3 (38%)	14	7 (50%)	
III	8	0 (0%)	14	2 (14%)	
Light chain MM (*N*)	18	11 (61%)	45	28 (62%)	.940
Hemoglobin (g/dL)	16	11.0 (8.4-14.0)	43	10.5 (7.1-13.9)	.430
GFR (mL/min)	9	45 (9-99)	39	69 (25-99)	.050
Serum ca (g/dL)	15	10.0 (9.0-12.7)	39	9.5 (8.1-18.4)	.080
Serum albumin (g/dL)	11	3.6 (2.6-4.9)	42	3.7 (2.5-5.0)	.890
Serum B2M (g/dL)	12	3.2 (1.7-17.8)	46	3.7 (0.7-18.6)	.600
Lytic lesions (*N*)	12	10 (83%)	31	26 (84%)	.970
Flow cytometry (*N*)					
CD38	6	6 (100%)	9	9 (100%)	N/A
CD138	6	6 (100%)	9	9 (100%)	
CD20	6	0 (0%)	9	1 (11%)	
CD56	6	3 (50%)	3	3 (100%)	
Cytogenetic data (*N*)					
t(11;14)	11	2 (18%)	20	3 (15%)	N/A
del13q	11	2 (18%)	20	4 (20%)	
del17p	11	2 (18%)	20	3 (15%)	
t(14;4)	11	1 (9%)	20	3 (15%)	
t(14;16)	11	0 (0%)	20	1 (5%)	

Abbreviations: ISS, International Staging System; R-ISS, Revised International Staging System; GFR, glomerular filtration rate; B2M, beta-2-microglobulin; N/A, not applicable. Results presented as medians (ranges) or numbers (percentages).

findings are consistent with those data, implying that prognosis in patients with IgE MM treated with IMIDs (38%) and/or PIs (63%) and ASCT (44%) may be no worse than in IgG MM.

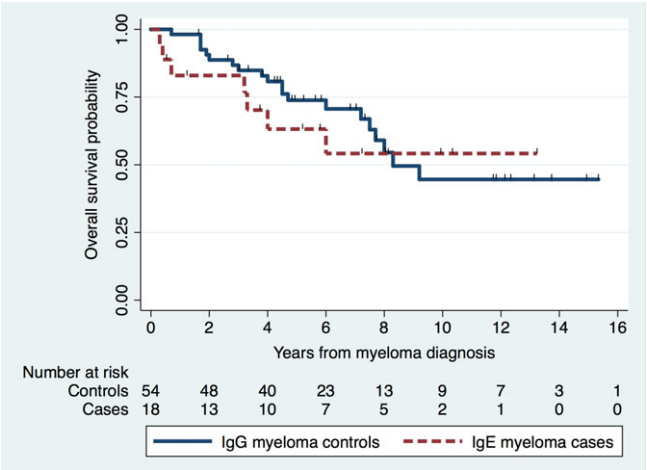

FIGURE 1 OS estimates in 18 patients with IgE MM and 54 controls with IgG MM [Color figure can be viewed at wieyonlinelibrary.com]

This study was not free from potential limitations, such as the presence of missing data on clinical and laboratory findings, especially immunophenotypic and cytogenetic characteristics of IgE MM. Moreover, it should be remembered that IgE status is not routinely examined in many centers and hence, some patients with IgE MM may be misdiagnosed with light chain MM. Consequently, our series might not be fully representative for the whole population of patients with IgE MM. Nevertheless, our results suggest that the clinical and laboratory characteristics of IgE MM are similar to IgG MM, and in the era of novel therapeutic agents, the prognosis in this rare condition may be better than previously reported.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest with the contents of this article.

AUTHOR CONTRIBUTIONS

All authors read and approved the final version of the article.

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