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Letter to the Editor

Clinical and epidemiological features of multiple myeloma patients from a low socio-economic region of Brazil



Dear Editor,

Multiple myeloma (MM) represents 1% of all new cases of cancer worldwide.¹ The International Myeloma Foundation estimates that about 30,000 MM patients are currently under treatment in Brazil. Since few studies have reported the clinical and epidemiological features of MM in this country,^{2,3} we aim to contribute to the clinical panorama of the disease by describing a series of 65 patients (median age: 64 years; range: 35–80 years) diagnosed with MM between 2006 and 2014 at the Hospital da LIGA ($n=55$) and Oncoclínica São Marcos ($n=10$), Natal, RN. Patients diagnosed with monoclonal gammopathy of undetermined significance, asymptomatic MM, POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes), solitary plasmacytoma, and primary plasma cell leukemia were excluded. The majority of myeloma proteins were of the IgG isotype (69.2%). The Kappa light chain was associated with the heavy chain isotypes in 64.7% of cases. Most patients were in stage IIIA of the Durie and Salmon (DS) classification (80.4%) and in Stages I, II and III of the International Staging System (ISS) (41.7%, 22.9% and 35.4%, respectively). Thirty-three patients (50.7%) were submitted to conventional chemotherapy based on cyclophosphamide, thalidomide and dexamethasone (CTD), with 16 of them undergoing autologous hematopoietic stem cell transplantations. Sixteen patients (24.6%) were treated with a melphalan, prednisone and thalidomide (MPT) protocol. Eight (12.3%) patients were treated with thalidomide with dexamethasone and eight (12.3%) with vincristine, doxorubicin and dexamethasone (VAD). Sixteen patients took bortezomib as second line treatment after disease progression.

In our cohort, the clinical presentation and response to treatment revealed gender-related differences not found worldwide, with women being more frequently affected than men (gender ratio M/F=0.6) and exhibiting lower creatinine levels at diagnosis than men (<1.3 mg/dL) (p -value=0.032). These epidemiological and clinical characteristics are not

similar to the disease descriptions in the more developed southern regions of Brazil.^{2,3} In fact, in most countries, MM is more frequent in men than in women.^{4,5} The causes of the gender bias herein reported, whether related to referral (for instance, due to women's health campaigns which have been intensified in Brazil over the last decades) or biological characteristics of the population, are not evident and warrant further studies. Regarding biological factors, Boyd et al.⁶ analyzed cytogenetic alterations in a large MM cohort and suggested that gender differences are influenced by the primary genetic events, with immunoglobulin translocations being more common in women and hyperdiploidy in men. In the southern regions of Brazil, where genetic alterations have been studied in MM, no such bias was described.⁷

Plasmacytoma was defined as bone and extramedullary tumors that were identified upon physical examination and by imaging studies, including a complete X-ray investigation, computed tomography scan and magnetic resonance imaging. Plasmacytoma was detected in 43.4% (23/53) of MM patients at diagnosis. The thoracic curve of the vertebral column was the most common site (40%), followed by the lumbar spine, femur, skull and pelvis. The frequency of plasmacytoma was higher than that reported worldwide,^{8,9} but similar to another report from Brazil.¹⁰ Although not being considered a marker of advanced disease or progression, since it can occur at any stage of myeloma, plasmacytoma has been more frequently found in patients with higher tumor burden,^{9,10} which can account for the increased incidence of plasmacytoma in our study.

Overall (OS) and progression free survival (PFS) were 78% and 50.9%, respectively. OS and PFS did not vary according to ISS, DS staging or the presence of plasmacytoma (p -value >0.5). Gender had an impact on OS with women having twice the survival time as men [mean time: 136 months; 95% confidence interval (95% CI): 10.2–116 months vs. 72 months; 95% CI 35–109 months, respectively – p -value = 0.005]. Low calcium levels (less than and greater than or equal to 8 mg/dL) were predictive of disease progression (mean time: 5 months;

95% CI: 0–15 months vs. 37 months; 95% CI: 16–57 months – p -value=0.011) and OS (mean time: 16 months; 95% CI: 3.1–21.8 months vs. 81 months; 95% CI: 24.5–137.4 months – p -value=0.006).

We acknowledge the limitation imposed by the reduced number of patients; however, our results in a particular series of MM patients point to the need of improving strategies for early diagnosis and prognosis of MM in less privileged settings.

Conflicts of interest

The authors declare no conflicts of interest.

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REFERENCES

- Kyle RA, Greipp RP. Plasma cell dyscrasias: current status. *Crit Rev Oncol Hematol*. 1988;8(2):93–152.
- Hungria VT, Maiolino A, Martinez G, Colleoni GW, Coelho EO, Rocha L, et al. Confirmation of the utility of the International Staging System and identification of a unique pattern of disease in Brazilian patients with multiple myeloma. *Haematologica*. 2008;93(5):791–2.
- Silva P, Brandão K, Pinto P, Faria R, Clementino N, Silva C, et al. Mieloma múltiplo: características clínicas e laboratoriais ao diagnóstico e estudo prognóstico. *Rev Bras Hematol Hemoter*. 2009;31(2):63–8.
- Sant M, Minicozzi P, Mounier M, Anderson LA, Brenner H, Holleczer B, et al. Survival for haematological malignancies in Europe between 1997 and 2008 by region and age: results of EURO CARE-5, a population-based study. *Lancet Oncol*. 2014;15(9):931–42.
- Raab MS, Podar K, Breitkreutz I, Richardson PG, Anderson KC. Multiple myeloma. *Lancet*. 2009;374(9686):324–39.
- Boyd KD, Ross FM, Chiecchio L, Dagrada G, Konn ZJ, Tapper WJ, et al. Gender disparities in the tumor genetics and clinical outcome of multiple myeloma. *Cancer Epidemiol Biomarkers Prev*. 2011;20(8):1703–7.
- Linardi CC, Martinez G, Velloso ED, Leal AM, Kumeda CA, Buccheri V, et al. Evaluation of chromosomal abnormalities by cIg-FISH and association with proliferative and apoptotic indexes in multiple myeloma. *Braz J Med Biol Res*. 2012;45(11):1074–9.
- Varettoni M, Corso A, Pica G, Mangiacavalli S, Pascutto C, Lazzarino M. Incidence, presenting features and outcome of extramedullary disease in multiple myeloma: a longitudinal study on 1003 consecutive patients. *Ann Oncol*. 2010;21(2):325–30.
- Iriuchishima H, Saitoh T, Handa H, Isoda A, Matsumoto M, Sawamura M, et al. A new staging system to predict prognosis of patients with multiple myeloma in an era of novel therapeutic agents. *Eur J Haematol*. 2015;94(2):145–51.
- Crusoe Ede Q, Higashi F, Padilha MP, Miranda EC, Quero AA, Almeida M, et al. Outcomes of autologous transplantation for multiple myeloma according to different induction regimens. *Rev Bras Hematol Hemoter*. 2014;36(1):19–24.

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