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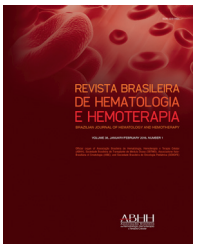

Original article

For survival, the emergence of oligoclonal bands after multiple myeloma treatment is less important than achieving complete remission

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ABSTRACT

Background: The emergence of oligoclonal bands, proteins differing from those originally identified at diagnosis, has been reported in multiple myeloma patients after high-dose chemotherapy followed by autologous stem cell transplantation and after successful conventional chemotherapy. The clinical relevance of oligoclonal bands remains unclear, but their emergence has been associated with better prognosis. The aim of the present study was to determine the prevalence, clinical characteristics and prognostic impact of the presence of oligoclonal bands in multiple myeloma patients.

Methods: A retrospective cohort study was conducted. The study included newly diagnosed multiple myeloma patients with at least very good partial response after conventional dose or high-dose chemotherapy followed by autologous stem cell transplantation. The emergence of oligoclonal bands was identified using serum protein electrophoresis as well as serum and urine immunofixation techniques.

Results: A total of 101 patients were included with a median follow-up of 42 months. In total, 55% were male, and the median age was 58 years (29–87 years). Fifty-one (50.5%) patients developed oligoclonal bands. They comprised 60% (45/75) of patients treated with autologous stem cell transplantation and 23% (6/26) of those who were not transplanted. Patients with oligoclonal bands showed better progression-free survival than those without the emergence of oligoclonal bands (p-value = 0.0075).

Conclusion: The prevalence of oligoclonal bands in this study population was 50.5% with its frequency being greater in cases treated with autologous stem cell transplantation and in those attaining complete remission. Complete remission was more important than the emergence of oligoclonal bands on progression-free survival.

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Introduction

Multiple myeloma (MM) is a hematologic disorder that is characterized by the clonal expansion of plasma cells in the bone marrow. These plasma cells are responsible for the production of a unique monoclonal immunoglobulin with a constant isotype and light chain restriction that can be found in serum and/or urine and is termed paraprotein or the M component.[1] The measurement of this monoclonal protein by serum protein electrophoresis (SPE) and immunofixation is invaluable for monitoring patients with MM.[1]

Since the introduction of high-dose melphalan followed by rescue using autologous hematopoietic stem cell transplantation (ASCT), the emergence of oligoclonality or oligoclonal bands (OB) has been described in numerous studies.[2–9] This is defined as follows: (1) a new monoclonal component identified by SPE, (2) a variation of the immunoglobulin subtype, and/or (3) the emergence of more than one immunoglobulin subtype detected by serum or urine immunofixation that differs from the initial pattern observed at diagnosis.[2–5] These invariably small components can remain undetected by SPE but are identified by immunofixation in up to 66% of cases.[3]

The prevalence of OB varies, ranging from 6.6% to 73%.[3,6] They are commonly found in patients who have undergone ASCT.[2,3,7,8] However, OB can also emerge after conventional chemotherapy, particularly following the use of the novel agents, such as immunomodulators (IMIDs) and proteasome inhibitors (PI).[4,5] The presence of OB has been associated with superior response rates.[2,5] While initially described as a mere transient phenomenon of immunologic recovery, some authors have suggested that the appearance of these bands is associated with improved prognosis and longer survival.[2–4,9,10]

The emergence of OB can be mistaken as disease progression, leading to unwarranted changes in treatment. Thus, to better understand the frequency, the clinical characteristics and the prognostic impact of OB, the clinical records and the results of SPE and immunofixation tests of MM patients who had at least very good partial response (VGPR) after treatment were analyzed. This is the first study analyzing the impact of OB in MM patients treated in Brazil.

Methods

The medical records of 328 patients who were treated at two referral centers for MM in the Brazilian national health system (Santa casa de São Paulo Hospital and University Hospital of the Universidade Federal da Bahia) from July 2003 to June 2013 were reviewed. Participants had achieved at least VGPR, defined as serum and urine M-protein detectable by immunofixation, but not by SPE, or who achieved ≥90% reduction in serum M-protein plus urine M-protein level <100 mg/24 h after first-line therapy,[11] specifically, conventional doses of chemotherapy or high-dose chemotherapy and ASCT. A total of 101 patients were included for the identification of the emergence of OB using the SPE and immunofixation techniques. The study was approved by the Research Ethics Committees of both institutions.

Table 1 – Clinical and laboratory characteristics of the study population.

Characteristic	
Age at diagnosis – years (n = 101)	
Range	29–87
Median	58
Sex – n (%) (n = 101)	
Male	55 (54.5)
Female	46 (45.5)
ECOG – n (%) (n = 101)	
0	34 (33.7)
1	18 (17.8)
2	16 (15.8)
3	17 (16.8)
4	2 (2.0)
Not assessed	14 (13.9)
DS – n (%) (n = 100)	
I	2 (2.0)
II	6 (6.0)
III	92 (92.0)
ISS – n (%) (n = 94)	
I	33 (35.1)
II	30 (31.9)
III	31 (33.0)
M-component – n (%) (n = 101)	
IgA	24 (23.8)
IgG	61 (60.4)
IgM	1 (1.0)
Kappa (free)	7 (6.9)
Lambda (free)	8 (7.9)

ECOG: Eastern cooperative oncology group; DS: Durie-Salmon; ISS: International staging system; M-component: monoclonal component.

The analyzed variables were sex and age at diagnosis, type of immunoglobulin secreted, Eastern cooperative oncology group (ECOG) performance status, staging systems (Durie-Salmon and International staging system – ISS), treatment (high-dose chemotherapy and ASCT or conventional chemotherapy), response assessment and emergence of OB.

The emergence of OB was defined as (1) new monoclonal spike on SPE, which differed from the initial pattern evidenced by direct comparison of assays, (2) immunoglobulin subtype switching, and/or (3) more than one immunoglobulin subtype at serum and urine immunofixation.

The response criteria were based on the 2006 International myeloma working group.[11] Overall survival was calculated from the start of treatment to death or loss to follow-up and progression-free survival (PFS) was calculated from the start of treatment to progression, death or loss to follow-up.

Categorical variables were compared using the Chi-square or Fisher exact tests, the *t*-test was used to compare age among groups and the Kaplan–Meier curve was employed for survival analysis, with comparison across groups using the log rank test. Kaplan–Meier analyses were also used to identify potential predictor variables for PFS. These variables were included

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