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PB1971 FREQUENCY AND CHARACTERISTICS OF DEL(6Q) IN PATIENTS WITH MULTIPLE MYELOMA FROM LATIN-AMERICAN COUNTRIES. A REAL-WORLD STUDY

Topic: 13. Myeloma and other monoclonal gammopathies - Biology & Translational Research

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Background: Multiple myeloma (MM) is a clonal B cell malignancy characterized by the presence of multiple structural and numerical genetic alterations, including gains, losses and rearrangements of different chromosomal regions. Among them, the partial deletion of the long arm of chromosome 6 [del(6q)] is a common recurrent abnormality in MM, observed in 20-35% of patients. Despite this, there is no data about this alteration from MM patients in Latin America (LA).

Aims: To evaluate frequency, distribution and clinical characteristics of MM patients with del(6q) in a multicenter study from the GELAMM (Grupo de Estudio Latinoamericano de MM).

Methods: We retrospectively reviewed MM patients from Argentina, Chile, Ecuador and Uruguay, whose specimens were assessed by conventional cytogenetics and tested using interphase FISH between 2010 and 2020. Conventional cytogenetic analysis was performed on unstimulated bone marrow (BM) cells cultured. G-banded technique was used. FISH analysis was performed on unstimulated BM samples or on isolated plasma cells. The MM DNA probe panel was used. To compare clinical characteristics, a reference group of 105 MM patients without cytogenetic and FISH alterations (w/alt) (57 males; R-ISS: 1: 10.6%, 2: 50.3%, 3: 39.4%) was included. The study was approved by the local Ethics Committees of each Institution, in compliance with the Declaration of Helsinki.

Results: A total of 220 patients with abnormal karyotypes were detected; 55 (25%) of them showed del(6q) (28 males; R-ISS: 1: 27.5%, 2: 31.1%, 3: 41.4%). Cytogenetic analysis showed simple karyotypes (SK; one or two alterations) in 51% of cases and complex karyotypes (CK; 3 or more alterations) in 49%. The distribution of modal number was: hypodiploid (33% of cases), hyperdiploid (30%), hypertriploid (11%), hyperhaploid (8%), pseudodiploid (7%), hypotriploid (7%) and hypotetraploid (4%). The most frequent breakpoints were 6q23 and 6q25 (32.7% each), followed by: 6q21 (29.1%), 6q13 (18.2%), 6q15 (16.4%) and 6q27 (10.9%). Most common alterations associated to del(6q) involved chromosomes: 1 (38.7% of cases), 13 (32.7%), 11 (30.9%), 3 (27.3%), 14, 15 and 19 (25.5% each). By FISH analysis, patients with CK showed high frequency of del(17p) (63.5%) and chromosome 1 alterations (61.5%). Translocations t(11;14) and t(4;14) were observed in 15% of cases each and t(14;16) in 10% of patients. Cases with del(6q) were older (61.4 years) than those w/alt (57.6 years) (p=0.0216). Analysis of clinical parameters showed increased lactate dehydrogenase and serum monoclonal M protein levels in patients with del(6q) than those

w/alt (p<0.0001 and p=0.0353, respectively). Cases with CK also had higher creatinine levels (p=0.0276). Seventy percent of patients received proteasome inhibitor and immunomodulatory agents at induction. No differences in overall survival (OS) between patients with SK (82.2 months) compared to those w/alt (78.2 months) was seen, but a significant short OS in cases with del(6q) and CK (36.1 months) (p=0.003) was observed.

Summary/Conclusion: To our knowledge, this is the first analysis of del(6q) in MM patients from LA. Our cohort had a similar frequency of del(6q) than published series, with particular involvement of 6q23 and 6q25 breakpoints. Interestingly, patients with del(6q) showed high frequency of chromosome 1 alterations, particularly in the context of CK, associated to poor clinical outcome. Our study reinforces the importance of conventional metaphase karyotyping, and its contribution to a better stratification and biologic characterization of MM patients.