Concordance between Conventional and Molecular Cytogenetic Techniques in Identification of Genetic Abnormalities among Newly Diagnosed Multiple Myeloma Patients

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Background/Purpose: Multiple myeloma (MM), also known as plasma cell myeloma, is a clonal hematological malignancy accompanied by abnormal proliferation of plasma cells that is related to an underlying genetic alteration. It is a relatively common neoplasm in elderly with deleterious end organ damage, if left untreated. Identifying of the genetic basis of the disease aids in prognostication as well as disease progression monitoring. Unfortunately, there is no published data about the genetic abnormalities in MM Saudi patients. Previously, genetic abnormalities were detected only in 50-60% of newly diagnosed patients. However, with the advent of plasma cell enrichment techniques, detection rate has been substantially enhanced reaching over 90%. This study reviewed the genetic abnormalities of newly diagnosed patients in our center by two methods and comparing the results with a well-established international data.

Methodology: This retrospective study identified 69 newly diagnosed patients with MM in King Abdulaziz Medical City, National Guard Hospital, Riyadh, between 2012 and 2015. However, only 58 patients were included in this study since they had complete cytogenetic investigations. All of these 58 pat*ents underwent MM-panel testing with florescence in situ hybridization (FISH) technique as well as classical cytogenetic analysis by karyotyping. The validated MM-FISH panel included five different probes; trisomy 12q15, 13q14/13q34 deletion, 17p13.1 deletion, translocation (11;14) and immunoglobulin heavy chain (IGH) rearrangement on chromosome (Ch) 14.*

Results: *In this cohort, the median age at diagnosis was 64.5 years, ranging from 39-91 years with only two cases were younger than 40 years. Male cases were predominant with the male to female ratio of 3.1:1. Karyotype analyses were done on 54 cases, showing failure or very low yield in 10 cases (18.5%) and evident structural or numerical chromosomal abnormalities in 11 cases (20.4%). In contrast, FISH studies were able to detect 41 positive cases out of 58 cases (70.7%). The overall concordance rate between both methods was only 46.3% (table 1). Only a single case showed a genetic abnormality by karyotyping not detected by MM FISH panel. Hyperdiploidy (including trisomies), IGH rearrangements, deletion of Ch 13/13q and Ch 17/17p and hypodiploidy were detected by FISH in 43.1%, 20.7%, 24.1%, 3.5% and 10.3%, respectively (table 2).*

Conclusion: *This study shed light on the pattern of genetic alterations among multiple myeloma patients in Saudi Arabia. In such contexts, FISH turns out to be a superior tool for detection of cytogenetic abnormalities compared with conventional karyotyping, yet rarely some cytogenetic abnormalities not included in the MM FISH panel, may be missed. Implementation of plasma cell enrichment technique to increase the detectability of cytogenetic abnormalities by karyotyping is urged. Finally, correlation of these findings with the clinical behavior of each individual patient will refine our understanding of the impacts of a specific or combined genetic abnormality(ies) on our population.*

Table 1: The concordance between karyotype and FISH studies in 58 newly diagnosed MM patients.

Result/Test	Karyotype	FISH
Tested Samples	54 (100%)	58 (100%)
Failure Samples	05 (9.3%)	00
Inadequate Samples (i.e., very low yield)	05 (9.3%)	00
Negative Cases	33 (61.1%)	17 (29.3%)
Positive Cases	11 (20.4%)	41 (70.7%)
Overall Concordance	25 cases (10 positive and 15 negative), 46.3%	

Table 2: Detailed genetic abnormalities in 58 newly diagnosed MM patients by FISH studies.

Abnormality	Cases with a single abnormality		Cases with other abnormality(ies)		Total	
Negative Cases	17	29.31%	NA	NA	17	29.31%
Hyperdiploidy/Trisomy	15	25.86%	10	17.24%	25	43.10%
Hypodiploidy [del 13 or 17 excluded]	0	NA	6	10.34%	6	10.34%
Deletion 13/13q	5	8.62%	9	15.52%	14	24.14%
deletion 17/TP53	0	NA	2	3.45%	2	3.45%
IGH rearrangement [t(11;14) excluded]	1	1.72%	5	8.62%	6	10.34%
t(11;14) alone	5	8.62%	1	1.72%	6	10.34%
Chromosome 1q gain	0	NA	1	1.72%	1	1.72%
Other abnormalities	0	NA	4	6.90%	4	6.90%