Chromosome aberration in Chinese patients with multiple myeloma: more high-risk MM was found

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Background: Although cytogenetics abnormalities in myeloma have been well documented, there are quite a few reports from chinese patients , what's more, not all FISH testing in China were performed in purified PCs or in combination with immunofluorescent detection of light chain-restricted PC cytoplasmic immunoglobulin enhanced FISH (cIg-FISH). The objectives of this study was to analyze a large series of cases to define the general patterns of cytogenetic abnormalities in chinese patients with MM and to assess the prognostic value of the chromosome aberration.

Materials and methods: Purified $CD138^+$plasma cells were obtained from 306 patients with newly diagnosed MM and 80 relapsed/refractory patients presenting to Blood Diseases Hospital, Chinese Academy of Medical Science & Peking Union Medical College from 2006-2012. Del(13q) abnormality was analyzed with the following probes specific for the 13q14.3 locus (LSI D13S319, Abbott Laboratories) and the 13q34 locus (LSI 13q34, Abbott Laboratories). del(17p13) was assessed using a probe specific for the 17p13.1 locus (LSI p53, Abbott Laboratories). The LSI IGH/ FGFR3dual-color probe (Abbott Laboratories) was used to detect t(4;14), LSI IGH/ CCND1(Abbott Laboratories) XT to t(11;14), and IGH/MAF DF to t(14;16).

A total of 200 interphase nuclei were analyzed. Cut-off values recommended by the European Myeloma Network (EMN) were used: for deletions and numerical aberrations, the cut-off level was set at 20%; for translocations in IgH locus as well as other translocations, the cut-off level was set at 10%.

Results:

Of the 306 newly diagnosed patients investigate by FISH, more than one molecular cytogenetic aberrations were found in 85.4% patients. 13q deletions，17p deletions, illegitimate IGH rearrangement, chromosome 1q amplification, t(11;14), t(4;14), t(14;16) were detected in 46.8%, 7.9%, 59.6%, 50.2%, 22.7%, 22.7%, 3.9% cases. According to Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) model, high-risk MM was defined as the presence of any one or more of the following: hypodiploidy, monosomy of chromosome 13, deletion of 17p13, or t(4;14), or t(14;16). 33.2% cases were indentified to belong to high-

risk group.

For newly diagnosed patients, detection of t(4;14), 1q21 gain, and 17p- by FISH suggested poor outcome, and del13 or 13q detected only by FISH in the absence of other abnormality did not demonstrate prognostic value, whereas t(11;14) did not predict superior outcome.

Of the 80 relapsed patients investigate by FISH, more than one molecular cytogenetic aberrations were found in 96.3% patients. 13q deletions，17p deletions, illegitimate IGH rearrangement, chromosome 1q amplification, t(11;14), t(4;14), t(14;16) were detected in 61.3%, 22.5%, 68.9%, 75.6%、18%, 32.9%, 2.8% cases. 53.8% patients were indentified to belong to high-risk group accoeding to mSMART model.

For relapse/refractory patients, only t(4;14) and 1q21 gain predicted worse outcome, whereas 17p deletions had no impact on survial.

Conclusion:

It seemed that more high-risk MM were found in Chinese patients with newly diagnosed multiple myeloma, and a direct comparison between Western and Asian patients is relevant. High incidence of genetic abnormalities that reflect progression include deletions at 17p13, chromosome 1 abnormalities were founded in relapsed/refractory patients. The prognositic value of chromosome aberration possibly changes with advancing stages of the disease, and should be Reevaluated in the context of relapsed and refractory disease.