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ELEVENTH ANNUAL MEETING

KRAS, NRAS, BRAF GENES MUTATIONS IN THE TUMOR SUBSTRATE FROM BONE MARROW, CTDNA AND PLASMACYTOMAS IN MULTIPLE MYELOMA (MM)

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INTRODUCTION

To assess the heterogeneity of MM, not only the tumor substrate in the bone marrow and plasmacytoma, but also in plasma circulating tumor DNA (ctDNA) could be effectively analyzed[1,2].

AIM

To study the mutational status of *KRAS*, *NRAS*, *BRAF* genes in the tumor substrate from bone marrow, ctDNA and plasmacytomas in MM patients.

METHOD

The study from October 2021 to February 2023 included 72 patients with symptomatic MM (30 men, 42 women) aged 35 to 84 years (median - 58). In 64% of patients with MM, according to CT data, plasmacytomas were detected (in 40 patients: bone and in 6: extramedullary). DNA was isolated from samples of various localization: CD138+ bone marrow cells (n=60), ctDNA (n=19), bone (n=9) and extramedullary (n=6) plasmacytoma. The mutational status of *KRAS*, *NRAS*, and *BRAF* genes was studied in the tumor substrate from different loci.

RESULTS

KRAS gene mutations were detected in 16% of patients, of which less than a third of patients (27%) had high-risk cytogenetic abnormalities. *NRAS* gene mutations were detected in another 16% of patients, while more than half of the patients (55%) were assigned to a high cytogenetic risk group. *BRAF* gene mutations were found in 9% of patients, one third of whom had high-risk aberrations (fig. 1). Paired tumor samples (plasma ctDNA and CD138+ bone marrow cells) were analyzed in 15 patients. No cases with *KRAS*, *NRAS*, or *BRAF* gene mutation detected in the plasma and the absence of the corresponding mutation in the bone marrow were found. It turned out that only *KRAS* gene mutations (7% of cases) were detected in the samples of bone plasmacytomas, and only *NRAS* gene mutations (50% of cases) were detected in the samples of extramedullary plasmacytomas (fig. 2).

Fig.1 Cytogenetic abnormalities in MM patients with *KRAS, NRAS* or *BRAF* gene mutations

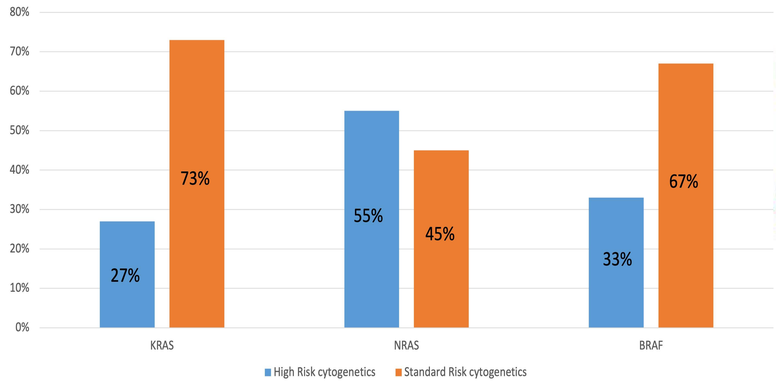
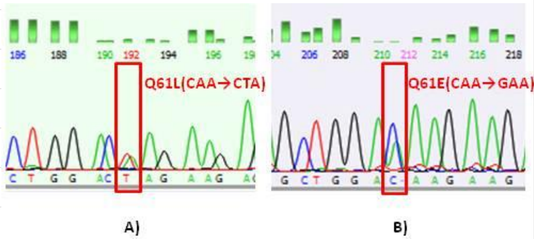


Fig.2 *NRAS* gene mutations in the extramedullary plasmacytoma in 2 patients with MM (A, B)



CONCLUSIONS

There was a trend towards higher frequency of high-risk cytogenetic aberrations in patients with *NRAS* gene mutations compared to patients with *KRAS* gene mutations (55% *vs* 27%).

It was also determined that the NRAS gene was mutated in 50% of extramedullary plasmacytomas samples.

REFERENCES

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