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IS THERE A PLACE FOR C-MYC IHC STAINING IN MULTIPLE MYELOMA REAL-WORLD CLINICAL SETTING? - single centre experience

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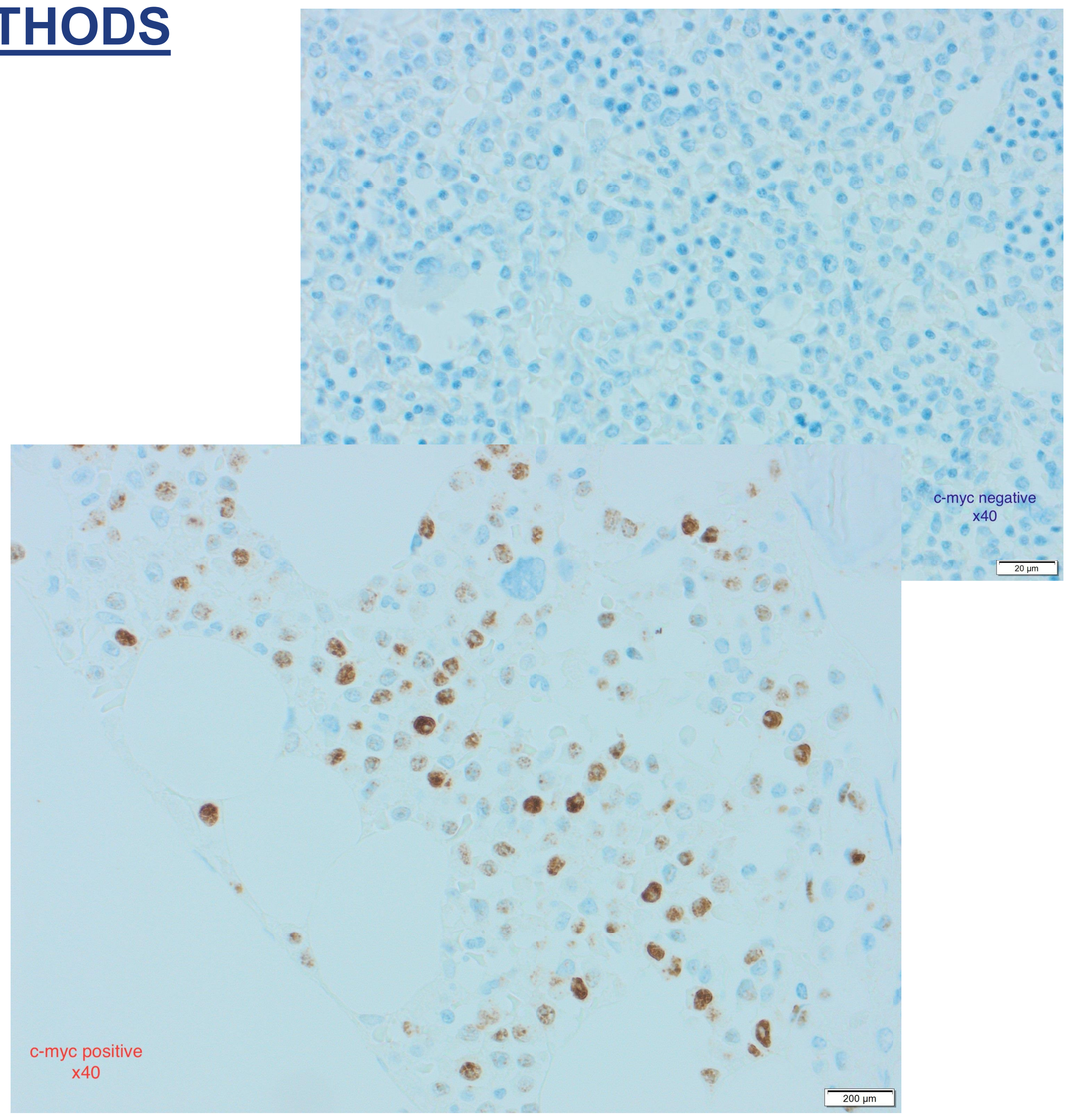
INTRODUCTION

C-myc, as a proto-oncogene, functionally participates in a broad spectrum of intracellular biological processes, including proliferation, differentiation, apoptosis, DNA damage repair, metabolism, and extracellular biological events such as angiogenesis and stromal remodelling. As a potent driver gene in multiple human cancer, this oncoprotein has been listed on the top of the putative drug target list[1]. In multiple myeloma (MM) it is enhanced[2], with range of overexpression between 10-67% depending on detection method. Overexpression of this proto-oncogene has been associated with hypercalcemia, extramedullary myeloma and shorter survival of the MM patients.[3,4] However, its role in MM is still controversial and there is lacking clinical data about c-myc overexpression and its effect regarding response to first line treatment.

MATERIALS AND METHODS

Patients: In a retrospective analysis we included 42 newly diagnosed MM patients in Clinical Hospital Center Rijeka, following international IMWG criteria for diagnosis. We evaluated clinical and prognostic markers: International Staging System (ISS), type of paraprotein in serum, presence of Bence-Jones protein in urine, serum values of haemoglobin, calcium, creatinine, lactate dehydrogenase, beta-2-microglobuline, albumin and presence of osteolytic lesions. Patients received VCD protocol (bortezomib, cyclophosphamide, dexamethasone) or VD protocol (bortezomib, dexamethasone). Response to treatment was assessed with IMWG criteria as complete remission (CR), very good partial remission (VGPR), partial remission (PR) and progression.

Immunohistochemical analysis (IHC): In trephine biopsies we carried out IHC using the following commercially available antibodies: anti-CD138 (mouse anti-CD138 (clone MI15, m7228, DAKO Glostrup, Denmark, ready to use), anti-c-MYC (anti C-MYC (y69, rabbit monoclonal primary antibody, Ventana, ready to use). In each single biopsy, we compared the CD138-stained myeloma cells with the c-myc nuclear staining. According to literature data over-expression was defined with cut-off of 30% c-myc positive myeloma cells.



RESULTS

In our group of MM patients only 2 (4.6%) over-expressed c-myc. However, 23 (54.8%) had some c-myc positive myeloma cells (5-30% of cells were positive) while 19 (45.2%) were negative. Median age was 80 years (47-89) in positive, and 78 (55-87) in negative group with no statistical difference (p=0,527). Prevalence of women was observed in both groups (13/23, 56.5% and 13/19, 68.5%, respectively). Paraprotein IgG kapa was the most represented in both groups (52.17% and 36.84%, respectively). Due to small sample size, significance of paraprotein values between groups was not measured. 12 (52.17%) and 16 (84.21%) patients received VCD protocol, respectively, while 7 (30.43) and 3 (15.79%) received VD protocol, respectively. Response to treatment in c-myc positive group was: CR 52.17%, VGPR 17.39%, PR 30,43%, while response to treatment in c-myc negative group was: CR 26.32%, VGPR 42.10%, PR 26.32%, progression 5.26%. There was no statistical difference in response to treatment between groups (p=0.937). In c-myc positive group 82.61% of patients had osteolytic lesions and 63.16% in negative group, with no statistical difference (p=0.159). Between the two groups, there was no statistical differences in values of haemoglobin (p=0.899), sedimentation rate (p=0.648), lactate dehydrogenase (p=0.390), albumin (p=0.455), calcium (p=0.667), creatinine (p=0.22), beta-2-microglobulin (p=0.095) or ISS stage (p=0.278).

CONCLUSION

Our preliminary results of immunohistochemical analysis determined very small percentage of MM with c-myc overexpression and expression in less than 30% of tumor cells had no clinical implication. Further studies of c-myc over-expression in larger cohort of patients with MM are required.

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