PB1962 COMPARISON OF EXPRESSION OF NSD2, CYCLIN D1 AND C-MAF BY PLASMA CELLS IN BONE MARROW AND BONE PLASMACYTOMA IN PATIENTS WITH PLASMA CELL MYELOGENOUS

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

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Background: Bone plasmacytomas form as a result of destruction of bone structures by tumor proliferate and its escape out of the medullar cavity. According published data, the incidence of bone plasmacytomas at the time of plasma cell myeloma (PCM) diagnosis ranges from 7 to 32.5%, whereas rates are higher in a relapse. Bone plasmacytomas in most cases are composed of mature plasma cells, while immature morphology is mainly characteristic for extramedullary plasmacytomas. It is shown, that plasmacytoma cells are the descendants of bone marrow tumor plasma cells. Due to acquisition of new qualities as a downregulation of adhesion molecules, secretion of growth factors, activation of oncogenes and antiapoptotic factors, new subclones of tumor cells can survive without support from bone marrow microenvironment.

Aims: to compare morphological consistency and immunohistochemical characteristics of PCM substrate in bone marrow trephines and bone plasmacytomas biopsy specimens.

Methods:

In retrospective study were included 13 patients with PCM aged from 36 to 67 years (median 55 years). At the time of diagnosis all patients underwent biopsy of bone plasmacytoma. The diagnosis of PCM verified according to IMWG criteria (2014). All patients have been examined with routine laboratory tests, immunochemical analysis of serum proteins and urine, cytologic examination of bone marrow smears, histologic and immunohistochemical examinations of bone marrow trephines and bone plasmacytomas biopsy specimens, instrumental examinations (CT, MRI).

Immunohistochemical staining of bone marrow trephines and bone plasmacytomas biopsy specimens made with using a stainer Leica Bond-Max, reactions with antibodies to CCND1 (clone SPA4, Cell Marque), NSD2 (clone 29D1, Abcam), c-MAF (clone ERP16484, Abcam). The cut-off scores for determining positivity for markers have been taken 5% for CCND1, 10% for NSD2 and c-MAF (by T. Murase et al., 2019). Microscopic examination of histologic and immunohistochemical slides have been done on light microscope Leica 3000.

Results:

PCM substrate by histologic examination in bone marrow trephines and bone plasmacytomas biopsy specimens were presented by mature plasma cells. In two patients (1 and 8) in bone plasmacytoma have been seen proplasmocytes between mature plasma cells, but in bone marrow have been seen only clusters of mature plasma cells.

According to the results of immunohistochemical examination the expression of proteins-products of oncogenes have been revealed in most patients (12 of 13) in plasma cells of bone marrow and bone plasmacytomas, wherein in half of the patients (patients 7-12) the expression of proteins-products of oncogenes coincides in bone marrow and bone plasmacytoma. We have revealed a discordant expression in another patients (tabl. 1). We've paid a special attention to the patients 1-3, in whom in bone marrow have been revealed an expression of 1/3 protein, but in bone plasmacytoma – 2/3 (patients 2 and 3) or all of 3 studied proteins (patient 1). This phenomenon is possible to consider...
as a heterogeneity of clonal composition of bone plasmacytoma as a consequence of tumor evolution.

**Summary/Conclusion:** Discordant expression of proteins-products of oncogenes NSD2, cyclin D1 and c-Maf in tumor cells in bone marrow and bone plasmacytoma could be evidence of different tumor clones activation in PCM.

| Number of patient | The presence of proteins-products of oncogenes expression in plasma cells in bone marrow trephines | The presence of proteins-products of oncogenes expression in plasma cells in bone plasmacytomas |
|-------------------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
|                   | NSD2 | Cyclin D1 | C-Maf | NSD2 | Cyclin D1 | C-Maf |
| 1                 | +    | -         | -     | +    | +         | +     |
| 2                 | +    | -         | -     | +    | +         | -     |
| 3                 | -    | +         | -     | +    | +         | -     |
| 4                 | +    | +         | -     | -    | +         | -     |
| 5                 | +    | +         | -     | -    | +         | -     |
| 6                 | +    | +         | -     | -    | +         | -     |
| 7                 | -    | +         | -     | -    | +         | -     |
| 8                 | +    | -         | -     | +    | -         | -     |
| 9                 | +    | -         | -     | +    | -         | -     |
| 10                | -    | +         | -     | -    | +         | -     |
| 11                | +    | -         | -     | +    | -         | -     |
| 12                | -    | +         | -     | -    | +         | -     |
| 13                | -    | -         | -     | -    | -         | -     |