MASS SPECTROMETRY-BASED PROTEOMIC ANALYSIS IN RENAL AL AMYLOIDOSIS PROGNOSIS

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Introduction. Amyloidosis is a rare but devastating condition caused by deposition of misfolded proteins as aggregates in the extracellular tissues of the body, leading to impairment of organ's function. Correct identification of the causal amyloid protein is absolutely crucial for clinical management. In this study, we describe three cases of amyloidosis, which is resistant to the novel drugs used and whose poor prognosis seems to correlate to a particular results of mass spectrometry (MS)-based proteomic analysis.

Methods. We compared the data of 6 patients with biopsy diagnosis of renal amyloidosis. All patients showed renal involvement (mean MDRD 34,6 ml/min; heavy proteinuria 15,1± 4,21 gr/24h), moderate cardiac involvement (mean Pro-BNP 361.1 and mean SIV 12.5 mm), serum free light k chains (k dFLC) in 4/10 patients and lambda dFLC in the others six, normal percentage of plasmacells of the bone marrow biopsy (5-10%). The genetic variant of transthyretin (TTR) did not occur. In order to detect serum protein network associated to the Amyloidosis, a proteomic approach was applied using serum and subcutaneous fat and two-dimensional gel electrophoresis separation, Western Blotting and Mass-Spectrometry. All patients received 9 cycles of chemotherapy with Bortezomib (1.3 mg/m^2 subcutaneously on days 1-4-8-11) + Cyclophosphamide (200 mg/m^2 on days 1-8-15-22) + Dexamethasone (40 mg on days 1-8-15-22).

Results. In two of 6 patients there was no remission of amyloidosis disease: however, we observed improvement of renal failure with ESRD, no hematologic response (less than 50% reduction in dFLCs) and an increased NT-proBNP. The others 6 patients showed a complete renal, cardiac and hematologic remission. In 2 patients non-responding we observed an abnormal protein pattern if when compared to a responding patient. In particular in the basic region and with an apparent molecular weight of 60.000 Dalton there was a high presence of an abnormal protein band, which was completely absent in the others patients. With Mass spectrometry analysis we have been able to single out the abnormal protein as a heavy chain IgG subtype 3. This globulin protein, which is usually present in the range of the 1-7% level of total IgG has been found at >90% in the 2 patients' serum.

Conclusion. In this study, we describe two cases of amyloidosis resistant to the novel drugs used, whose poor prognosis seems to correlate to the particular results of mass spectrometry (MS)-based proteomic analysis. This has provoked abnormal levels such as a heavy chain IgG subtype 3 with different physico-chemical properties. We conclude that, in the future, proteomic analysis could impact and orient early prognosis.

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