Meningioma metabolic subgroups revealed by NMR spectroscopy

D. Monleon[1], J. M. Morales[2], A. Gonzalez-Segura[1], C. Lopez-Gines[3], J. M. Gonzalez-Darder[4], R. Gil-Benso[3], and M. Cerda-Nicolas[3]

[1]Fundacion Investigacion HCUV, Valencia, Valencia, Spain, [2]Universidad de Valencia, Valencia, Valencia, Spain, [3]Universidad de Valencia, [4]Hospital Clinico Valencia

Purpose

Meningiomas add up to 30% of CNS tumours. The World Health Organization (WHO) classifies meningiomas into three histologic grades: grade I (benign), grade II (atypical), and grade III (anaplastic) in accordance with the clinical prognosis. Atypical meningiomas show a high index of recurrence 5 years after complete resection. Sometimes, meningiomas with histological diagnosis of benign meningioma show clinical characteristics of atypical meningioma. Additional criteria for better classification of meningiomas will improve clinical decisions like resection extension, additional radiotherapy needs, treatment selection and patient follow up strategy after surgery. In this communication, we used NMR metabolic profiling for molecular characterization of 30 benign and 10 atypical meningiomas.

Methods

Samples Tumor samples were obtained from 40 patients with meningioma from the Clinic Hospital of Valencia. The samples were categorized (30 benign and 10 atypical menigniomas) according to the WHO classification. Karyotypic analyses were performed according to ISCN (1995) for the determination of chromosomally normal benign meningioma.
NMR spectroscopy Metabolic profiling of the samples was performed on frozen tissue by HR-MAS (High resolution Magic Angle Spectroscopy). The whole HR-MAS study was performed at 4 C. HR-MAS spectra were recorded in a Bruker AVANCE spectrometer at 600 MHz. Samples were spun at 5kHz. All samples were analyzed by post-HRMAS histopathology to assess the tissue integrity and double validate histological diagnosis.
Statistical analysis Statistical analysis was performed using in-house MATLAB scripts and the LIBRA statistical multivariate analysis library. Principal Component Analysis (PCA) was applied to the set of spectral vectors. Principal components chosen explained at least 90% of the variance. A Partial Least squares Discrimination Analysis (PLS-DA) model for discrimination between atypical and chromosomally normal benign meningioma was built.

Results

The PLS-DA analysis of the NMR metabolic profile for chromosomally normal and atypical meningioma shows clear separation between groups (Figure 1). The major features for this separation were higher concentrations of glycine, glutamate, phosphocholine, and uracil and lower concentrations of global fatty acids, ascorbate, acetate, creatine, glucose, choline and ethanolamine. For most of these metabolites the values for benign meningioma with chromosomal instabilities were closer to atypical meningioma than to chromosomally normal benign meningioma (Figure 2). Most of the metabolic changes observed in benign meningioma with chromosomal instabilities and in atypical meningioma reflect a higher tumor metabolism (higher glycolysis, resistance to apoptosis, higher membrane turnover, etc).

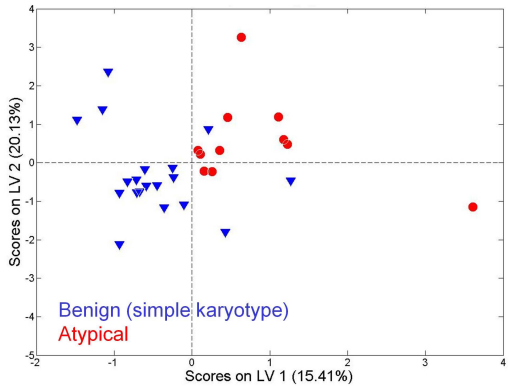

Figure 1. Scores plot of PLS-DA to compare the metabonome of the chromosomally normal benign meningioma (blue triangles) and the atypical meningioma (red circles).

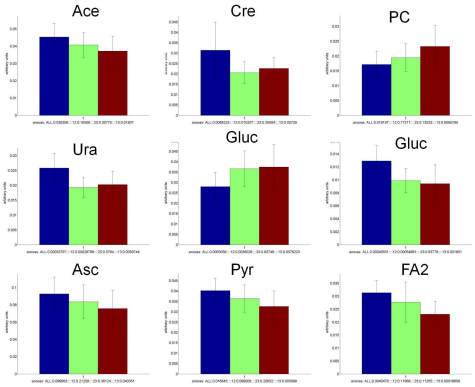

Figure 2. Histograms showing relevant metabolite levels for the chromosomally normal benign meningioma (blue), the benign meningioma with chromosomal instabilities (green bars) and the atypical meningioma (red bars).

Discussion / conclusion

The metabolic phenotype measured by HR-MAS allows detecting metabolic aggressiveness in otherwise benign tumors. The metabolic and genetic profile obtained for this new subgroup of meningiomas place them biochemically closer to atypical meningioma than to the conventional benign meningioma. Our study revealed a subgroup of benign meningiomas with aggressive metabolism and chromosomal instabilities. This is the first time than differential metabolic profiles are reported for tumors with the same histological grade. The methodology used in this study may also open new possibilities in the diagnosis of meningioma.

Acknowledgements

Ministry of Science and Innovation of Spain (SAF2008-00270) and Generalitat Valenciana (GVASAN AP014/2009 and GVAEDU/ACOMP/184/2010) are gratefully acknowledged for financial support. DM gratefully acknowledges a Ramon y Cajal contract from the Ministry of Education of Spain.