THESES

PRIMITIVE NEUROECTODERMAL TUMOR OF THE POSTERIOR FOSSA: MEDULLOBLASTOMA. EVALUATION OF THE PROLIFERATIVE INDEX BY MEANS OF MONOCLONAL ANTIBODY MIB-1, ITS PROGNOSTIC CORRELATION AND THERAPEUTICS IMPLICATIONS (ABSTRACT)*. **THESIS**. **SÃO PAULO**, **2002**.

*ANTONIO FERNANDES FERRARI***

Tumors result from the unbalance between cellular proliferation and its death. As cellular proliferation increases, the more aggressive the tumor gets. The gold-standard method for labelling which cells are proliferating is the immunohistochemistry using monoclonal antibodies that recognize these cells. In the past few years, the monoclonal antibody Mib-1 has been used by researchers in order to retrospectively study paraffin imbed tumor fragments. The medulloblastoma is the most frequent maling central nervous system tumor in childhood. It seems to be originated from the inferior medullary velum and it occupies the fourth ventriculum invading cerebellar hemispheres and brain stem.

This retrospective study presents an analysis of the cellular proliferation index of the posterior fossa medulloblastomas collected from 22 patients at A. C. Camargo Hospital, from January 1999 to December 1999. The histopathological diagnosis was confirmed by H.E. and LI was acquired by Mib-1 which detects proliferating cells during G1, G2, S and M phases. The objectives were: determination of the mean Mib-1 LI value from these patients, correlating sex, age, race, clinical and radiological findings and treatment as well as the prognostic value of the method.

The results demonstated that the mean Mib-1 value has no significant statistic correlation with sex, age, race, clinical and radiological findings and p53, although patients harboring tumor with proliferation indexes lower than the mean value had a better prognosis.

In conclusion, these methods have to be placed as routine for patients harboring medulloblastomas, and the ones who have LI greater than the mean value found in this study have to be treated aggressively.

KEY WORDS: primitive neuroectodermal tumor, posterior cranial fossa, medulloblastoma, proliferative index.

*Tumor neuroectodérmico primitivo da fossa posterior: meduloblastoma. Avaliação do padrão proliferativo celular, sua correlação prognóstica e implicações terapêuticas (Resumo). Tese de Doutorado, Faculdade de Medicina da Universidade de São Paulo (Área: Neurologia). Orientador: José Píndaro Pereira Plese.

*** Address: Rua Mario Moretti 76, 19060-570 Presidente Prudente SP.*

THE INFLUENCE OF THE APOLIPOPROTEIN E POLYMORPHISM IN THE LIPID PROFILE OF ALZHEIMER'S DISEASE OR VASCULAR DEMENTIA PATIENTS. (ABSTRACT)*. **DISSERTATION**. **SÃO JOSÉ DO RIO PRETO**, **2002**.

*SILVIA APARECIDA SOARES***

The apolipoprotein E (apo E) plays an important role in the modulation of atherogenic lipoproteins and in the pathogenesis of Alzheimer's disease. Recognizing the association between these two functions would make early clinical intervention possible, with obvious benefits in terms of patient care.

This study aimed to assess the influence of the apo E genetic polymorphism in the lipid profile of late onset Alzheimer's disease (LAD) and vascular dementia (VD) patients and controls. The possibility that the apo E polymorphism could become a risk factor for dementia because of its influence on the lipid profile in those patients was investigated.

A total of one hundred and sixty-one subjects were studied (mean age 72 years) and divided into three groups: Group 1 (G1) = 63 patients with AD; Group 2 (G2) = 38 patients with VD; Group 3 (G3) = 60 individuals without clinical signs of these diseases. All patients were clinically assessed following standard protocol and guidelines (NINCDS-ADRA).

DNA was extracted from leukocytes by means of amplification of the apo E gene through polymerase chain reaction, and the products were submitted to enzymatic restriction with *Hha* I. Investigation of the lipid profile included measurement of the levels of triglycerides (TG), total cholesterol (TC), and cholesterol

fractions of low density lipoprotein (LDLc), high density lipoprotein (HDLc) and very low density lipoprotein (VLDLc). All data were submitted to statistical analysis.

The frequency of e4 allele was significantly higher in AD (0.27) compared with controls (0.10; p= 0.004).The ε3/ε3 genotype was prevalent in all groups, mainly in G2 and G3 (71.0%; 73.3%, respectively). ε4 genotypes had the highest incidence in G1 (47.6%), while ε3/ε3 genotype was more frequent in G3 (73.3%). Mean values of TC and LDLc in G2 for ε3/ε3 genotype were significantly higher specifically for ε-/ε4 (223.6± 57.7; 300.4±61.3 mg/dL, respectively) compared with G1 (161.3±38.7; 236.8±45.7 mg/dL, respectively) and G3 (142.7±29.2; 220.3±33.6 mg/dL, respectively). Mean TG levels in G2, independent of apo E genotypes, also showed a significant increase, compared to G1 and G3. Mean values of HDLc and VLDLc remained within the desirable range in all groups and genotypes, although in G2 the mean level of HDLc was significantly lower (36.9±12.9 mg/dL) compared to G1 (51.3±17.5 mg/dL) and G3 (51.5 ±14.1 mg/dL), exclusively for the ε3/ε3 genotype. Conversely, the prevalence of ε-/ε4 genotypes was significantly higher in AD patients with increased TC, LDLc and TG levels when compared to the control group. There was, however, no significant difference between AD and VD or between VD and the control group.

In conclusion, the incidence of the ε4 allele and ε-/ε4 genotypes allows discrimination between AD patients and controls and characterizes ε4 as a risk factor for AD. Its prevalence, however, does not differentiate VD patients from controls, which suggests that the apo E polymorphism plays a less significant role in VD than in AD. A higher incidence of ε4 in AD patients with an altered lipid profile suggests that both factors play a role in the pathogenesis of the disease. The similarity between AD, VD and controls is indicative of the presence of other factors that might influence lipid metabolism besides the ε4 allele in VD.

KEY WORDS: apolipoprotein E, lipid profile, vascular dementia, Alzheimer's disease.

* Estudo do polimorfismo genético da apolipoproteína E e sua influência no perfil lipídico em pacientes com demência (Resumo). Dissertação de Mestrado. Faculdade de Medicina de São José do Rio Preto- FAMERP (Área: Neurogeriatria). Orientadora: Dorotéia Rossi Silva Souza. Co-orientador: Waldir Antonio Tognola.

***Address: Rua Dom Afonso Henrique 901 / 54, 15085-030 São José do Rio Preto SP, Brasil. E-mail: silviarp@zaz.com.br*

THESES é seção de *Arquivos de Neuro-Psiquiatria* que divulga os resumos em inglês de teses defendidas e aprovadas. O assunto da tese deve estar relacionado a aspectos clínicos ou experimentais de interesse em neurologia, ciências a ela afins e psiquiatria.

Para publicação, o Autor deve encaminhar ao Editor: *abstract* da tese, acompanhado do *título em inglês* e em português; *key words*; *disquete* com a reprodução desses dados.

Adicionalmente, o Autor deve informar: a natureza da tese (Dissertação/Tese de Mestrado, Tese de Doutorado, Tese de Livre-Docência - como exemplos); nome da instituição na qual foi defendida e respectiva área de concentração; nome do Orientador, quando for o caso; endereço para correspondência.