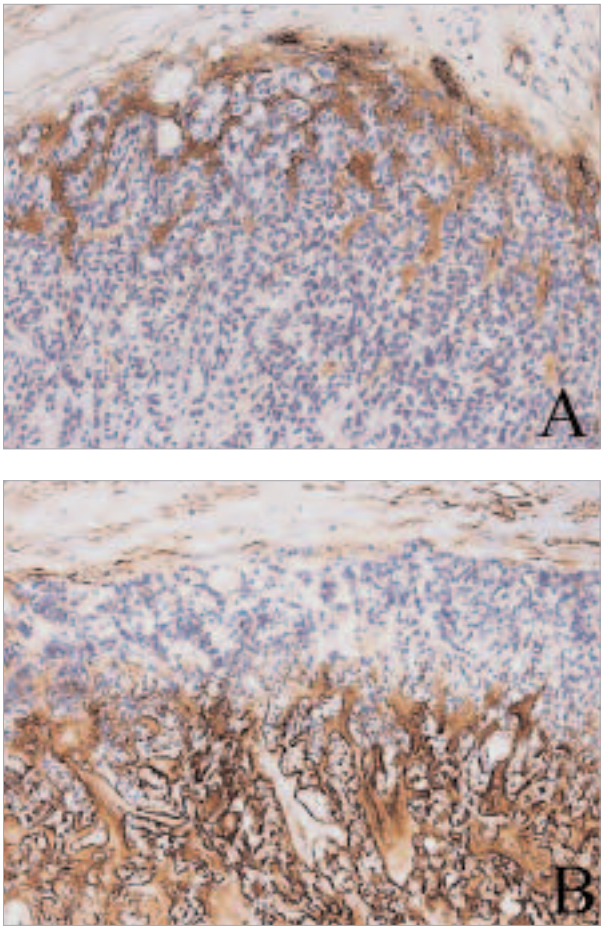
STUDY OF THE ALTERATIONS RESULTING FROM THE MALIGNANT TRANSFORMATION OF PLEOMORPHIC ADENOMA INTO CARCINOMA EX-PLEOMORPHIC ADENOMA

Vera Cavalcanti de ARAÚJO

Centro de Pesquisas Odontológicas São Leopoldo Mandic (SLMA)



CXPA minimally invasive type, with epithelial component. A and B: different expression of tenascin and fibronectin. Tenascin is expressed only in the invasion front (A) meanwhile, fibronectin is expressed only in the deep area (B) of the same specimen

Carcinoma ex-pleomorphic adenoma (CXAP) is a salivary gland tumor resulting from a malignant transformation of pleomorphic adenoma, usually recurrent or of long duration. It accounts for 5 to10% of all salivary gland tumors. It is considered a high grade tumor with frequent metastasis and death. Since it is a rare malignant transformation of a benign tumor, the CXAP is an interesting model for studying the events that take place during the malignant transformation, such as the acquired metastasis, the alteration of cellular fenotype, the modification of the environment, the occurrence of anti-invasive and invasive components and the chromossome alteration related to the material loss and gain. The aim of this project is to study the CXPA according to the following subjects: i) immunohistochemical profile of tumoral cells in relation to cytoskeleton proteins, adhesion proteins (cadherin and catenin),inhibitor of protease (Maspin);
ii) immunohistochemical profile of tumoral stroma;
iii) study of tumor oncogenes and suppressor genes;
iv) analysis of genetic alterations by comparative genomic hybridization. All the results will be analyzed by comparing the benign area with the malignant area and, when it exists, with the transitional area.

SUMMARY OF RESULTS TO DATE AND PERSPECTIVES

The study of CXPA in its different phases of malignant progression allowed comparative studies between benign and malignant area, including transitional area, contributing to the knowledge of this tumor oncogenesis. The cytoskeletal protein analysis has classified CXPA in tumors with epithelial component and epithelial and/or mioepithelial and highlighted the *in situ* conditions. This way we have contested the literature which considers intracapsular tumor as *in situ* tumor. It has been shown that benign myoepithelial cells surrounding malignant luminal cells of *in situ* areas become more differentiated and produce important proteins related to the tumor suppressor role. It has been observed that maspin was present in the myoepithelial cell possibly as a suppressor tumor preventing tumor growth and metastasis as well as the invasion and motility. P53 protein and C-ERB-2 were observed even in the early phase of malignant transformation contributing to the differential diagnosis between atypical cells without oncogenic potential and carcinomatous group of cells. Concerning tumoral stroma it has been observed that tenascin and collagen type I of fibrilar pattern probably highlight the real invasive front of the tumor. Desmoplasia increases with the tumor progression, being rare at CXPA presenting myoepithelial component. About vascularization, it was observed that the lymphatic vessels were the ones previously present in the benign tumor and that neoangio genesis increased during adenoma progression to carcinoma and it was lower in tumors presenting myoepithelial differentiation, although showing high microvascularization total area. Cromossomic analysis has identified regions which genes potentially involved in tumoral process or the ones responsible for tumor severity.

MAIN PUBLICATIONS

Altemani A, Martins MT, Freitas L, Soares F, Araujo NS, Araujo VC. 2005. Carcinoma ex pleomorphic adenoma (CXPA): immunoprofile of the cells involved in carcinomatous progression. *Histopathology*. **46(6)**:635-41.

reitas LL, Araujo VC, Martins MT, Chone C, Crespo A, Altemani A. 2005. Biomarker analysis in carcinoma ex pleomorphic adenoma at an early phase of carcinomatous transformation. *Int J Surg Pathol*. **13(4)**:337-42.

Martins MT, Altemani A, Freitas L, Araújo VC. 2005. Maspin expression in carcinoma ex pleomorphic adenoma. *J Oral Pathol Med*. **58**:1311-4.

de Araujo VC, Altemani A, Furuse C, Martins MT, de Araujo NS. 2006. Immunoprofile of reactive salivary myoepithelial cells in intraductal areas of carcinoma ex-pleomorphic adenoma. *Oral Oncol.* **42(10)**:1011-6.

Soares AB, Ponchio LA, Juliano PB, De Araujo VC, Altemani AM. 2007. Lymphatic vascular density and lymphangiogenesis during tumor progression of carcinoma ex-pleomorphic adenoma. *J Clin Pathol*. **60(9)**:995-1000.

Araújo VC, Furuse C, Cury PR, Altemani A, Alves VAF, Araújo NS. 2008. Tenascin and fibronectin expression in carcinoma ex-pleomorphic adenoma. *Appl Immunohistochem Mol Morphol*. **16(1)**:48-53.

Soares AB, Juliano PB, Araujo VC, Metze K, Altemani A. 2007. Angiogenic switch during tumor progression of carcinoma ex-pleomorphic adenoma. *Virchows Arch*. **451(1)**:65-71.

Araújo VC, Furuse C, Cury PR, Altemani A, Alves VAF, Araújo NS. 2007. Desmoplasia in different degrees of invasion of carcinoma Ex–Pleomorphic Adenoma. *Head and Neck Pathology*. **1**:112-7.

Vera Cavalcanti de ARAÚJO

Centro de Pesquisas Odontológicas
São Leopoldo Mandic/SLMA
Rua Abolição, 1827 – Swift
13045-610 – Campinas, SP – Brasil

+55-19-3237-3611 r. 225
veraa@slmandic.com.br