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ARTICLE

Estrogen Receptor Expression in Salivary Gland Mucoepidermoid Carcinoma and Adenoid Cystic Carcinoma

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Estrogen receptor (ER) expression in salivary gland carcinomas is controversial, and most published studies considered no more than 10 cases. We analyzed ER expression by immunohistochemistry in 136 mucoepidermoid carcinomas and 72 adenoid cystic carcinomas. All cases were negative. These results do not support a role for estrogens in salivary gland mucoepidermoid carcinoma and adenoid cystic carcinoma. (Pathology Oncology Research Vol 10, No 3, 166–168)

Keywords: mucoepidermoid carcinoma, adenoid cystic carcinoma, salivary gland tumors, immunohistochemistry, estrogen, estrogen receptor

Introduction

Estrogen receptor (ER) expression has been demonstrated in hormone-dependent organs such as breast, endometrium, colon, prostate and their cancers.[3,9] In salivary gland tumors ER expression has been reported in a limited number of cases.[4,7,10,13] Salivary gland tumors refractory to conventional therapy (surgery, radiotherapy and chemotherapy) would possibly benefit from by hormonal therapy, but it is important to identify therapeutic targets to these agents. The aim of this study was to evaluate the expression of ER in a large series of salivary gland mucoepidermoid carcinomas (MEC) and adenoid cystic carcinomas (ACC).

Material and Methods

A hundred and thirty six MECs and seventy two ACCs, from the files of the AC Camargo Cancer Hospital, São Paulo, Brazil, were used in this study. Clinical data were obtained from the patients' records. MECs were graded according to Ellis and Auclair[5] as low, intermediate and high grade, and ACCs classified as cribriform, tubular and solid types. Immunohistochemical reactions against ER (mouse monoclonal antibody against estrogen receptor, clone NCL-ER-6F11, Novocastra Laboratories, UK, dilution 1:50) were performed on 3 µM histological sections. Microwave antigen retrieval using EDTA pH 8.0, overnight incubation with the primary antibody and secondary antibodies conjugated to a streptavidin-biotin-peroxidase system (Strept ABComplex/HRP Duet, Mouse/Rabbit, Dako A/S, Denmark) were used, followed by diaminobenzidine as the chromogen. Slides were counterstained with Carazzi hematoxylin. Positive (benign fibrocystic disease of breast) and negative (absence of the primary antibody) controls were included in all reactions.

Results

For MECs, the mean age of the patients was 45 years (ranging from 6 to 96 years) and 77 (57%) were males. Site of the tumors included 69 minor (50.7%) and 67 major (49.3%) salivary glands, with parotid affected in 50 cases (37%). TNM staging revealed 59% clinical stages I + II and 41% stage III + IV patients. MEC histological grade showed 58 (45%) low-grade, 24 (18%) intermediate-grade and 48 (37%) high-grade tumors. For ACCs, the mean age was 50 years (ranging from 10 to 82

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Table 1. **Summary of the reports of estrogen receptor (ER) expression in salivary gland mucoepidermoid carcinoma (MEC) and adenoid cystic carcinoma (ACC).**

Authors	*Year*	*MEC*		*ACC*	
		No. of cases	*ER positive*	*No. of cases*	*ER positive*
Dimery et al.[3]	1987	2	1 (50%)	4	3 (75%)
Lamey et al.[9]	1987	1	0	NP	NP
Wilson et al.[14]	1993	1	0	NP	NP
Miller et al.[10]	1994	NP	NP	5	0
Shick et al.[13]	1995	NP	NP	12	0
Gaffney et al.[6]	1995	6	0	7	0
Jeannon et al.[8]	1999	10	3 (30%)	6	0
Dori et al.[4]	2000	NP	NP	27	0
Nasser et al.[11]	2003	10	1 (10%)	10	0
Our study	2004	136	0	72	0

NP – not performed

years), and 37 were males (51.4%). Minor and major salivary glands were affected in 45 (62.5%) and 27 (37.5%) cases, respectively. According to clinical stages, 53 (73.6%) tumors were classified as stage III+IV and 19 (26.4%) as stage I+II. Microscopically, 34 cases (47.2%) were cribriform, 21 (29.2%) tubular and 17 (23.6%) solid. ER expression was not detected in any of the MEC or ACC cases.

Discussion

Hormone therapy has been succesfully used as adjunctive treatment in some cancers, but its efficacy in salivary gland tumors has not yet been demonstrated.[8] Ozono et al.[12] demonstrated the expression of ER in DMBA-induced epidermoid carcinoma of the submandibular glands in rats, experimentally supporting its participation in tumorigenesis and the use of hormone therapy in salivary gland tumors. However, studies in humans have shown that the expression of hormones and their receptors in salivary gland tumors is not frequent or even absent.[4,6,7,9,10,13,14] These findings do not support a role for hormones role in salivary gland function and tumorigenesis.[4,9,10] Nevertheless, hormone therapy trials have been suggested as adjunctive protocols in salivary duct carcinoma and adenoid cystic carcinoma unresponsive to conventional therapeutic strategies, in view of their aggressive behavior.[2]

ER expression in MEC is controversial. Jeannon et al.[8] have shown ER in 3 out of 10 MECs, supporting the use of hormone therapy in some tumors, and Dimery et al.[3] found ER expression in one of their 2 MECs studied. More recently Nasser et al.[11] have shown ER expression in one of their 10 MECs studied. In contrast, Gaffney et al.[6] studying 6 parotid MECs, Lamey et al.[9] and Wilson et al.[14] in one case of MEC each, found no estrogen receptor expression. Our 136 cases of MEC were negative for ER expression (*Table 1*).

ER expression in ACCs was negative in most reports.[4,6,8,10,11,13] We confirmed these results in 72 cases of ACC. However, Dimery et al.[3] found ER expression in 3 out of 4 ACC (*Table 1*). Interestingly, Arpino et al.[1] found 46% expression of ER in breast ACC, supporting that although it is rare in salivary gland tumors, ER expression is influenced by anatomical sites.

Our results support that estrogen do not participate in salivary gland MEC and ACC tumorigenesis. Consequently there is no rationale for hormone therapy trials because probably it would not be a useful strategy in the management of these tumors.

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