Archives of Oral Biology 60 (2015) 1437–1441

Contents lists available at ScienceDirect

Archives of Oral Biology

journal homepage: www.elsevier.com/locate/aob

Review

p53 expression in pleomorphic adenoma of salivary glands: A systematic review and meta-analysis

Nader Ahmed Alaizari [a,b,*], Bassel Tarakji [a], Sadeq Ali Al-Maweri [a,b], Hashem Motahir Al-Shamiri [a], Shourouk Darwish [a], Feras Baba [c]

[a] Department of Oral Maxillofacial Sciences, Al-Farabi College of Dentistry and Nursing, Riyadh, Saudi Arabia
[b] Department of Oral Medicine and Pathology, Faculty of Dentistry, Sana'a University, Yemen
[c] Aleppo University, Faculty of Dentistry, Syria

ARTICLE INFO

Article history:
Received 17 February 2015
Received in revised form 29 May 2015
Accepted 15 June 2015

Keywords:
p53
Immunohistochemical
Systemic review
Meta-analysis
Pleomorphic adenoma

ABSTRACT

Objective: There are conflicting data regarding immunohistochemical expression of p53 in pleomorphic adenoma. This systematic review and meta-analysis aimed to examine whether p53 expression has a role in the pathogenesis of pleomorphic adenoma.
Design: A comprehensive literature search for relevant studies published from 2000 up to end of 2014 was performed using PubMed, EMBASE and the Cochrane Library Databases. Only articles in which p53 detected by immunohistochemical staining were included. The meta-analysis was done using Comprehensive Meta-Analysis software.
Results: Eighteen eligible studies were included in this meta-analysis. Heterogeneity measures showed a statistically significant Cochrane *Q* value (*P*-value < 0.001). The random effects model showed an effect size of 0.254 with a 95% CI (0.139–0.417). The overall p53 positivity is 25.4%.
Conclusion: Mutant p53 has to be detected by more precise techniques to emphasize on its role in development of pleomorphic adenoma of salivary gland.

Contents

1. Introduction

The most common salivary gland tumor is the pleomorphic adenoma (PA), which represents 40–45% of all salivary gland neoplasms. Most of pleomorphic adenomas occur in the parotid glands, although submandibular glands, sublingual glands or

* Corresponding author at: Department of Oral and Maxillofacial Sciences, Al-Farabi College of Dentistry and Nursing, Riyadh, Saudi Arabia.
E-mail address: dr2007nader@yahoo.com (N.A. Alaizari).

http://dx.doi.org/10.1016/j.archoralbio.2015.06.019
0003-9969/

minor salivary glands could be affected less frequently (Speight & Barrett, 2002). The histopathological pattern of PA is characterized by morphological heterogeneity, great cellular diversity, as well as changes in the differentiation pattern and in the architecture of the gland. These changes can be predominantly epithelial or predominantly mesenchymal (Ianez et al., 2013; Ito, Jorge, Vargas, & Lopes, 2009).

Understanding the molecular biology of salivary gland tumors plays a crucial role in their diagnosis, treatment and prognosis. The evaluation of different proteins expressed in these tumors can reflect facts about the biology and behavior of a tumor (Ozono, Onozuka, Sato, & Ito, 1992).

Inhibition of apoptosis and activation of cell proliferation is the leading mechanism of malignant transformation and progression due to disturbances in cell cycle regulation. Accordingly, the study of tumor suppressor p53 is of particular importance (Coradini & Daidone, 2004).

Normally, p53 gene acts as genome protector, DNA rescuer, and apoptosis inducer. It blocks the cell cycle in the G1 phase, initiates the processes of DNA repair and determines the fate of cells. Currently, two types of the p53 gene are distinguished: normal (wild-type, wt) that is present in all proliferating and regenerating tissues and determining the apoptotic pathway of cell elimination and mutant (mt) (Levine, Momand, & Finlay, 1991).

Mutations of p53 have been demonstrated in a subset of salivary gland tumors and are thought by some authors to be an early event in malignant transformation of pleomorphic adenomas. There are conflicting data regarding immunohistochemistry for p53 in pleomorphic adenomas, with p53 expression seen in 0–54% of cases (Nordkvist et al., 2000; Ohtake et al., 2002). Therefore, we present a systemic review and meta-analysis of published studies on the expression of 53 in pleomorphic adenoma to assess the involvement of this tumor suppressor gene in the pathogenesis of this tumor.

2. Material and methods

2.1. Literature search and eligibility criteria

A systematic literature search of the electronic database PubMed, EMBASE and the Cochrane Library Databases from 2000 to November 2014 was performed. A random combination of the following terms was used for the search: 'p53, immunohistochemical, expression, pleomorphic adenoma, salivary gland tumors, salivary gland neoplasms'. Irrelevant and repeated studies were identified and excluded and the potential publications were screened. All of the remaining literature on the topic of interest was reviewed for additional pertinent studies. Finally after screening by full text reading, publications lacking eligibility were further excluded and the eligible studies were included in the study to evaluate the implication of p53 in pathogenesis of primary pleomorphic adenoma.

2.2. Inclusion into the current review was based on the following criteria for all retrieved studies

Tumor type of study performed was primary pleomorphic adenoma. Papers were reviewed to determine whether immunohistochemical assessment of p53 had been performed. Studies that did not involve pleomorphic adenoma, performed only on cell lines, western blotting and gene profiling studies (non-IHC studies) have not reviewed.

2.3. Data extraction and quality assessment

A total number of 18 final papers were included in this study and two authors independently evaluated the studies for eligibility. Data retrieved from the reports included author, publication year, number of cases, gender, mean age, type of salivary gland involved, the choice of cutoff scores for the definition of positive staining or staining intensity and positive percentage (Table 1). If data from any of the above categories were not reported in the primary study, items were treated as "not applicable". Actually, we did not use prespecified quality-related inclusion or exclusion criteria and did not weigh each study by a quality score due to the following two reasons: first, the eligible studies are case reports or series and most of them were on tissue samples with limitations in follow up of the patients and scoring the survival rates. Second, there is no consensus on a generic candidate too for assessing quality of observational epidemiological studies (Sanderson, Tatt, & Higgins, 2007).

2.4. Statistical analysis

Meta-analysis of the present study was performed using Comprehensive Meta-Analysis version 2.2.048 software. Cochran's Q provides a P-value for the test of homogeneity (Biggerstaff & Jackson, 2008). I^2 is deemed to be more reliable in assessing inconsistency between studies, with values of 25%, 50% and 75%

Table 1
Characteristics of the included studies.

First author, year	No. of cases	Gender M/F	Mean age years	Type of gland	Definition of positivity (%)	Positive expression (%)
Al-Rawi, 2010	10	NR	NR	3 P, 7 MSGs	≤5	30
Alves, 2002	60	23/37	36.3	SM	NA	0
Alves, 2004	15	NR	NR	P, MSGs	>5	0
Da Cruz Perez, 2004	26	4/22	15.7	11SM, 10P,5MSGs	>5	0
DeRoche, 2008	41	15/26	48.4	35P, 1 SM, 5MSGs	≥5	12
Ferreira, 2014	31	9/22	35	MSGs	NA	0–1
Gomes, 2011	18	NR	46	NA	≥1	27.70
Gomes, 2012	14	NR	45.6	6 P, 2 SM, 6 MSGs	>5	42.80
Gordón-Núñez, 2008	19	NR	NR	NA	≥5	73.70
Jorge, 2001	5	1/4	15.8	MSGs	NA	0
Lazzaro, 2000	38	NR	NR	MSGs	>1	73
Maquez, 2007	10	NR	NR	NA	>5	0
Nagler, 2003	6	NR	NR	P, SM, MSGs	>10	0
Ohki, 2001	14	NR	NR	NA	>10	1–40
Ohtake, 2002	101	40/61	46.4	18P, 14SM, 1SL, 68 MSGs	NA	54.50
Soares, 2011	10	6/4	46	8 P, 2 SM	NA	0.20
Tarakji, 2010	29	10/19	52	P	≥1	75.90
Weber, 2002	42	NR	NR	P	NA	9.50

P, parotid gland; SM, submandibular gland; SL, sublingual gland; MSGs, minor salivary glands; NA, not applicable; NR, not reported.