

## Original Article

# Pleomorphic adenoma of salivary gland and synchronous/metachronous invasive ductal breast cancer: a casual coincidence or a clinical presentation resulting from common genetic events?

Francesco Longo<sup>1</sup>, Rocco Sabatino<sup>2</sup>, Gabriella Aquino<sup>2</sup>, Nunzia Simona Losito<sup>2</sup>, Monica Cantile<sup>2</sup>, Franco Ionna<sup>1</sup>, Gerardo Botti<sup>2</sup>

<sup>1</sup>Head and Neck Surgery Unit, <sup>2</sup>Pathology Unit, Istituto Nazionale per lo Studio e la Cura dei Tumori "Fondazione G. Pascale", IRCCS, Naples, Italy

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**Abstract:** Breast and salivary glands have similar morphological and pathological features; however genetic relation between these lesions were not described. In this report we described a small series of biomarkers that developed synchronously or metachronous pleomorphic adenoma of the salivary glands and invasive breast cancer, on which we have tested, by immunohistochemistry, several of bio-markers that may be associated with the pathogenesis of both malignancies. In conclusion, we suggest to better investigate early genetic alterations that could underlie of the synchronous occurrence of these lesions.

**Keywords:** Synchronous/metachronous tumors, pleomorphic adenoma, breast cancer

## Introduction

The manifestation of multiple tumors in the same individual, synchronous or metachronous, are taking in recent years an increasing clinical relevance. Causal mechanism of this event can include environment but mainly relevant genetic events, or combination of both. However, genetic predisposition to develop multiple cancers is still currently the subject of numerous studies [1].

Breast and salivary glands are both tubulo-acinar exocrine glands sharing similar morphological features. Their similarity also accompany their pathological processes of neoplastic transformation. For this reason many benign and malignant mammary tumors often are defined as Salivary Gland-like Tumors of the Breast [2].

Pleomorphic adenoma (PA) is one of the most frequent tumors in salivary glands, and it can develop simultaneously with other salivary gland tumors or can develop at different sites

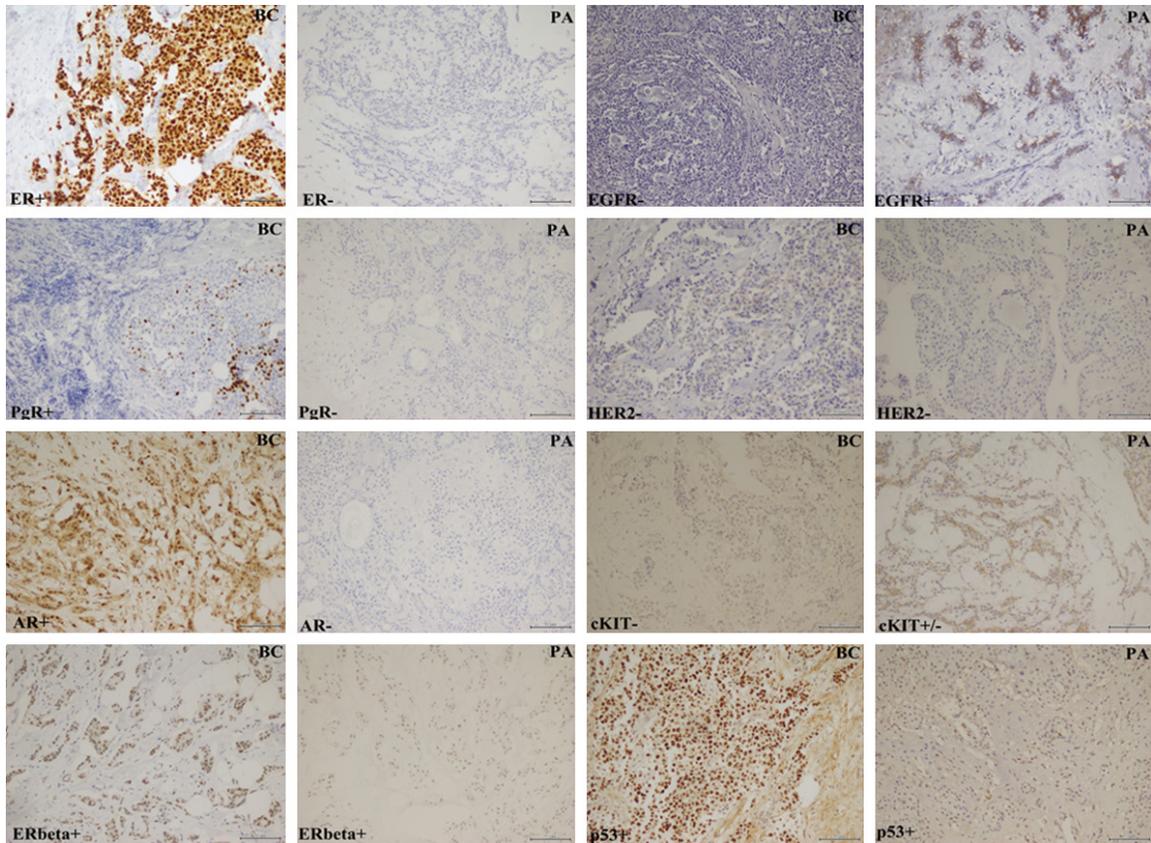
simultaneously [3]. PA was described also in human breast with a histology similar to its salivary gland counterpart [4].

It is known that the pleomorphic adenoma can evolve into carcinoma and its morphological and immunophenotypic characteristics suggest a potential derivation from cells already committed to differentiation into ductal luminal cells [5].

Some molecular characteristics, in particular the aberrant expression of certain tumor-related protein receptors, as HER-2, EGFR, AR, ER $\alpha$ , ER $\beta$ , PgR, and as the tumor suppressor p53, again highlight the biological similarities between the two lesions [3].

In addition, the identification of a breast cancer gene that encodes a secreted protein designated *BASE* (breast cancer and salivary gland expression) even more supports the common biology of these tumors. *BASE* is expressed in many breast cancers, but in none normal tissues only in salivary gland [6]. However, the

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**Figure 1.** Immunostaining of ER $\alpha$ , PgR, AR, Er $\beta$ , EGFR, HER2, cKIT, p53 in Breast Cancer (BC) and Pleomorphic Adenoma (PA) from the same patient (magnification 20 $\times$ ).

presence of both lesions in the same patients is a clinical condition that was never molecularly deepened.

Over the past 6 years, we had the possibility of recovering a series of 8 patients who developed synchronously or metachronous pleomorphic adenoma of the salivary glands and invasive breast cancer, over which we have tested a number of biomarkers that may be associated with the pathogenesis of both malignancies (**Figure 1**).

Whereas steroid receptors were found expressed only in breast samples, Er $\beta$  and p53 proteins were detected in both lesions.

Larger molecular characterization studies should be realized for these tumors, above all collecting wider case series. To date this has represented a main problem because generally a second lesion in a different location from the first, is diagnosed later in other hospital structures. The establishment of an efficient and

comprehensive cancer registry made available to clinicians and researchers would adequately define the incidence and distribution of these clinical manifestations, and would carry out studies aimed at understanding the possible molecular mechanisms that determine it.

In conclusion, although genetic relation between Pleomorphic adenoma of salivary gland and invasive ductal breast cancer were not described, we can speculate that some common biological characteristics and early genetic alterations may underlie the concomitant occurrence of these lesions.

### Disclosure of conflict of interest

None.

**Address correspondence to:** Monica Cantile, Pathology Unit, Istituto Nazionale Tumori “Fondazione G. Pascale”, via Mariano Semmola, Napoli 80131, Italy. Tel: +390815903745; Fax: +390815903718; E-mail: m.cantile@istitutotumori.na.it

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