The neural crest transcription factor SOX 10 is preferentially expressed in triple negative breast carcinomas

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ABSTRACT

Background*:* The expression of SOX 10 by immunohistochemistry has been documented in benign breast myoepithelial cells and in ductal carcinomas classified by the molecular subtype defined by immunohistochemistry. **Material and methods***:* 77 cases of infiltrating ductal carcinomas of the mammary gland with Sox 10 reactivity were analyzed and subdivided by immunohistochemistry into the different molecular subtypes. The IHC panel used to define the molecular subtypes included Estrogen Receptors (R.E), Progesterone Receptors (R.P), Her 2, Cytokeratin (C.K) 5/6, Epidermal Growth Factor Receptor (E.G.F.R). **Results***:* In our study we demonstrated in 31 cases (44.25%) of 77 infiltrating ductal carcinomas SOX 10 immunoreactivity, which was observed only in basal and undifferentiated subtype triple negative carcinomas. **Conclusion**: The expression of Sox 10 in triple infiltrating ductal carcinomas Negative supports the concept that these neoplasms show myoepithelial differentiation.

KEYWORDS

Breast carcinoma, Triple Negative, SOX10, Ductal carcinomas, Myoepithelial cells

El factor de transcripción de la cresta neural SOX 10 se expresa preferentemente en los carcinomas de mama triple negativos

RESUMEN

Introducción: La expresión de SOX 10 por inmunohistoquímica ha sido documentada en células mioepiteliales de mama benignas y en carcinomas ductales clasificados por el subtipo molecular definido por inmunohistoquímica. **Material y métodos**: Se analizaron 77 casos de carcinomas ductales infiltrantes de glándula mamaria con reactividad Sox 10 y se subdividieron por inmunohistoquímica en los diferentes subtipos moleculares. El panel de IHC utilizado para definir subtipos moleculares incluyó receptores de estrógeno (ER), receptores de progesterona (PR), Her 2, citoqueratina (CK) 5/6, receptor del factor de crecimiento epidérmico (EGFR). **Resultados**: En nuestro estudio demostramos en 31 casos (44,25%) de 77 carcinomas ductales infiltrantes la in-

munorreactividad SOX 10, que solo se observó en carcinomas basales e indiferenciados subtipo triple negativo. Conclusión: La expresión de Sox 10 en carcinomas ductales infiltrantes triple negativos apoya el concepto de que estas neoplasias muestran diferenciación mioepitelial.

PALABRAS CLAVE

Carcinoma de mama, Triple negativo, SOX10, Carcinomas ductales, Células mioepiteliales

INTRODUCTION

The transcription factor Sox 10 is involved in the survival and differentiation of glial cells and melanocytes [1,2]. The antibody Sox 10 uses by inmunohistoqu í mica (IH Q), mainly for precis ar diagnosis of melanoma [3-5] and your Mores nerve sheaths [3,4]. Both of which are interpreted to derive from the neural crest.

Expression of Sox 10 by IHC has been documented in breast myoepithelial cells, salivary glands, and bronchial glands [3,4].

Ashley- Cimino - Mathew s et al. [6], published the expression of Sox 10 in infiltrating ductal carcinomas previously subclassified in the different molecular subtypes.

Our objective consisted in evaluating the expression of Sox 10 ductal carcinomas, subdivided by IHC 5 molecular subtypes: Luminal A, Lum inal B, Her 2 and negative Triple with two variants similar basal and Undifferentiated and assessing whether the dominant expression this marker and n triple negative could lead one to conclude its origin in cells myoepithelial these neo p lasias.

MATERIALS AND METHODS

IHC panel used to define molecular subtypes included Receptors Estrogens (RE.), Progesterone receptor (R. P.), Her 2, cytokeratin (CK) 5/6, Receptor Growth Factor Epidermal (EGFR) [7].

Luminal A breast carcinomas are positive for hormone receptors (ER Positive and / or PR Positive), negative for Her2 and have low levels of Ki 67 (> 14%).

Luminal B breast carcinomas are positive for hormone receptors (ER. Positive and / or PR. Positive) and positive for Her2 or negative for Her2 with high levels of Ki 67 <14%.

Her2 enriched breast carcinomas are RE. and RP. negative and Her 2 positive.

Triple negative breast carcinomas are ER negative, RP. and Her 2. In turn, a subtype of this type of carcinoma express CK 5/6 and EGFR and are called basal types and another subtype that does not express CK5 / 6 and EGFR are called undifferentiated or quadruple negative.

We evaluated the expression of Sox 10 in a total of 77 cases of infiltrating duct carcinomas of the mammary gland, subdivided by IHC into the different molecular subtypes. 27 undifferentiated triple negative carcinomas, 21 cases of baseline type triple negative, 10 Luminal A, 10 Luminal B and 9 Her2 3+ (Positive).

IHC techniques were performed with the antibody polyclonal Sox 10 obtained in rabbit, with a dilution of 1 in 100, Brand Cell Marque, a automator of immunostaining Bench mark GX, Brand Window.

SOX 10 staining was observed at the level nuclear in carcinomas du infiltrating ctales mammary gland. As a positive internal control, strong Sox 10 nuclear staining was observed in the myoepithelial cells of the mammary gland at the level of the normal lobules.

RESULTS

Expression of Sox 10 was observed in 16 of 27 undifferentiated triple negative carcinomas (59.25%).

In 15 of 21 baseline triple negative carcinomas (71.42%). In the 10 Luminal A, 10 Luminal B and 9 Her2 3+. N or expression was observed for Sox 10.

(Table 1). Immunohistochemistry of Sox 10 breast cancers.

	N ° Cases	TotalPositives
Luminal Carcinoma Type A	10	0 (0%
Luminal carcinoma type B	10	0 (0%
Her 2 Carcinoma	09	0 (0%

BasalTripleNegativeCarcinoma	21	15(71.42%)
TripleNegativeUndifferentiated Carcinoma	27	16(54.25%)

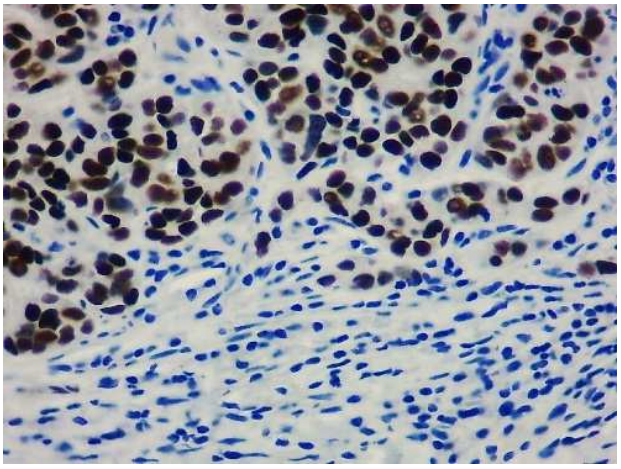


PHOTO A: SOX 10 IN UNCLASSIFIABLE TRIPLE NEGATIVE CARCINOMA X 400.

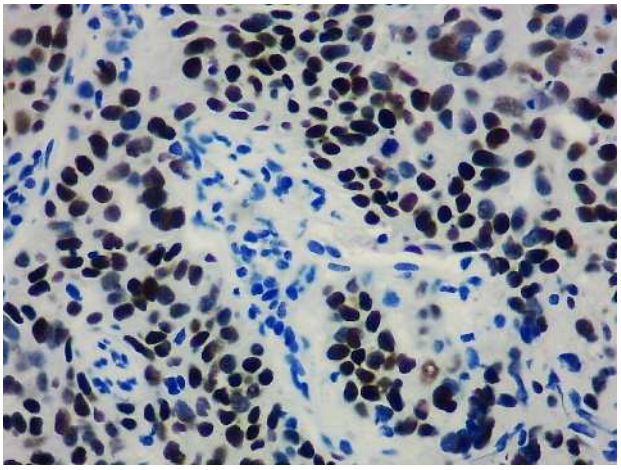
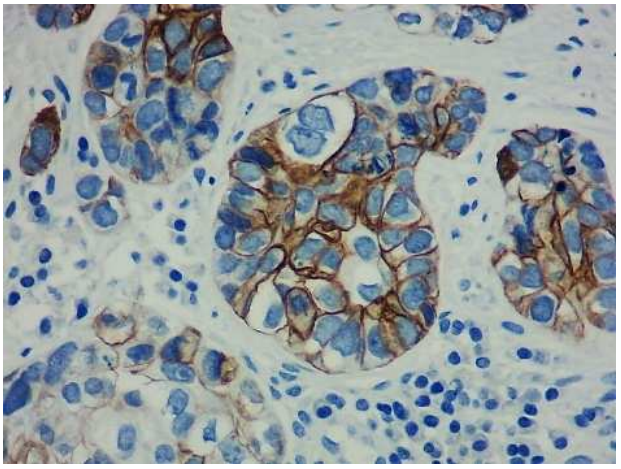


PHOTO B: SOX 10 IN BASAL SIMILE CARCINOMA X 400.



PICTURE C: 5 CK CARCINOMA SIMILE BASAL X 400.

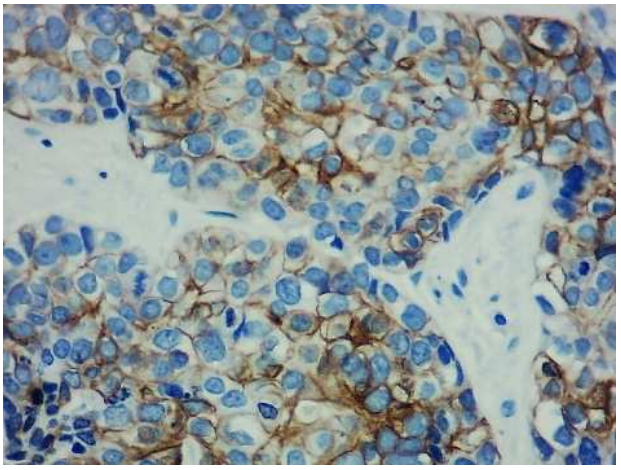


PHOTO D: E. G.F.R. IN BASAL SIMILE CARCINOMA X 400.

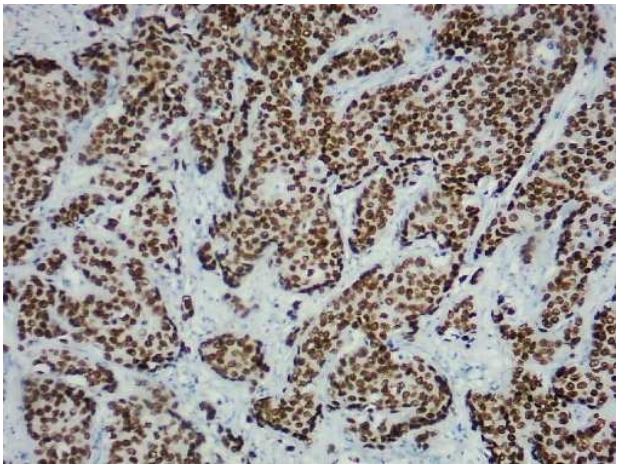


PHOTO E: R. ESTROGENS IN TYPE A LUMINAL CARCINOMA X 100.

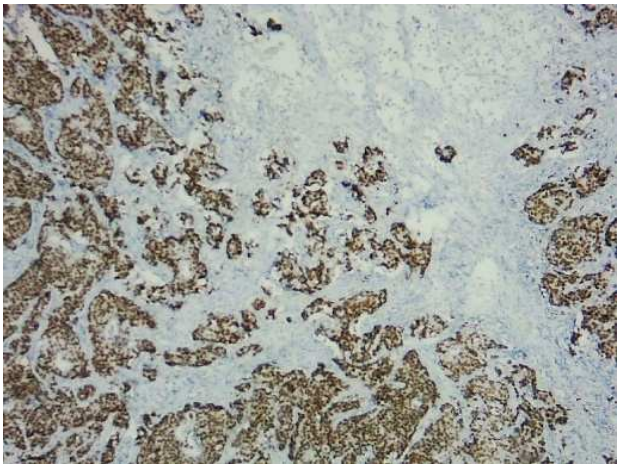


PHOTO F: R. PROGESTERONE IN LUMINAL CARCINOMA TYPE A X 100.

DISCUSSION

The Sox genes are a family of transcription factors with HMG-DNA-binding domains that play a role in numerous developmental processes, including the development of the nervous system, skeletal system, and immune system [8]. The Sox 10 gene was first discovered in mouse embryos in 1993 [9] and was subsequently described in the human genome in 1998 [10]. All family proteins Sox, the function of Sox10 protein has been one of the most studied, largely due to the association of Sox 10 mutated neuroc ristopatias clinical like syndrome Waardenburg-Shah [2] . Sox 10 appears to play a role in the survival of neural crest cells and in their maturation and differentiation into neural crest-derived melanocytes and glia [1,2].

In the breast, via Notch signaling it is essential for controlling the maintenance of stem cells and cell differentiation [11], and the Notch gene is activated in progenitor cells luminal duct signals of lobes breast [12]

The immunostaining with Sox 10 IHC demonstrated in cells myoepithelial breast [3,4] but in Sickle Cell ductal epithelial benign s.

Ashley- cimino - Mathew s et al [6] demonstrated for the first time nuclear marking with S ox 10 by SSI in infiltrating breast carcinoma, more precisely in 66% of basal subtype triple negative breast carcinomas and in unclassifiable ones. not observed reactividadad with Sox 10 and n carcinomas luminal A, and very limited in carc inomas luminal B and carcinomas Her2.

In our work we have shown by dialing Sox10 by immunohistochemistry infiltrating breast carcinomas, more exactame nte in 64.58% of carcinom as triple - negative breast, basal subtype and the unclassifiable.

We did not observe reactivity with sox 10 with luminal A, luminal B, Her 2 carcinomas.

Triple negative breast carcinomas are a heterogeneous group of infiltrating carcinomas that lack expression of RE, R. P, and Her2 [13,14]. Currently there is no specific targeted therapy for these tumors and as a group, they are associated with poor overall survival.

Basal-type tumors comprise a subset of triple negative carcinoma, because they lack expression of RE, RP, and Her2 and express markers seen in basal myoepithelial cells of the breast such as CK 5 / 6 and / or E.G.F.R.[15,16]. Our findings on the expression of Sox 10 in a subset of infiltrating breast carcinomas present us with several points:

First: The expression of sox 10 in normal breast myoepithelial cells, as well as in triple negative carcinomas, basal subtype supports the myoepithelial differentiation of these types of neoplasms.

Second: it also suggests that unclassifiable triple negative carcinomas have demonstrated reactivity with sox 10 and also evidenced a basal or myoepithelial differentiation, which is not detected by IHC with EGFR or Ck 5/6.

Third: Immunoreactivity for Sox 10 may be useful to pinpoint a mammary origin of a metastasis from a basal or undifferentiated triple negative carcinoma.

A study in the inst itutu Salk study biological s found that the gene Sox 10 is expressed as specific in mammary cells showing typical activity of stem cells or progenitors, ie those with greater capacity to generate cell types.

Furthermore, analysis of Sox 10 expression in a panel of breast tumor samples revealed a tendency for triple negative breast cancers to present higher Sox 10 levels than the rest of the tumors.

The resulting two of this work indicate an IM plication of the g in Sox 10 in the acquisition of cellular characteristics that favors aggressiveness and spread of tumors triple negative breast and point to new ways about the need to investigate the development of trafficking ment for the same [17].

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