FOXP3 AND CD8 EXPRESSION IN DUCTAL CARCINOMA OF THE BREAST AND ITS RELATION TO THE CLINICOPATHOLOGICAL PARAMETERS

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Introduction

Globally, breast cancer is the most frequently diagnosed cancer in women. Tumor microenvironment (TME), soluble, cellular and physical components plays a pivotal role in tumor progression. Tumor infiltrating lymphocytes (TILs) in ductal carcinoma in situ (DCIS), with and without invasive carcinoma is an emerging area of clinical research. Recent studies have linked high FOXP3 expression in T regulatory (Treg) tumor infiltrating lymphocytes (TILs) with higher grade and stage and poor clinical outcome. CD8+ cytotoxic T lymphocytes have antitumor effects by induction of tumor cell cytostasis, apoptosis, angiostasis and macrophage tumoricidal activity.Thus, examination of the balance between CD8+ and FOXP3+ T cells is crucial in breast cancer prognosis.

Aim of the work

The current work was carried out to evaluate the expression of CD8 and FOXP3 in DCIS and invasive breast cancer as well as CD8/FOXP3 ratio in relation to clinicopathological parameters.

Material and Methods

Material:
The present study comprised 70 retrospective cases of breast cancer .Paraffin blocks of these cases were obtained from the archives of the Pathology Department, Faculty of Medicine, Alexandria University, from January 2018 till December 2022.

Methods:
The current study entailed clinical data collection, pathological assessment as regards H&E staining, and Immunohistochemical staining. The latter was conducted using the avidin-biotin peroxidase complex method according to the instruction manual. IHC was assessed as regards density of FOXP3 and CD8 TILs (both stromal and tumoral TILs) in interface and intratumoral compartments.

Results

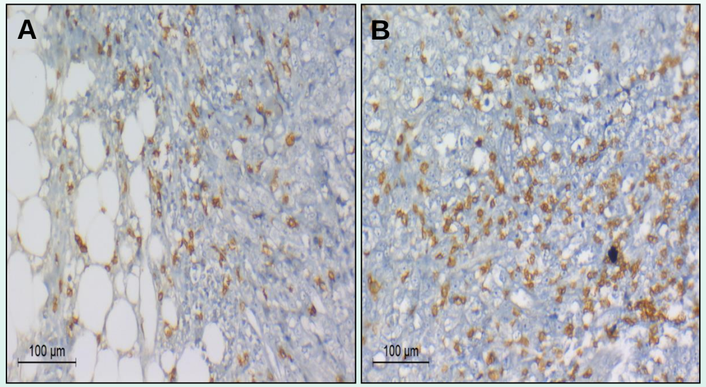

Fig. 1: CD8 expression in IDC cases
A. CD8 TILS in stromal TILS (x40). **B.** CD8 TILS in tumoral TILS. (x40)

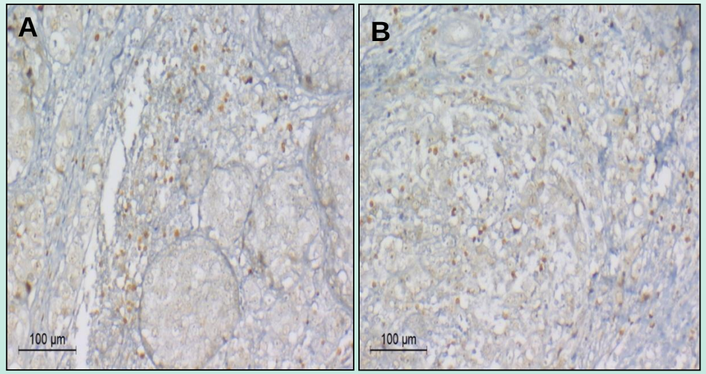

Fig. 2: FOXP3 expression in IDC cases.
A. FOXP3 in stromal TILS (x40). **B.** FOXP3 in tumoral TILS. (x40)

CD8 staining showed positive significant correlation with density of TILs (P=0.032), extranodal extension (P=0.043), ER staining (P=0.045), PR staining (P=0.037), HER2 staining(P=0.024) and negative significant correlation with tumor focality (P=0.011).
FOXP3 staining showed positive significant correlation with density of TILs (P=0.035) and with extranodal extension (P=0.022).
CD8 and FOXP3 showed positive significant correlation with each other (P<0.001).
CD8/FOXP3 ratio showed negative significant correlation with tumor focality (P=0.040)and positive significant correlation with ER staining (P=0.007) ,PR staining (P= 0.018) and HER2neu staining (P= 0.044).

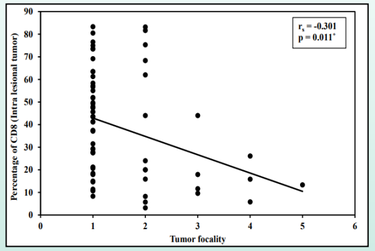

Fig. 3: Correlation between percentage of CD8 in intra lesional tumor with tumor focality (n = 70).

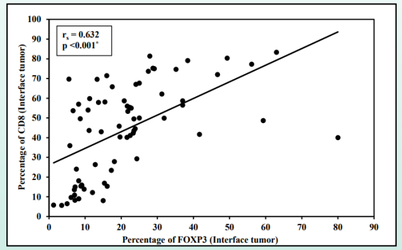

Fig. 4: Correlation between percentage of FOXP3 with percentage of CD8 in interface tumor (n = 70).

Conclusion

From the results of the current study, it can be concluded that:

- CD8 cytotoxic T lymphocytes were associated with good prognostic parameters.
- While FOXP3 (Treg) were associated with poor prognostic parameters in breast cancer patients.
- CD8 and FOXP3 can be used as potential prognostic markers in breast cancer.