TWIST-1 EXPRESSION AND ITS ASSOCIATION WITH CANCER STEMNESS IN COLORECTAL CARCINOMA

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Introduction

Colorectal cancer (CRC) is considered to be the third most common malignancy worldwide, It is the fourth cause of cancer related death. Epithelial mesenchymal transition (EMT) plays a pivotal role in tumor invasion and metastasis. Recent studies have linked Twist-1 expression with EMT in different cancer cells including CRC bonding its expression with a more aggressive tumor phenotype and a poorer clinical outcome. The EMT phenotype has been also implicated in the acquisition of cancer stem cell (CSC) like properties. CD44 is believed to represent one of the main colorectal cancer stem cell markers. It plays a role in tumorigensis through stimulating several signaling pathways that maintain stemness of malignant tumors. Thus, Twist-1 and CD44 represent potential prognostic markers.

Aim of the Work

The current work was carried out to study the immuno-histochemical (IHC) expression of both Twist-1 and CD44 in CRC and to correlate this expression with the different clinicopathologic parameters and patients' outcome .

Material

The current study comprised 50 retrospective cases of colorectal cancer . Cases were obtained from the archives of the Pathology Department, Faculty of Medicine, Alexandria University, from January 2014 till December 2016.

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 staining intensity and distribution percent then combined scores were assigned.

Results

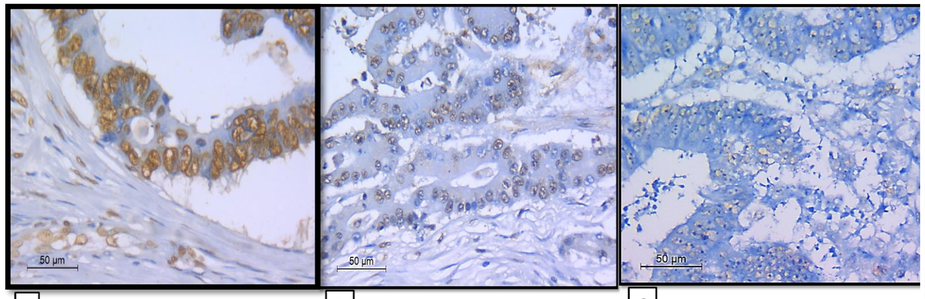

Fig. (1): Twist-1 expression in CRC cases (Anti-Twist-1).
A. Intense nuclear staining in tumor cells (x400).
B. Moderate nuclear staining in tumor cells (x400).
C. Weak nuclear staining in tumor cells (x400).

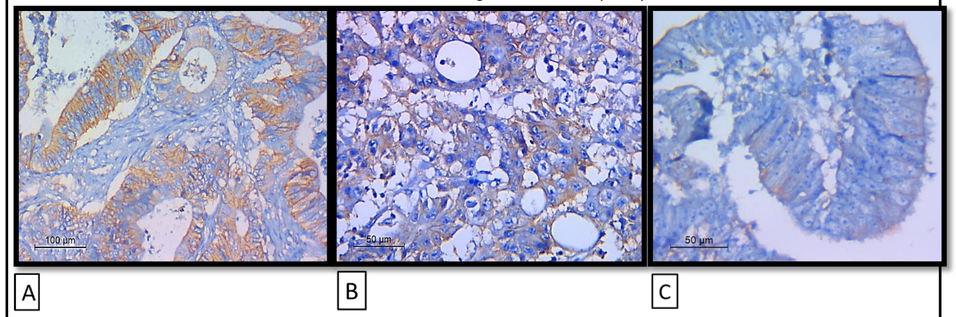

Fig. (2): CD44 expression in CRC cases (Anti-CD44)
A. Intense membranous staining in tumor cells (x200)
B. Moderate membranous staining in tumor cells (X400)
C. Weak membranous staining in tumor cells (x400)

CRC cases with high positive expression of Twist-1 were associated with tumor aggressive phenotype characteristics such as lymphovascular invasion, perineural invasion , lymph node metastasis and more advanced TNM stage. In addition to higher percent of recurrence and development of metastatic deposits that showed increases incidence with higher Twist-1 expression despite lacking statistical significance. In contrast, CD44 expression showed inverse relation with lymphovascular invasion , perineural invasion, tumor depth, lymph node metastasis and tumor TNM stage although being statistically insignificant. A statistical significance was found between CD44 expression with 2 year survival outcome (p=0.05) and tumor size (p=0.033). There was no correlation between Twist-1 expression , CD44 expression and overall survival time .

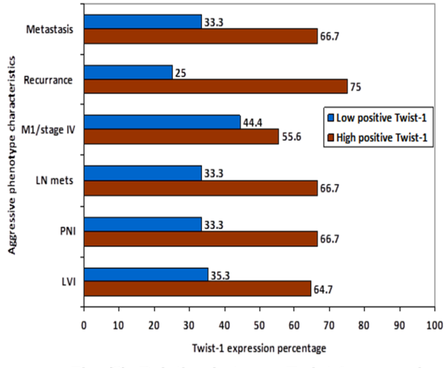

Fig. (3): Relation between Twist-1 expression and CRC aggressive phenotype.

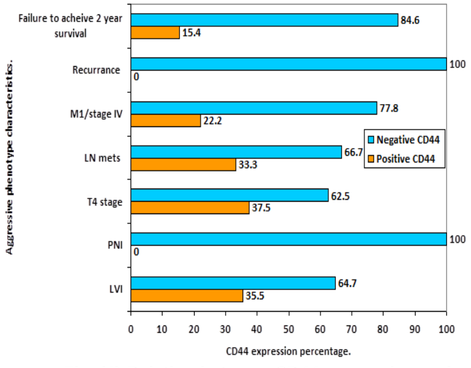

Fig. (4):Relation between CD44 expression and CRC aggressive phenotype.

Conclusion

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

- High Twist-1 and low CD44 expression could be used as predictive markers of CRC aggressive phenotype.
- Increased Twist-1 expression is associated with increased adverse events during postsurgical therapy such as recurrence and the development of metastatic deposits.
- High CD44 expression predicted a better 2 year survival outcome .
- Twist-1 and CD44 are promising CRC prognostic markers that need further studies on a larger number of cases with more diverse study sample .