Summary

Cancer stem cells hypothesis suggest that cancers are driven by cancer stem cells that originate in tissue stem or progenitor cells probably through dysregulation of self-renewal pathways(e.g. Wnt, Hedgehog, and Notch). This leads to expansion of this cell population that then may undergo further genetic or epigenetic changes to become fully transformed ,in other words, the cancer stem cell is the cell responsible for tumor self-renewal and not the differentiated cells that make up the bulk of the tumor.

Breast cancer is the most frequent malignant tumor in females. The role of breast cancer stem cells hypothesis was confirmed by Al ,Hagg, etal (2003) who reported that that $CD44^{+}/CD24^{-/low}$ human breast tumor cells have an increased ability to form tumors when injected into the cleared mammary fat pad of NOD/SCID mice.

The present work evolved 30 cases of ductal carcinoma, 10 cases of ductal carcinoma insitu, 20 cases of invasive ductal carcinoma including eight cases of recurrent ductal carcinoma in addition to six cases of fibrocytic diseases were taken as control .All cases aged between 25 to 75 years with the mean age 42 years old.

Histopathological examination was done for confirmation of histopathological data.TNM staging and grading were applied for all cases and two years survival was recorded for all cases.

Double staining immunohistochemistery technique using CD44 and CD24 cell surface markers was applied for identification of $CD44^{+}/CD24^{-/low}$ breast cancer stem cells. Correlation between expression of breast cancer stem cells and other clinco pathological parameters was done .

The present work reported $CD44^{+}/CD24^{-/low}$ breast cancer stem cells are expressed in different percentages in ductal carcinoma varying from 0 % to more than 50% of total number of cancer cells.

There was no significant correlation between $CD44^{+}/CD24^{-/low}$ breast cancer stem cells and age of patients ,size of tumors ,family history, grade of tumors, lymph node metastasis and stage of the tumors.

There was significant correlation between $CD44^{+}/CD24^{-/low}$ breast cancer stem cells and both vascular invasion and distant metastasis .

Also, there was significant correlation between $CD44^{+}/CD24^{-/low}$ breast cancer stem cells and hormonal status as their expression increased in estrogen negative and progesterone negative tumors.

Significant correlation between $CD44^{+}/CD24^{-/low}$ breast cancer stem cells and recurrence was detected as their expression increased in recurrent cases .this may explain resistance of breast cancer stem cells to chemotherapy and their role in distant metastasis and recurrence.

As regard to two years disease free survival, significant correlation was detected between $CD44^{+}/CD24^{-/low}$ breast cancer stem cells and two years disease free survival as their expression increased in poor survival patients having recurrence or death.

Conclusion

In conclusion expression of $CD44^{+}/CD24^{-/low}$ breast cancer stem cells show no increase in ductal carcinoma progression from ductal carcinoma insitu to invasive ductal carcinoma. $CD44^{+}/CD24^{-/low}$ breast cancer stem cells are associated with ER-PR- tumor, recurrence ,distant metastasis, vascular invasion and poor survival .

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These finding may help in planning new therapy strategies for breast carcinoma, however further invivo and invitro studies are required to confirm significance of $CD44^{+}/CD24^{-/low}$ breast cancer stem cells in ductal carcinoma and other types of breast cancer.

Recommendation

(1) $CD44^{+}/CD24^{-/low}$ breast cancer stem cells may be helpful in predicting the prognosis, distant metastasis and recurrence of breast ductal carcinoma.

(2) Further in vivo and in vitro studies should be carried out on $CD44^{+}/CD24^{-/low}$ breast cancer stem cells and other other markers of breast cancer stem cells as Aldehyde dehydrogenase , CD 133 and other markers in order to investigate from which they originate, their molecular alteration and how they interact with microenvironment. Elucidation of these points is essential to develop new therapeutic strategies and to improve the diagnosis and prognosis of breast cancer.