EXCELLENT PUBLISHERS

International Journal of Current Research and Academic Review

ISSN: 2347-3215 Volume 2 Number 12 (December-2014) pp. 91-96

www.ijcrar.com

Quantitative analysis of mast cells in invasive ductal carcinoma

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KEYWORDS

Mast cells,
MCD,
Breast cancer,
Toluidine blue

A B S T R A C T

Role of mast cells in invasive breast carcinoma has always been debated as they are capable of facilitating tumor growth by aiding angiogenesis and also secrete cytokines and enzymes detrimental to tumor growth. Hence the study was undertaken to evaluate the impact of mast cells in invasive breast carcinomas. Mast cell seen both intratumoral and peritumoral, quantitative analysis using toluidine blue technique was done in a series of 55 cases of invasive carcinomas and the results were correlated with tumor grade. Mast cells were found to correlate with low grade tumors. A higher number of mast cells were seen in tumors of lower grade suggesting a detrimental role on tumor grade by mast cells in invasive breast carcinomas.

Introduction

Neoplastic transformation elicits an immune response which causes inflammatory cell infiltrate like mast cells and macrophages to accumulate around tumor tissue, which is recruited and activated by tumor cells (Gui Young Kwon *et al.*, 2005).

The presence of mast cells in the tumor tissue is reported since Ehrlich first described them in 1878 (Filippo *et al.*, 2007).

Mast cell (Mastocyte) is a resident cell of several tissues and contains many granules rich in histamine. They have various roles which have inflammatory, Immunoregulatory and biological consequences such as mitogenesis, extracellular matrix degradation and spread of tumors by recruiting various growth factors and cytokine (Theoharides and Conti, 2004; Shaked and Kerbel, 2007; Kobayashi *et al.*, 2000; Galinsky and Nechustan, 2008).

Mast cells are derived from a specific bone marrow progenitor cells which migrate into tissue where they mature depending on micro environmental conditions. They are usually present in the vicinity of blood vessel, skin and intestinal submucosa (Amini *et al.*, 2007)

Role of mast cells in tumor development is being investigated in various tumors. Mast cell accumulation can be beneficial for tumor growth by facilitating tumor angiogenesis through heparin like molecules and detrimental by releasing various mediators and cytokines like Tumor necrosis factor alpha (TNFα), Interleukin 1 and 6 (IL 1 & 6) which has inhibitory effect on tumor growth participating in apoptosis of malignant cells (Samoszuk *et al.,* 2005; Ching *et al.,* 2006; Heidarpour *et al.,* 2008).

Dual role of mast cells in inhibiting and promoting tumor growth needs to be further investigated.

The aim of this study is to determine the role of mast cells in breast cancer prognosis.

Materials and Methods

Histologic sections of invasive breast carcinoma retrieved from the archives of Department of Pathology, Sri Devraj Urs Medical College, and Kolar from 2008 to 2013 were selected.

A total of 55 cases were selected. Non neoplastic lesions of breast, which were on or receiving radiotherapy and chemotherapy were excluded from the study. All sections were examined and reviewed by two pathologists for histological grading according to Modified Bloom Richardson. Then representative tissue sections (4–5µm thickness) were prepared from formalin fixed, paraffin embedded tissues and stained with 0.1 % toluidine blue.

Mast cell count (MCD)

Mast cells are identified by round to oval mononuclear cells with granular cytoplasm. These cells are stained by basic aniline dyes (metachromatic staining) like toluidine blue and methylene blue, where they stain granules to give purplish pink in color.

The slides were scanned at low power objectives and mast cells were counted in three high power fields(20x objective) and average of three high power field were estimated both intratumoral and peritumoral of the lesion.

For MCD- intratumoral were defined as mast cells within the main tumor mass surrounded by tumor cells and mast cells seen more than one high power field (200 X) magnification away from the invasive tumor front were considered as peritumoral mast cells. This will give the number of mast cells per defined field.

Statistical analysis

Data was analyzed using SPSS software version. Frequencies, mean and standard deviation were used to describe the data. Further ANOVA was used to describe the association between mast cells density and histological grade.

'P' value less than 0.05 would be considered as significant.

Result and Discussion

A total of 55 cases were included in the study. The mean age was 52 years (Range 35–85 years). Infiltrating ductal carcinoma was the most common histological type of breast carcinoma seen in 45 (82%) cases followed by medullary 5 (9%) cases. Other subtypes are infiltrating, lobular, metaplastic and papillary carcinoma formed less than 10% of total cases.

Grading was done according to Nottingham Modification of Bloom Richardson system. 38 (69%) cases had grade II, followed by grade I tumors which comprised of 11

(20%) cases and remaining 6 cases (10.9%) were in grade III tumor (Table 1).

Mast cells were found mainly in tumor stroma adjacent to neoplastic cells and also seen infiltrated within the islands of tumor cells. The presence of intratumoral and peritumoral or stromal mast cells was highest in grade I tumors and the value decreased as the tumor grade increases. However p value was more than 0.05 implying lack of significance between both intratumoral and peritumoral mast cell density with histological grade (Table 2, Table 3 and Figure 1).

The importance of reciprocal relationship between the tumor and stroma is being increasingly recognized and role of inflammatory cells likes mast cells, macrophages, fibroblasts and lymphocytes in cancer initiation and progression are being continuously evaluated (Ellis *et al.*, 2006)

There is an ongoing debate about possible role of mast cell accumulation in stroma, which can be detrimental or beneficial and the effects on tumor cells and growth (Nassar *et al.*, 2006).

Mast cells secrete various growth factors and cytokines like heparin, interleukin 8 and vascular endothelial growth factor that promote neovascularization (Angiogenesis) (Duduch *et al.*, 2012)

Mast cells promote cancer growth by modulation of immune response by secretion of histamine, interleukin 10 and Tumor necrosis factor alpha which leads to suppression of cellular immunity (Almholt and Johnsen, 2003) Along with these mast cells also secrete proteases (matrix metalloproteases-MMP2) which contribute to the majority of proteolytic components necessary for tumor invasiveness (Folkman *et al.*, 1971; Weidner *et al.*, 1995).

On the other hand, mast cells can be detrimental to tumor growth by secreting several cytokines such as Interleukin 4 and proteolytic enzymes participating in inducing apoptosis of malignant cells (Gooch *et al.*, 1998). Opposite effects of mast cells depend on its ability to degranulate or secrete various mediators in response to stimuli. Tryptase causes tumor cell disruption and chondroitin sulphate may inhibit tumor cell dissemination and metastasis formation (Ching *et al.*, 2006)

Mast cell release certain mediators like interleukin 1 and 6 which has inhibitory effect on tumor growth and angiogenesis (Weidner *et al.*, 1996).

In a study done by Heidarpour *et al.* (2008) showed that presence of mast cells was associated with low grade tumors. Another study by Kwon *et al.* (2005) showed that peritumoral mast cell density was highest in grade III tumors.

In his study on breast cancer, Amini *et al.* (2007) showed that, the presence of mast cells is associated with low grade tumors and estrogen receptor positivity.

In the present study mast cell counts both in intratumoral and peritumoral were highest in grade I tumors, it may be due to mast cells which are attracted by tumor derived chemo attractants to degranulate and release potential tumor cytotoxic compounds depending upon the local tumor conditions. They also release certain mediators like TNF α, IL -1 and IL -6 which has inhibitory effect on tumor growth and angiogenesis (Ribatti and Crivellato, 2011; Rajput *et al.*, 2008).

Table.1 Distribution of cases with regard to histological grade

Grade	No. of cases	Percentage (%)
I	11	20.0
II	38	69.1
III	6	10.9
Total	**55**	**100.0**

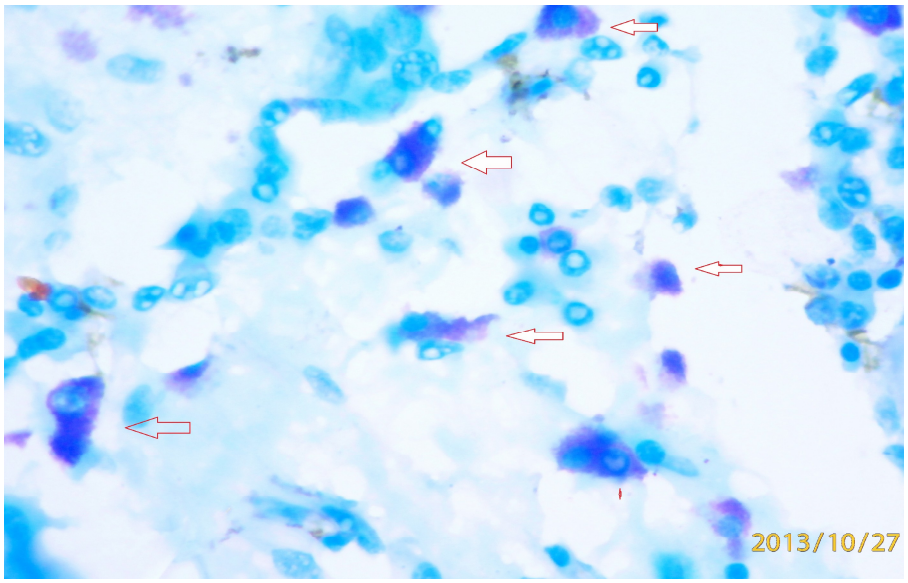
Table.2 Association between intratumoral MCD and grade of the Tumor

Grade of the tumor	Mean MCD	SD	p value
I	3.27	2.00	0.68
II	2.82	2.24	
III	2.00	1.54	
Total	**2.82**	**2.12**	

Table.3 Association b/w peritumoral MCD & grade of the tumour (ANOVA)

Grade of the tumor	No. of subjects	Mean	Std. deviation	F	p value
1	11	16.64	11.129	0.36	0.69
2	38	15.79	9.84		
3	6	12.50	6.921		
Total	**55**	**15.22**	**9.626**		

Fig.1 Photomicrograph showing mast cells (red arrow) 200x magnification (toluidine blue)



However the p value calculated indicated lack of significance between mast cell count and tumor grade. This may be due to small sample size and also depend on the local stromal conditions. In present study mast cell counts were highest in low-grade tumors which show the protective effect of mast cells, possibly exerting a cytoxic effect on the tumor cells. However, the studies are still few and further investigations are needed in order to elucidate the precise role of mast cells in the tumorogenesis.

In conclusion, the presence of mast cells in breast carcinoma was seen highest in low grade tumors, suggesting the protective role of mast cells in breast cancers. However using quantitative mast cells analysis routinely in reporting breast carcinomas warrants further studies.

Acknowledgement

Sri Devraj Urs University, Kolar for giving me an opportunity to do the study. Dr. Harendra Kumar M.L HOD & professor department of pathology, Kolar supported and helped me in completion of this study. Dr.Suresh TN, Dr.CSBR Prasad, Dr.Aparna Narasimha, Dr.Swaroop. Raj, Dr. Manoranjan UD, Dr.Swaroop Narayan (Staff) and Virendra (Technician) who have helped me through out the study.

References

Almholt, K., Johnsen, M. 2003. Stromal cell involvement in cancer. *Recent Results Cancer Res.*, 162: 31–42.

Amini *et al.* 2007. Mast cells and Eosinophils in invasive breast carcinoma. *BMC Cancer,* 77: 1–5.

Ching, S., Wallis, R.A., *et al.* 2006. Mast cells and cutaneous malignancies. *Mod Pathol.*, 19: 149–159.

Duduch, G., Kaczmarczyk, K., *et al.*, 2012. Mast cells and cancer: Enemies or allies. *Pol. J. Pathol.*, 1: 1–7.

Ellis, I.O., Galea, M., *et al.* 1992. Pathological prognostic factors in breast cancer. Histopathological type. Relationship with survival in a large study with long term follow up. *Histopathol.*, 20: 479–489.

Filippo, D.R., *et al.*, 2007. Mast cells in invasive ductal breast cancer: different behavior in high and minimum hormone receptive cancer. *Anticancer Res.*, 27: 2465–2472.

Folkman, J., Merke, E., *et al.* 1971. Isolation of tumor factor responsible or angiogenesis. *J. Exp. Med.*, 133: 275–288.

Galinsky, D.S., Nechustan, H. 2008. Mast cells and cancers no longer just basic science. *Crit. Rev. Oncol. Hematol.*, 68: 115–130.

Gooch, J.L., Lee, A.V., *et al.*, 1998. Interleukin 4 Inhibits growth and induces apoptosis in human breast cancer cells. *Cancer Res.*, 58: 4199–4205.

Gui Young Kwon., *et al.* 2005. Mast cells and Macrophage Counts & microvessel density in invasive breast carcinoma-analysis with clinico pathological parameters. *Cancer Res Treat.*, 37: 103–108.

Heidarpour, M., Rajabi, M.A., *et al.*, 2008. Mast cells in invasive ductal breast carcinoma. *JRMS*, 13: 255–259.

Kobayashi, H., Ishizuka, T., *et al.*, 2000. Human mast cells and basophils as sources of cytokines. *Clin. Exp. Allergy*, 30: 1205–1212.

Kwon, G.Y., Lee, S.D., *et al.*, 2005. Mast cell and macrophage counts and microvessel density in invasive breast carcinoma – comparison analysis with clinicopathological parameters. *Cancer Res. Treat.*, 37: 103–108.

Nassar, H., Qureshi, H., Volkanadsay, N., *et al.* 2006. Clinico pathological Analysis of solid papillary carcinoma of the breast and associated invasive carcinoma. *Am. J. Surg. Pathol.,* 30: 501–507.

Rajput, A.B., Turbin, D.A., *et al.,* 2008. Stromal mast cells in invasive breast cancer are a marker of favorable prognosis: A study of 4,444 cases. *Breast Cancer Res. Treat.,* 107: 249–57.

Ribatti, D., Crivellato, E. 2011. Mast cells, angiogenesis and cancer. *Adv. Exp. Med. Biol.,* 716: 270–88.

Samoszuk, M., Kanakubo, E., *et al.* 2005. Degranulating mast cell fibrotic regions of human tumors and evidence that mast cell heparin interferes with the growth of tumor cells through mechanisms involving fibroblasts. *BMC Cancer,* 21: 121.

Shaked, Y., Kerbel, R.S. 2007. Anti-angiogenic strategies on defence: on the possibility of blocking rebounds by tumor vasculature after chemotherapy. *Cancer Res.,* 67: 7055–7058.

Theoharides, T.C., Conti, P. 2004. Mast cells: Jekyll and hyde of tumor growth. *Trends Immunol.,* 25: 235–241.

Weidner, N. 1995. Intratumoral microvessel density as a prognostic factor in cancer. *Am. J. Pathol.,* 147: 9–19.

Weidner, N. *et al.,* 1996. Angiogenesis in breast cancer. *Cancer Treat Res.,* 83: 265–301.