Original Article

MAST CELLS IN BASAL CELL CARCINOMA

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ABSTRACT

Objective: Many researchers have been more interested in inflammatory changes in tumor stroma recently. Recent studies have shown that mast cells are significantly increased in human skin basal cell carcinoma (BCC) and are associated with tumor aggressiveness. In this study, we compared the number of mast cell population expressing c-kit in the BCC samples and normal skin. We also evaluated the number of this cell type in infiltrative and noninfiltrative subtypes of this tumor.

Methodology: Tissue sections containing 30 cases of BCCs and 30 normal skins were prepared and after staining with c-kit were analyzed for the number of stromal mast cells.

Results: Our results indicate that the number of c-kit positive mast cells was significantly higher in BCC when compared with normal skin (P <0.01), and number of mast cells in the stroma of infiltrative subtypes of this tumor is higher than noninfiltrative subtypes (p <0.04). In our study there wasn’t any correlation between sex and age with mast cells count.

Conclusion: Our results are in line with previous studies indicating that mast cell numbers are increased in BCC. In addition, the results suggest that mast cell populations may contribute to BCC progression. Besides, we demonstrated that this increase in mast cell density was independent of the patients’ ages and sexes.

KEY WORDS: Mast cell, Basal cell carcinoma, C-kit.

INTRODUCTION

It is known that cancer is not a single transformational event. It is rather a multistage process involving complex interactions with the surrounding cellular microenvironment. Different studies have argumentary discussions about the inflammatory and immunological responses that occur in the tumor microenvironment. Mast cells accumulate at sites of tumor growth in response to numerous chemoattractants and mast cell hyperplasia was found in many malignant tumors, but the significance of this phenomenon is still unknown. Basal cell carcinoma is the most common invasive malignant tumor of the skin. This tumor may occur at any age but the peak incidence is after age of 40,
although its incidence is significantly increasing in younger population due to increased sun exposure.

In spite of the increased incidence of skin tumors, there are few data about mast cell reaction in malignant neoplasms of the skin, such as basal cell carcinoma (BCC) in the literature. Our goal was to investigate mast cell populations expressing c-kit in normal skin and BCC and their relationship with sex, age and microscopic subtypes of BCC.

**METHODOLOGY**

Biopsies of 30 patients with BCC were retrieved from the archives of Alzahra Hospital. The microscopic features were evaluated by the analysis of one 5 μm section of each sample, stained routinely with hematoxylin and eosin, by two independent pathologists. After review of the slides, BCCs were classified as infiltrative and noninfiltrative BCCs according to the histologic criteria of Lever’s Histopathology of the Skin. The control group was 30 biopsies of normal skin. Then tissue sections (3µm thickness) were prepared from formaline-fixed, paraffine-embedded tissues and stained with CD-117 antibody. Rabbit anti-human c-kit (CD 117) polyclonal antibody (A4502, DAKO) was utilized at 1:800. Briefly, serial sections were collected on glass slides coated with poly-l-lysine.

The sections were deparaffinized by immersion in xylene, and this was followed by immersion in alcohol and then immersion in citrate buffer, pH 6.0, for 20 minutes at 95°C for antigen retrieval. Next, the sections were incubated with 3% hydrogen peroxide for 10 minutes. The slides were then incubated with the primary antibody at room temperature for 60 minutes. After washing in Phosphate Buffer Saline (PBS), the sections were treated with polymer envision for 20 minutes. The sections were then incubated with Diaminobenzidine (DAB) in a chromogen solution for 5 minutes at room temperature. Finally, the sections were stained with hematoxylin and were mounted. Then, mast cells were counted in high-power field (×400 magnification) in each tissue section.

**RESULTS**

In BCC cases C-kit positive mast cells were observed at the lamina propria especially around the tumor nests and in papillary dermis (Figure-1). Increased numbers of mast cells were also found around the vessels. Ovoid cells whose positivity could be definitely appreciated were counted. The results are expressed as
The mean mast cell count in normal specimens was 26.1 (± 3.6) and was 30.3 (± 7.7) for BCC specimens. With performing t-test for equality of means the differences between MC count in normal skin and BCC was significant (p<0.01). In the BCC group there were 13 infiltrative cases and 17 noninfiltrative cases. The mean mast cell count in noninfiltrative BCC cases was 28.3 (± 5.8) and for infiltrative BCC cases was 34.4 (± 9.7). These difference between infiltrative and noninfiltrative groups was significant doing the same test (p<0.04).

The average age of the cases analyzed in this study was 64±9 years, with a range of 46-87 years. In both the case and control groups there were 14 males and 16 females. We did not find any correlation between age or sex of the cases and their mast cell count (p< 0.05).

DISCUSSION

The inflammatory responses that occur in the tumor microenvironment have been a matter of debate and the subject of several studies. Several studies have searched the role of different inflammatory cells and genes in different tumors. The results of these studies are to be used in immunotherapy and gene therapy of these tumors in the near future.2-4,7

Although inflammatory cells may reduce tumoral invasion, these cells may also contribute to cancer progression and Metastasis.2-4,8 In this context, mast cells play an important role in host defense, due to their ability to release mediators that could contribute to immunoregulation, matrix degradation, elastose change and angiogenesis.4,9,10 The significance of stromal mast cells count in tumor prognosis has been reported in different studies including colon, lung, breast, uterine cervix and skin tumors.11-15

Erkilic et al15 reported that an increase in the density of mast cells is seen in BCC compared with normal skin and that morpheaform of BCC has significantly more mast cells than its other variants. We analyzed the correlation between stromal mast cell count and BCC histopathological subtypes. The results of our study show that there is a significant difference between mast cell count in BCC and normal skin. Regarding BCC subtypes we found that infiltrating subtypes had more mast cells in their stroma. As there is a strong correlation between BCC’s subtype and its recurrence, we can infer that there must be a correlation between BCC mast cell count and the tumor prognosis.

As it can be seen in the results, the more mast cells are present in BCC stroma, the more infiltrating the tumor would be. This is opposite to what has been depicted in other studies concerning other tumors like breast, which report that the presence of mast cell in these tumors stroma predicts a more favorable prognosis and treatment outcome.13

Oliveira-Neto et al,16 examined the mast cells in oral cavity squamous cell carcinoma and demonstrated that the densities and migration of these cells are significantly reduced in this tumor, when compared with control and premalignant lesions. In the same study, the survival analysis demonstrated that the patients with highest numbers of mast cells demonstrated better prognosis than patients with low counts.16 It is opposite to what we found in BCC and its subtypes but is consistent with the results of our study on breast cancer patients.13

On the other hand, some studies have shown a direct correlation between the number of dermal mast cells and the degree of immunosuppression, suggesting that mast cells are related to a worse prognosis.4,9 Other studies have demonstrated that mast cell density could be influenced by chemical and physical carcinogens, such as tobacco and sun exposure.4,17 Grimbaldeston et al.18 demonstrated an increase in mast cell count in human photodamaged skin and suggested that this increase could represent a significant predisposing factor for the development of BCC. However, these authors have not yet been able to establish a link between prevalence of dermal mast cell presence and the presence of BCC.4

So, it’s clear that a definite and established role for mast cells in different tumors of human body has a long way to be elucidated and further research is necessary to confirm their role in acceleration or retardation of tumor progression.
REFERENCES


