Inflammatory cells, the Lymphocyte to Monocyte Ratio and the Lymphocyte to Eosinophil Ratio as inexpensive prognostic/diagnostic markers of Cancer

Malathi Veeramani
Assistant Professor, Department of Biochemistry, Ethiraj College for Women, Chennai-8, TamilNadu, India.

Abstract: The link between inflammation and the development of cancer has gained interest in recent years. The interplay between chronic inflammation and cancer is very complex. In the present study, the alterations in lymphocytes, monocytes and eosinophils counts in four major types of cancer namely Ovarian cancer, Colon cancer, Liver cancer and Prostate cancer was studied. The levels of the inflammatory cells were then compared with the counts in normal subjects. Upon comparison a statistically significant increase in monocyte and eosinophil levels and significant decrease in lymphocyte levels was observed. The LMR and LER in normal and cancer subjects were also calculated. These alterations of inflammatory cells can be inexpensive diagnostic/prognostic markers in cancer.

Key words: Lymphocyte, Monocytes, Eosinophils, Prostate cancer, Ovarian Cancer

I. Introduction

Inflammation has been identified to be a critical component of tumor progression. With growing evidence on the role of inflammation in Cancer biology, the systemic inflammatory response has been postulated as having prognostic significance in wide range of cancer types. Inflammatory cells can release growth and survival factors promoting angiogenesis and lymphogenesis, stimulate DNA damage and promote tumor evasion of the host defense mechanism (De visser et al., 2006). Although the inflammatory response can be expected to have tumor suppressive role, cancer patients often lack sufficient inflammatory response (Finn, 2012). For different solid tumors as well as Lymphomas, inflammation parameters, including Leukocytes, Neutrophils, Lymphocytes and C-reactive protein have been associated with high mortality rates (Mohri et al., 2010; Cao et al., 2012).

The inflammatory component of a developing tumor may include a diverse leukocyte population including neutrophils, eosinophils, mast cells and lymphocytes, all of which are capable of producing a wide variety of mediators (Wahl et al., 1998). By the release of specific chemokines, the tumor microenvironment controls leukocyte migration and other functions of these cells after their arrival at the tumor site. The autocrine production of chemokines by tumor cells attracts the inflammatory cells and increase their survival, proliferation and dissemination (Balkwill et al., 2004).

In addition to absolute counts of inflammation parameters, the neutrophil to lymphocyte ratio (NLR) has been identified as an independent prognostic factor for overall survival in various types of cancer (Walsh et al., 2005; Zhang et al., 2012; Pichler et al., 2013; Skandera et al., 2013). In various types of cancers for example, Breast cancer, melanoma and lymphoma, innate immune cells like granulocytes, macrophages and mast cells correlate with increased angiogenesis and/or poor prognosis, which in past explained by upregulation of cyclooxygenase-2 or suppression of anti-tumor adaptive immune response (Leek et al., 1996; Liu et al., 2001; Schoppman et al., 2002; Dannenberg and Subbaramanian, 1997; Ribatti et al., 2003). The neutrophil–lymphocyte ratio, the platelet–lymphocyte ratio and the C-reactive protein or fibrinogen levels have been proposed as prognostic parameters that adequately reflect the systemic inflammatory response in cancer (Troppan et al., 2014). Thus the host response to malignant tumors comprises not only local changes in tumor microenvironment but also systemic effects. These haematological findings significantly correlate with advanced tumor stage and poor disease prognosis.

II. Materials and Methods

Subjects
A total of 120 patient histologically confirmed of the four major types of cancer namely Colon, Liver, Ovarian and Prostate cancer, 30 numbers in each category, were involved in the study after obtaining an informed consent for participation in the study and after obtaining ethical clearance for the same. All patients were treated at V.S. Cancer Hospital, Chennai, TamilNadu, India.
Inflammatory cells, the Lymphocyte to Monocyte Ratio and the Lymphocyte to Eosinophil Ratio ....

Samples
Blood was collected from all patients in suitable vials. The samples were collected after obtaining proper Institutional ethical clearance for the study.

Blood cell counts
The total count, Differential count and Haemoglobin % were calculated by routine laboratory procedure. From the blood counts the Lymphocyte to Monocyte Ratio (LMR) and the Lymphocyte to Eosinophil Ratio (LER) was calculated.

Statistical Analysis
Statistical analyses were carried out using the SPSS statistical software. The results were expressed as Mean ± Standard deviation. The significance of differences between groups was determined by the Student unpaired t test. Values of p< 0.05 were considered as significant.

III. Results
The Total Count, Differential Count and Hb % was evaluated in all blood samples and compared with the respective values in normal subjects

Colon cancer
A statistically significant decrease in the total counts was observed in colon cancer (p < 0.05 , p= 0.037 ). A significant decrease in lymphocyte levels was observed (p < 0.05 , p =0.019 ). A highly significant increase in monocyte levels (p < 0.001 ) was also observed in colon cancer samples. Even Eosinophil count showed a statistically significant increase (p < 0.001 ) (Table : 1)

Prostate cancer
In prostate cancer there was no significant change in the total count. However there was a significant increase in monocyte (p< 0.001, p =0.0007 ) and eosinophil levels p < 0.001 . Lymphocyte levels showed a statistically significant decrease (p = 0.01 , P < 0.05 ).There was no significant change in the levels of RBC and Hb % .(Table : 2)

Ovarian cancer
There was no significant change in the RBC count and HB %.However there was a statistically significant increase in the monocytes levels (p<0.05 , p=0.015) in the ovarian cancer sample. There was also a significant increase in the eosinophil count in the ovarian cancer sample (p=0.003, p<0.05) .(Table: 3)

Liver Cancer
In liver cancer sample also there was a significant increase in Monocytes levels (p=0.01; p=0.05) and highly significant increase in eosinophil count (Table : 4)

Lymphocyte to Monocyte Ratio (LMR) and Lymphocyte to Eosinophil Ratio (LER)
LMR and LER showed a significant decrease in cancer subjects than normal subjects (Table 5 & 6)

<table>
<thead>
<tr>
<th>Haematological parameters of Cancer patients compared with normal subjects. Values presented as mean cell count ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Table :1</strong> Colon Cancer</td>
</tr>
<tr>
<td><strong>RBC</strong></td>
</tr>
<tr>
<td>NORMAL SUBJECTS</td>
</tr>
<tr>
<td>NS</td>
</tr>
</tbody>
</table>

DOI: 10.9790/0853-152126569 www.iosrjournals.org 66 | Page
Inflammatory cells, the Lymphocyte to Monocyte Ratio and the Lymphocyte to Eosinophil Ratio ....

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Prostate Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RBC</td>
</tr>
<tr>
<td>CANCER PATIENTS</td>
<td>4.267 ± 0.672</td>
</tr>
<tr>
<td>NORMAL SUBJECTS</td>
<td>3.963 ± 0.704</td>
</tr>
<tr>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Ovarian Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RBC</td>
</tr>
<tr>
<td>CANCER LEVEL</td>
<td>4.055 ± 0.34</td>
</tr>
<tr>
<td>NORMAL LEVEL</td>
<td>4.175 ± 0.002</td>
</tr>
<tr>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Liver Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RBC</td>
</tr>
<tr>
<td>CANCER LEVEL</td>
<td>4.78 ± 0.67</td>
</tr>
<tr>
<td>NORMAL LEVEL</td>
<td>4.38 ± 0.67</td>
</tr>
<tr>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 5</th>
<th>LMR in normal and cancer subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Liver cancer</td>
</tr>
<tr>
<td>Normal</td>
<td>12.6 : 1</td>
</tr>
<tr>
<td>Cancer</td>
<td>5.8 : 1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 6</th>
<th>LER in normal and Cancer Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Liver cancer</td>
</tr>
<tr>
<td>Normal</td>
<td>25.2 : 1</td>
</tr>
<tr>
<td>Cancer</td>
<td>6.8 : 1</td>
</tr>
</tbody>
</table>

IV. Discussion

The influence of cancer and inflammation was well known but until now tumor –inflammation interaction has not been completely explained.

Variations in systemic inflammatory cell amount might be a valuable prognostic marker for stratifying patients at risk for tumor recurrence in cancer (Gomz et al., 2008, Cho et al., 2009, Idowu et al., 2012; Kwon et al., 2012;Raungkaemanee et al., 2012).

Earlier studies have reported that a lower lymphocyte count was associated with increased cancer mortality, especially from hepatoma, pancreatic carcinoma, colorectal, breast and prostate cancer (Fogar et al., 2006; Huang et al., 2003; Lissoni et al., 2006).

The host response to malignant tumors comprises not only local changes in tumor microenvironment, but also systemic effects. These haematological conditions significantly correlate with the advancement of tumor. It is interesting to know how tumor development contributes to alterations in the number of circulating leucocytes. One possible mechanism is the production of soluble factors such as granulocytes and macrophage colony stimulating factor (GM-CSF) by tumor cells, capable of mobilizing precursors in the bone marrow or vascular endothelial growth factor (VEGF) and interleukin -6, both of which alter cell differentiation (Pinzon – Charry et al., 2005).

Lymphocyte depletion with consequent depression of innate cellular immunity is severe clinical problem that can develop during cancer progression and cytoreductive therapies. Lymphopenia results from tumor induced mechanisms that include impairment of antigen presentation, activation of negative costimulatory signals, and production of immunosuppressive factors, resulting in a marked decrease in T-helper lymphocytes (Walsh et al., 2005 & Croci et al., 2007).

Another reason for these alterations might be accumulation of genetic failures over time, leading to oncogenic activation, simultaneously, inactivation of tumor suppressor genes, which are responsible for higher transcription of inflammatory mediators resulting in an inflammatory condition in the tumor cell environment.
Further tumor related leucocytes especially monocytes, are main regulators of cancer inflammation and have an essential role in systemic inflammatory response to tumor disease (Allavena et al., 2008; Mantovani et al., 2008).

There is less adequate data regarding Lymphocte to monocyte ratio in solid tumors as a prognostic marker. The LMR and LER might be a good reflection of both lymphopenia that is a surrogate marker of weak immune response and an increased monocyte count, suggestive of high tumor burden.

V. Conclusion

Cancer patients often develop para neoplastic syndromes. These conditions can be useful predictors of response to treatment and survival.

LMR, LER can be obtained from the data already routinely available, without additional costs. Further understanding of the mechanisms giving rise to these conditions may contribute to the development of new therapeutic strategies in cancer and could benefit disease prognosis.

Conflict of Interest

No potential conflicts of interest were disclosed.

Acknowledgements

I thank Dr.S.Subramaniam, Managing Director, V.S.Hospital, Chetpet, Chennai, for his support for the work.

References

Inflammatory cells, the Lymphocyte to Monocyte Ratio and the Lymphocyte to Eosinophil Ratio