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Pathology

INSIGHT INTO COMPLETE BLOOD COUNT IN MALIGNANCIES

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ABSTRACT It is very well known that the tumor-host interaction is not limited to the tumor microenvironment but to also alter the entire physiological process to help the development and progression of cancer. Our immune system does not escape from the clutches of the cancer, i.e altered hematological parameters can influence the progression of cancer and vice versa. With this in mind we conducted this study in the Department of Pathology MMC&RI with an attempt to reveal the pattern of complete blood count in malignancies and their difference in localized and metastatic cancer. All the cases included in this study were the ones referred to Cytopatholgy, and diagnosed with cancer. There was significant statistical correlation between the various hematological parameters and the metastatic cancers implying their use to predict the tumor behavior.

KEYWORDS : Complete Blood Count, Hematological Parameters , Metastatic Cancer.

INTRODUCTION:

One of the hallmarks of cancer is "Cancer related Inflammation". Under normal circumstances immune surveillance in our body prevents the emergence of malignant cells and destroys them[1], so development of cancer depends on the ability of malignant cells to alter the normal physiological processes of the host. Later on how the host responses affects tumor progression and prognosis is yet to be explored.[2]

Several studies have revealed that elevated neutrophils are found in many patients with advanced cancer. In agreement with this, the presence of neutrophils within certain tumors also seemed to be an indicator of poor prognosis.[5] There is also growing evidence that gene expression profiling of peripheral blood cells is a valuable tool for assessing gene signatures related to solid tumors[2]. Side by side the field of immunotherapy is growing, it endeavors to stimulate a host response that effectuates long-lived tumor destruction.[6]

With this in mind, we have studied the easily available major peripheral blood parameters in cancer and observed their patterns in metastasizing and localized cancers.

AIMS AND OBJECTIVES:

1) To study the complete blood count profile in malignancies.
2) To study the differential leucocyte count pattern in malignancies.

MATERIALS AND METHODS:

This study was conducted in the Department of Pathology Mysore Medical College and Research Institute. All the cases referred to Cytopatholgy, and diagnosed with Malignancy were included in this study. 2.5ml of blood was collected from each of them into EDTA bottle and full blood count analysis was done on the same day of collection. Complete blood count was done using the Sysmex XN-1000. Hemoglobin levels less than 8gm/dl was considered the lower limit. Upper limits for neutrophils and eosinophils were 70% and 6% respectively. 20% was considered as the lower limit for lymphocytes. The patients were stratified as the ones with Neutrophil to lymphocyte ratio(N:L) <3 and >3. To determine the statistical significance between the above parameters and metastatic cancers, Z-test for difference between proportions was used and the *p* value was obtained.

RESULTS:

In this study conducted in the department of Cytopathology, Mysore Medical College and Research Institute, the complete blood count of diagnosed cases of malignancy prior to treatment was observed. The male to female ratio was found to be 1:1.04, maximum number of patients were in the 6th decade and out of 100 patients studied 72 had metastatic disease. Breast cancers constituted the highest number in our study. 44% of the patients with metastatic cancers had low hemoglobin. 44% of the patients who had metastatic cancer had neutrophilia, 48% had lymphopenia and 34% had eosinophilia. 56% of patients who had metastatic cancer had N:L ratio >3. Significant statistical correlation was found between low hemoglobin, elevated neutrophils, low lymphocytes, N:L ratio and metastatic cancer(i.e *p* value <0.05)

Table 1: Age distribution

Age group	Frequency	Percentage(%)
20-29	1	1
30-39	8	8
40-49	26	26
50-59	28	28
60-69	18	18
70-79	15	15
80-89	3	3
90-99	1	1

Table 2:Age and sex-wise distribution of the Cases studied

Primary	Frequency		Total
	Males	Females	
Breast carcinoma	2	40	42
Squamous cell carcinoma-oral cavity	22	3	25
Squamous cell carcinoma-Pharynx and larynx	7	3	10
GIT malignancy	5	1	6
Thyroid malignancy	1	--	1
Parotid tumor	3	--	3
Lung cancer	1	--	1
Carcinoma cervix	--	1	1
Non-hodgkin lymphoma	1	--	1
Others	7	3	10
Total	49	51	100

Table 3: Pattern of hemoglobin in the present study

Hemoglobin(100 cases)			
Low Hemoglobin	38	Metastatic cancer	32
		No metastasis	6
Normal hemoglobin	62	Metastatic cancer	33
		No metastasis	29

Table 4: Pattern of various Blood counts in the present study

Neutrophlil pattern(100 cases)			
Increased neutrophils	38	Metastatic cancer	32
		No metastasis	6

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Decreased neutrophils	2	Metastatic cancer	1
		No metastasis	1
Normal neutrophils	60	Metastatic cancer	40
		No metastasis	20
Eosinophils pattern(100 cases)			
Increased eosinophils	32	Metastatic cancer	25
		No metastasis	7
Normal eosinophils	68	Metastatic cancer	47
		No metastasis	21
Lymphocyte pattern(100 cases)			
Decreased lymphocytes	42	Metastatic cancer	35
		No metastasis	7
Normal lymphocytes	58	Metastatic cancer	41
		No metastasis	17

Table 5: Pattern of N:L ratio in the present study

N:L ratio(100 cases)			
>3	50	Metastatic cancer	41
		No metastasis	9
<3	50	Metastatic cancer	29
		No Metastasis	21

DISCUSSION:

It was Paul Ehrlich who first conceived the idea that tumor cells can be recognized as 'foreign' and eliminated by immune system. Subsequently, Lewis Thomas and MacFarlane Burnet formalized this concept by coining the term 'immune surveillance' which implies that a normal function of the immune system is to constantly 'scan' the body for emerging malignant cells and destroy them. Even before all of this in 1863 Rudolf Virchow noted leucocytes in neoplastic tissues and made a connection between inflammation and cancer.[3] Rheinbach in 1893 was the first to report a case where he found the malignancy to be the cause of Eosinophilia.[4] This has been supported most recently and most directly by the response of advanced cancers to therapeutic agents that act by stimulating latent host T-cell responses.[1]

Neutrophils have a dual role in influencing the tumor behavior i.e clinical evidence has shown that neutrophils promote tumor progression in various ways by inducing tumor proliferation and angiogenesis and can enhance tumor cell migration and metastasis. Also a type of tumor associated Neutrophils(TANs), named N1, can display antitumor functions. Therapeutic ways to recruit and activate these N1 type neutrophils are being investigated in order to turn protumorigenic neutrophils into antitumor effector cells. Blocking neutrophil-derived components known to help tumor growth is a field of active research.[5]

In our study out of the 72 patients who had metastatic cancer 32(44.4%) had increased neutrophil count. There was a significant statistical correlation between elevated neutrophils and metastatic cancer(*p* value<0.05).

Norman et al published one of the first articles to find the relation of eosinophilia with malignancy titled "Eosinophilia in malignant tumors: Its significance" and concluded that Eosinophilia, when associated with a malignant tumor, with other causes ruled out, is indicative of dissemination of the malignant process. *Harsh Kumar et al* found an association between eosinophilia and disseminated disease. In our study out of the patients who had metastatic cancer 25(34.7%) had elevated eosinophils. There was no significant statistical correlation established between them in our study(*p* value >0.05).

It is very well known that there is increased incidence of some cancers in immunodeficient people. It has been studied that inhibiting immune suppression by blocking the activity of regulatory immune cells, or blocking self-suppression of the Cytotoxic T lymphocyte response by inhibitory molecules such as PD-1 and CTLA-4, holds great potential for improving anti-tumor responses.[7] Amongst the 72 metastatic cancers 33(48.6%) had decreased lymphocytes. Significant statistical correlation was found between the two parameters(*p* value <0.05)

Sarraf et al found that increasing Neutrophil/lymphocyte ratio(N:L Ratio) are associated with increasing tumor stage. In our study elevated N:L ratio was found in 41 out of 72 patients who had metastatic cancer, showing significant statistical correlation between them(*p* value <0.05)

Anemia is a frequently encountered complication in cancer, categorized as anemia of chronic disease. Clinical evidence shows that Hemoglobin level is a prognostic factor for overall survival and/or Disease free survival in several hematological malignancies and solid tumors. There is more than one reason to pay attention to Hemoglobin levels in cancer patients: not only is normalizing Hemoglobin important for improving quality of life, but it may also play a role in influencing outcome.[1] In our study 32(44.4%) had low hemoglobin in metastatic cancer. There was significant statistical correlation noted(*p* value<0.05).

CONCLUSION:

Our study showed difference in the pattern of differential leucocyte counts in metastatic and non-metastatic cancers that was found to be statistically significant. Hence the routinely used low cost, standardized complete blood count can provide information regarding behavior of different malignancies.

ABBREVIATIONS:

N:L ratio: Neutrophil: Lymphocyte ratio
EDTA: Ethylene Diamine Tetra acetic Acid
PD-1: Programmed cell death protein-1
CTLA-4: Cytotoxic T- Lymphocyte associated protein-4

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