Original Research Paper

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Pathology

DIFFERENT POSSIBILITIES OF WBC COUNT MORE THAN 50,000 ON MORPHOLOGICAL BASIS AT TERTIARY CARE CENTER JAMNAGAR IN DURATION OF TWO YEAR.

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ABSTRACT **Background:** The term leukemoid reaction describes an increased white blood cell count, which is a physiological response to stress or infection (as opposed to a primary blood malignancy, such as leukemia). It often describes the presence of immature cells such as myeloblasts or red blood cells with nuclei in the peripheral blood. It requires Peripheral blood smear and other methods for correct diagnosis. **Aims & Objectives:** To determine the difference between leukemia and leukemoid reaction in patients with WBC count more than 50,000 leukocytes/mL. **Patients and Methods:** Medical records of 140 consecutive patients who presented at the G.G. Hospital, Jamnagar between January 2021 to December 2023 with more than 50,000 leukocytes/mL blood were reviewed. Clinical cases was recorded and analysed. **Results:** Extreme leukocytosis was attributed to leukemoid reaction in 128 cases and advanced malignancy in 12 cases. Higher leukocyte counts were associated with malignancy. Most of them are Neutrophilic leukemoid reaction. Mortality is greater in patients with leukemia rather than patients with leukemoid reaction. Although incidence of leukemoid reaction is much higher than malignancy. **Conclusion:** Clinicians should be aware that extreme leukocytosis with a predominance of granulocytes is associated with leukemoid reaction. The presence of infective etiology increases the likelihood that leukemoid reaction as the cause.

KEYWORDS : Leukocytosis, Leukemoid reaction, Leukemia, LAP score.

INTRODUCTION

Elevated white blood cell count due to many potential cause, including malignant and nonmalignant causes.[1]

Leukocytosis is the elevated white blood cell (WBC) count, typically more than 11.0x10^9/L, on a peripheral blood smear collection. The exact value of WBC elevation can vary slightly between laboratories depending on their 'upper limits of normal' as identified by their reference ranges. The WBC value represents the sum-total of white blood cell subtypes, including neutrophils, eosinophils, lymphocytes, monocytes, atypical leukocytes that are not normally present on a peripheral blood smear (e.g., lymphoblasts), or any combination of these. The clinician should properly characterize the leukocytosis and determine if further evaluation and workup are indicated.[2]

Leukemoid Reaction

A leukemoid reaction is a transient increase in WBC count defined as significant increase >50x10^9/L in the absence of a myeloproliferative neoplasm. This acute inflammatory reaction can be mistaken for leukemia, but careful history, physical examination, and further laboratory evaluation can find that this reaction can occur in sepsis, organ rejection, solid tumors, and bacterial infections. Peripheral smears and radiological imaging may be necessary to identify the true cause of these reactive laboratory findings.[2]

The Differentiating Point From Leukemia

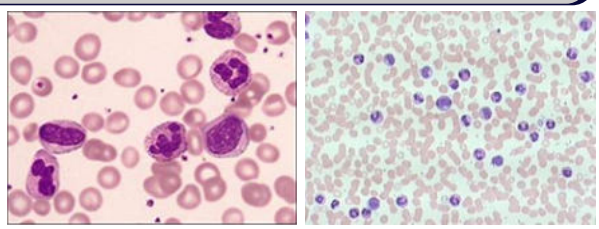
Leukemoid reaction is diagnosed after the exclusion of malignant haematological disorder. The diagnostic work up of leukemoid reaction include various testing to differentiate from leukemia. We should take into consideration WBC count and differential count, peripheral blood film, the Leukocyte alkaline phosphatase (LAP)score, cytogenetic studies, immunophenotyping of peripheral blood and bone marrow and serum levels of hematopoetic growth factors.

(1) WBC Count And Differential Count :-

In leukemoid reaction WBC count are >50,000/cu.mm and consists mostly of mature cells. The differential count discloses a marked left shift, as evidenced by the presence of myelocytes and metamyelocytes. In case of leukemia there are more immature cells.

(2) Peripheral Blood Smear :-

There are presence of immature cells, more eosinophils and basophils according to the type of leukemia. While in leukemoid reaction there is presene of neutrophiliiia, eosinophilia or monocytosis according to the type of leukemoid reaction. Leukemoid reaction shows toxic granules and dohle bodies in granulocytes.



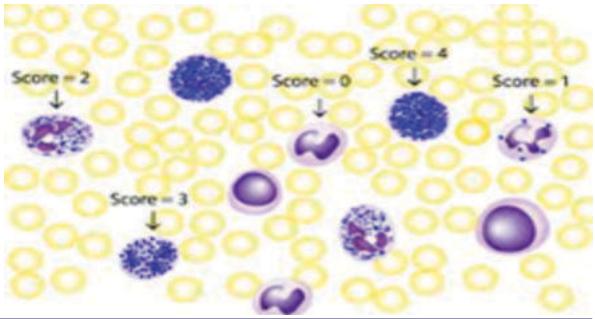
(a) (b)

Fig 1.(a,b)Leukemoid Reaction : Peripheral smears showing immature neutrophils, band cells and myelocytes. Few of the neutrophills show toxic granules.[9]

(3) Leukocyte Alkaline Phosphatase(LAP) Score :-

Leukocyte alkaline phosphatase(LAP) is an enzyme present in the cytoplasmic microsomes of neutrophils, bands, metamyelocytes and myelocytes. This enzyme removes phosphate group in the molecule and help in digestion of phagocytosed material in the neutrophils.

The activity is extremely high in mature leukocytes. Immature neutrophils, such as those observed in CML, have decreased LAP scores(0-20). Scores of LAP test can range from 0 to 400, with those between 30 to 185 being considered normal. The stimulated neutrophils of an leukemoid reaction have increased LAP scores. Principle of the test include naphthol AS phosphate as substrate which hydrolysed by leukocyte alkaline phosphate which leaves naphthol. Naphthol binds with dye and precipitates. We have to look for blue precipitate in neutrophils. Grading of LAP is done in this manner. One hundred consecutive band and segmented neutrophils are rated 0-+4 on the basis of quantity & intensity of the precipitated dye in their cytoplasm. The sum of the ratings of the 100 cells is the LAP score. Figure 2 showing how to grade the LAP score.



No stain	0
Faint stain	+1
Moderate stain	+2
Strong stain	+3
Strong stain without cytoplasmic background	+4

Fig 2. Lap score[3]

(4) Cytogenetic Testing :-
The presence of Philadelphia 1 chromosome in the karyotype or the detection of t(9:22)translocation (creating the bcr/abl oncogene) by molecular techniques is the hallmark for Chronic Myeloid Leukemia. No karyotypic abnormalities are expected in leukemoid reactions.

(5) Serum Levels Of Hematopoetic Growth Factors :-
Although G-CSF, GM-CSF, and IL-6 are not included in the routine diagnostic work-up, their determination by an enzyme-linked immunosorbent assay (ELISA) have been used by several physicians to demonstrate an association between a cytokine- producing tumor and the development of an LR. These glycoproteins are normally secreted by monocytes, macrophages, endothelial cells, and fibroblasts. Their functions include regulation of the growth and differentiation of hematopoietic progenitor cells and functional activation of mature neutrophils and macrophages. LR due to a GM-CSF-producing tumor is characterized by marked eosinophilia. CML and CNL patients have significantly low G-CSF levels, suggesting that the neoplastic granulopoiesis can exert a suppressor effect on G-CSF synthesis. [4]

DISCUSSION

Total 140 cases are devided based on age, sex and morphological basis. out of 128 of leukemoid reaction 50 of them were in age group 0-40 years and52 were in the age group 41-60 years, while 26 cases above 60 years shows leukemoid reaction. So leukemoid reaction is more common in age group below 60 years. In cases of leukemia 7 cases are below 0-40 years, while 2 cases are in age group of 41-60 years and 3 cases above 60 years which depicts that leukemia is more common in early age group of 0-40 years but it also depends on type of leukemia and other factors. Male are affected more than female in leukemoid reaction. While females are affected more in leukemia according to this study. But it has very little significance. Mostly wbcs are morphologically divided into granulocytes and mononuclear cells. Granulocytes includes neutrophils, eosinophils and basophils. Out of 128 cases 109 were neutrophilic while 19 were lymphocytic.

Table 1- Age Wise Distribution Of Cases

Age Group	No. of patients with leukemoid reaction (n1)	No. of patients with leukemia (n2)
0-40 years	50	7
41-60 years	52	2
>60 years	26	3

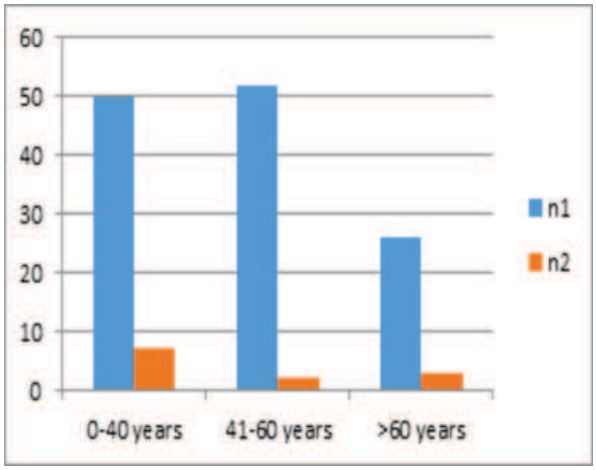


Chart 1.0 Age Wise Distribution

Table 2-sex Wise Distribution Of Cases

Sex	No. of patients with leukemoid reaction (n3)	No. of patients with leukemia (n4)
Male	80	5
Female	48	7

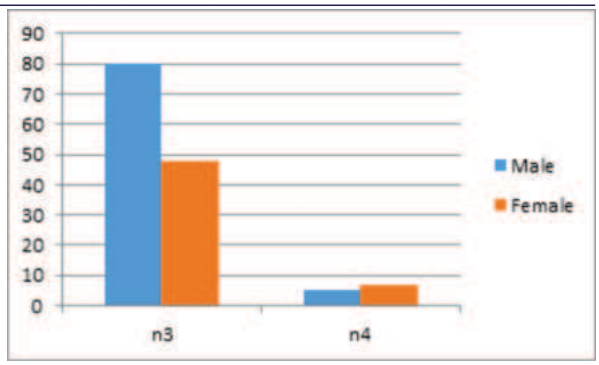


Chart 2.0 Sex Wise Distribution

Table 3- Type Of Leukemoid Reaction

Type of Leukemoid Reaction	No. of patients (n5)
Neutrophilic	109
Lymphocytic	19

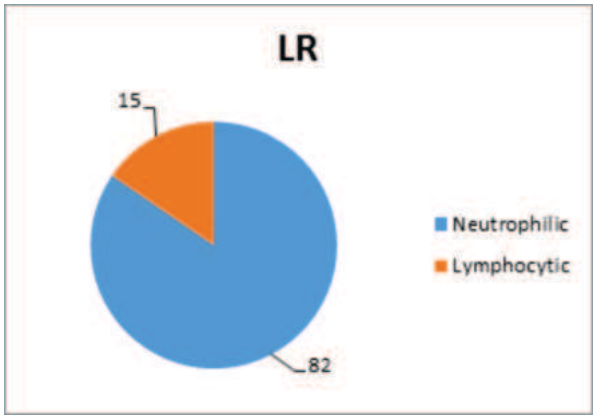


Chart 3.0- Type Of Leukemoid Reaction.

Most of the leukemoid reaction are neutrophilic while few are lymphocytic.

RESULTS OF RETROSPECTIVE ANALYSIS

Current knowledge about the incidence, spectrum, course, and prognosis of patients with LR is scarce. It is based on individual case reports and only a few series of specific groups of patients.[5,6,7,8] We retrospectively investigated a prevalence of leucocytosis(>$50x10^3$ cu.mm) in adult patients at G.G. Hospital, Jamnagar during two year period(2021-2023). In this period white blood cell count >$50x10^9$/l seen in 128 patients.91.43% patients had leukemoid reaction while 8.58% patients had leukemia. In all the patients described, leukemia was considered as the probable cause of leucocytosis however a leukaemoid reaction appears to be the cause of the leucocytosis. The major causes of leukemoid reaction includes infection presenting in 112 cases. Other common causes of leukemoid reaction include stress/ischemia presenting with 10 cases, followed by inflammation in 4 cases and other less common causes present in 2 cases.

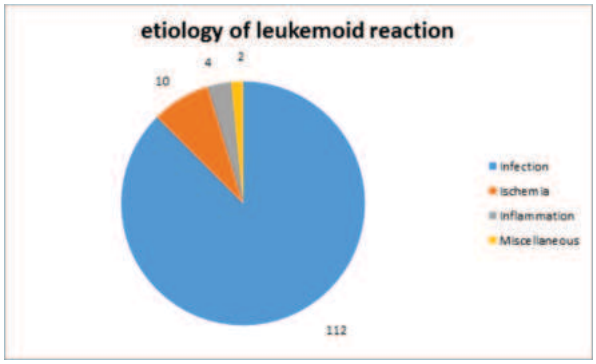


Chart 4.0- Etiology Of Leukemoid Reaction

I compared my results with article titled as "Leukemoid Reaction: Spectrum and Prognosis of 173 Adult Patients" and this article

revealed similar results on etiology of leukemoid reaction. According to this article, infection with or without positive blood cultures, was seemingly the most common cause of LR, occurring in 83 patients (47.9%). Other common causes of LR were ischemia/stress (n = 48, 27.7%) followed by inflammation (n = 12, 6.9%, mostly pancreatitis and splenectomy). Obstetric/gynecologic diagnoses were also common (n = 12), mostly vaginal delivery (n = 6) followed by cesarean section (n = 3), ectopic pregnancy, uterine contractions, and vaginal bleeding. Interestingly, although only 83 patients had an infection, 140 patients (80.9%) received antibiotics; apparently not only for obvious infectious diseases.[10]

If an increased amount of immature granulocytes such as myelocytes or metamyelocytes is seen, a leukaemoid reaction can imitate chronic myeloid leukemia. Investigation of bone marrow including immunophenotyping may help to differentiate between leukemia and leukaemoid reaction. Cytogenetic abnormalities associated with leukemia should be looked for by karyotyping and reverse transcriptase-polymerase chain reaction. The BCR-ABL protein can be found in CML and in some cases in acute lymphoblastic leukemia or acute myeloid leukemia.

CONCLUSION

We have analysed 140 cases of wbc count more than 50000 cells/cu.mm. We have examined peripheral smear of all the patients as well as other data such as history and clinical examination suggests that most of cases turned out to be leukemoid reaction and only 12 cases turned out to be malignant. This analysis provides clinicians with practical information to guide the diagnostic and therapeutic management of patients with extreme leucocytosis. Targeted blood smear review may be useful in selected patients when there is suspicion of underlying hematological malignancy.

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