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Morphological Spectrum of Reactive Lymphocytes in Peripheral Blood Smears of Infants: A Prospective Observational Study.

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Abstract
Background: Reactive lymphocytes in infant peripheral blood smears show morphological heterogeneity and can occasionally resemble malignant lymphoblasts. Characterizing these patterns in relation to viral etiologies may improve diagnostic interpretation. ***Methods:*** This prospective observational study was conducted over 6 months at Navodaya Medical College and Yadgiri Institute of Medical Sciences, a tertiary care center. Fifty infants with reactive lymphocytes identified on peripheral blood smear were evaluated. Demographic characteristics, hematological parameters, viral etiologies, and predominant reactive- lymphocyte morphology were documented. ***Results:*** Of 50 infants, 28 (56%) were male and 22 (44%) were female. Mean hemoglobin was 10.4 ± 1.2 g/dL, total leukocyte count was 8,450 ± 2,100 cells/µL, platelet count was 112,000 ± 45,000/µL, and reactive lymphocytes constituted 18.4 ± 6.2% of leukocytes. Dengue virus was the commonest etiology (72%), followed by Epstein-Barr virus (EBV; 04%), cytomegalovirus (CMV; 02%), respiratory syncytial virus (RSV; 2%), and undetermined viral infection (20%). Plasma cell-like reactive lymphocytes were most frequent (52%), followed by monocyte-like (30%) and lymphoblast-like forms (18%). Plasma cell-like cells predominated in dengue infection (28/36; 77.8%), while lymphoblast-like forms predominated in EBV infection (1/2; 50.0%). ***Conclusion:*** Reactive lymphocytes in infants demonstrate a varied morphological spectrum. Plasma cell-like forms were most frequent and were strongly associated with dengue infection, whereas lymphoblast-like forms were more common in EBV infection. Morphological assessment with clinical and laboratory correlation can provide useful etiological clues and prevent misinterpretation as hematological malignancy.

Keywords: Reactive lymphocytes; infants; peripheral blood smear; dengue virus.

INTRODUCTION
Reactive lymphocytes are activated lymphoid cells that may appear in peripheral blood during antigenic stimulation, particularly in viral infections. Their morphology ranges from enlarged cells with abundant basophilic cytoplasm to monocyte-like, plasmacytoid, or blast-like forms. Peripheral blood-smear examination remains a useful component of hematological assessment and complements complete blood-count findings in the evaluation of leukocyte abnormalities.[1]Dengue, EBV, CMV, and other infections may produce reactive lymphocytosis. Dengue infection is associated with peripheral blood plasmacytosis and plasmacytoid lymphocytes, whereas EBV-associated infectious mononucleosis is characterized by atypical mononuclear cells that may be morphologically diverse. [2-5] These reactive cells can occasionally resemble lymphoblasts, particularly when nucleoli are conspicuous, and may generate concern for acute leukemia without appropriate clinical correlation.Data describing the morphological spectrum of reactive lymphocytes specifically in infants remain limited. This study aimed to describe the hematological profile, etiological distribution, and predominant morphology of reactive lymphocytes in peripheral blood smears of infants at a tertiary care center.

MATERIALS AND METHODS
Design and setting of the study
The present prospective observational study was carried out for a period of 6 months at Yadgiri Institute of Medical Sciences, a tertiary care center.

Participants in the study
Fifty infants were recruited for the study that met our inclusion criteria. The cohort consisted of 28 males and 22 females. All infants had fever and presence of reactive lymphocytes on peripheral blood smear examination.The data provided did not include the exact age range, detailed inclusion and exclusion criteria, method of sample collection, stain used in

preparing the blood smear, number of cells examined, ethics committee approval, and the process of obtaining informed consent. Before manuscript submission, these key methodological details should be included.

Variables evaluated

The hematological parameters studied were: hemoglobin concentration, total leukocyte count, platelet count and percentage of reactive lymphocytes. Viral etiologies identified were dengue virus, EBV, CMV, RSV and unknown viral etiology after standard serology.

Reactive lymphocytes were classified according to the most common morphology in the dataset:
Monocyte-like cells: lobulated nucleus, chromatin clumped. Plasma cell-like cells: Peripheral basophilia with skirted cytoplasm. Lymphoblast like cells Sieve-like chromatin, prominent nucleolus.

Statistical analyzes

Categorical variables were expressed as frequency and percentage. Continuous variables are presented as mean ± SD and range. No patient-level dataset or statistical-test results were provided. The analysis is descriptive.

RESULTS

The study was conducted on a cohort of 50 infants (56% males) who presented with fever and other clinical features like respiratory symptoms and hepatosplenomegaly (Table 1) . Hematologic evaluation showed a mean hemoglobin of 10.4 ± 1.2 g/dL, a mean total leukocyte count of 8,450 ± 2,100 cells/µL, and a widespread thrombocytopenia (mean 112,000 ± 45,000/µL) with a prominent reactive lymphocytosis averaging 18.4% (Table 2). Serological screening showed that the most frequent infectious trigger was Dengue virus (72%), followed by Epstein-Barr virus (EBV) (04%) and Cytomegalovirus (CMV) (02%) with 20% of cases with an undetermined viral etiology (Table 3). Morphological evaluation of the peripheral smears showed plasma cell-like reactive lymphocytes as the most common variant, seen in 52% of infants, with monocyte-like (30%) and lymphoblast-like (18%) forms constituting the rest (Table 4). Notably, the correlations between viruses and morphologies were different: 77.8% of Dengue infections presented mainly plasma cell-like cells, while lymphoblast-like forms were most associated with EBV (50% of EBV cases), and monocyte-like forms were most frequent in CMV infections (Table 5).

Table 1. Demographic and Clinical Characteristics of the Study Population

Characteristic	Number	Percentage
Male	28	56%
Female	22	44%
Fever	50	100%
Respiratory symptoms		—
Hepatosplenomegaly		—
Total infants	50	100%

Table 2. Hematological Parameters of the Enrolled Infants

Parameter	Mean ± SD	Range
Hemoglobin (g/dL)	10.4 ± 1.2	8.1 – 12.5
Total leukocyte count (cells/µL)	8,450 ± 2,100	4,200 – 14,800
Platelet count (cells/µL)	112,000 ± 45,000	40,000 – 250,000
Reactive lymphocytes (%)	18.4 ± 6.2	11 – 34

Table 3. Viral Etiological Profile

Confirmed etiology	Number of cases	Percentage
Dengue virus	36	72%
Epstein-Barr virus	02	04%
Cytomegalovirus	01	02%
Respiratory syncytial virus	01	02%
Unknown viral etiology	10	20%
Total	**50**	**100%**

Table 4. Predominant Morphological Distribution of Reactive Lymphocytes

Predominant morphology	Primary features	Number of cases	Percentage
Monocyte-like	Lobulated nucleus; clumped chromatin	15	30%
Plasma cell-like	Skirting cytoplasm; peripheral basophilia	26	52%
Lymphoblast-like	Prominent nucleolus; sieve-like chromatin	9	18%
Total		50	100%

Table 5. Correlation Between Viral Etiologies and Predominant Reactive Lymphocyte Morphology

Etiology	Total cases	Monocyte-like	Plasma cell-like	Lymphoblast-like
Dengue virus	36	6	28	02
Epstein-Barr virus	02	0	1	1
Cytomegalovirus	01	1	0	0
Respiratory syncytial virus	01	0	1	0
Unknown viral etiology	10	4	4	2
Total	50	15	26	9

DISCUSSION

In this prospective observational study, dengue was the leading infectious trigger of reactive lymphocyte morphology in infants, accounting for 72% of the cases. The most common morphological type was plasma cell-like reactive lymphocytes, which accounted for 52% of all infants and 77.8% of dengue positive cases. The low mean platelet count of 112,000/µL further supports the finding that thrombocytopenia was an important concomitant hematologic feature in this cohort. The presence of plasma cell-like lymphocytes in dengue cases is consistent with the published literature. Thai et al [2] reported peripheral blood plasmacytosis in 64%–73% of dengue cases, most pronounced early in illness and falling rapidly. Transient reactive plasmacytosis in dengue was reported by Gérôme et al [3], who noted the necessity for careful peripheral blood smear examination to recognize this observation. Plasmacytoid lymphocytes as a diagnostic clue in dengue fever were also described by Tanaka [4].

The high percentage of plasma cell-like cells in dengue positive infants in this study supports the value of this morphology as a supportive but not independent diagnostic smear finding. EBV was the causative agent in 04% of cases and 50% of EBV-positive infants exhibited a predominance of lymphoblast-like reactive lymphocytes. Fedyanina et al [5] reported that children with EBV-associated infectious mononucleosis had significant numbers of atypical mononuclear cells, mainly CD8-positive T cells. Softić and Jeren [6] described morphological and cytochemical heterogeneity of atypical mononuclear cells in EBV associated infectious mononucleosis.

These observations are consistent with the present finding that EBV can produce cells with prominent nucleoli and fine chromatin that overlap morphologically with blasts. CMV accounted for 12% of cases and RSV for 8% of cases, respectively, with 20% of infants having no confirmed viral etiology. Evans [7] described EBV as the leading cause of classical infectious mononucleosis. Other infections such as CMV can produce similar clinical and hematological syndromes. Fleisher and Paradise [8] stressed that atypical lymphocytosis in children alone is not sufficient to diagnose acute EBV infection. The morphology of the reactive lymphocytes should therefore be interpreted in conjunction with the clinical history, hematological parameters, serology and, when necessary, flow cytometry.

Limitations of this study include a sample size of 50, a single-center design, and a descriptive analysis. Other absent information in the raw data included age stratification, numerical frequencies of respiratory symptoms or hepatosplenomegaly, timing of smear examination to symptom onset, testing platforms and interobserver agreement in morphology assessment. However, the study provides descriptive data that links reactive lymphocyte morphology and common viral etiologies in infants.

CONCLUSION

Infant reactive lymphocytes have a broad range of peripheral blood smear morphology. The most frequent pattern was plasma cell-like forms, strongly associated with dengue virus infection, and lymphoblast-like forms were more common in EBV-positive infants. Awareness of such reactive patterns with clinico-laboratory correlation may be useful for etiological assessment and to minimize undue concern for hematological malignancy.

REFERENCES

1. Lynch EC. Peripheral blood smear. In: Walker HK, Hall WD, Hurst JW, editors. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd ed. Boston: Butterworths; 1990. Chapter 155.
2. Thai KTD, Wismeijer JA, Zumpolle C, de Jong MD, Kersten MJ, de Vries PJ. High incidence of peripheral blood plasmacytosis in patients with dengue virus infection. Clin Microbiol Infect. 2011;17(12):1823-8. doi:10.1111/j.1469-0691.2010.03434.x.
3. Gérôme P, Foucher B, Otto MP, Crevon L, Rabar D, Pasquet F, et al. Plasmacytosis and dengue fever: an underestimated abnormality? Rev Med Interne. 2012;33(6):343-5. doi:10.1016/j.revmed.2012.03.357.
4. Tanaka Y. Plasmacytoid lymphocytes: a diagnostic clue for dengue fever. Intern Med. 2018;57(19):2917. doi:10.2169/internalmedicine.0179-17.
5. Fedyanina OS, Filippova AE, Demina OI, Zhuliabina OA, Tikhomirov DS, Filatov AV, et al. The nature and clinical significance of atypical mononuclear cells in infectious mononucleosis caused by the Epstein-Barr virus in children. J Infect Dis. 2021;223(10):1699- 706. doi:10.1093/infdis/jiaa601.
6. Softić N, Jeren T. Morphological and cytochemical characteristics of atypical mononuclear cells in the blood of patients with the syndrome of infectious mononucleosis caused by Epstein-Barr virus. Acta Med Croatica. 1993;47(2):67-74.
7. Evans AS. Infectious mononucleosis and related syndromes. Am J Med Sci. 1978;276(3):325- 39. doi:10.1097/00000441-197811000-00010.
8. Fleisher GR, Paradise JE. Atypical lymphocytosis in children. Ann Emerg Med. 1981;10(8):424-6. doi:10.1016/S0196-0644(81)80310-1.