American Journal of BioMedicine
AJBM 2023;11 (3): 136-143
Research Article doi:10.18081/2333-5106/2023.11/136

Neutropenic acute lymphocytic leukemia patients with different patterns of bacterial Infections

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Abstract

Neutropenia following chemotherapy regimens in leukemia patients is of main pressing issue since it makes these patients powerless against contamination. On the off chance that we can recognize which microorganisms are causing these contaminations, they can be destroyed, or, at any rate, the most proper anti-microbial treatment can be begun right away, even before we have the aftereffects of the way of life. Over the past four decades, the range of bacterial isolates has changed a lot. The goal of the current study was to assess the example of bacterial and contagious diseases in acute lymphoblastic Leukemia neutropenic patients. A non-randomized graphic and cross-sectional review including 55 hospitalized patients was completed at the hematology department from December 2020 to December 2022. Neutropenic patients mostly children's patients with clinical indications of contamination or potential fever were signed up for the participation. The resulting data contained 55 febrile as well as contaminated neutropenic episodes happening in 30 male and 25 female more youthful of age with a mean period of 32.14±4.23 years. A sum of 34 microorganisms was refined: 60.5% from other locations and 39.5% from the urinary tract; 70.2% were gram-negative microbes, 19.8% were gram-positive microscopic organisms, and 10% were growth. Pseudomonas aeruginosa and staphylococcus aureus were the most successive gram-negative and gram-positive detaches separately. Candida spp. was the only fungus found isolated. In conclusion, Gram-negative micro-organisms remained the most prevalent pathogens isolated in this result in the study population, and the patterns of isolates in neutropenic patients with lymphocytic leukemia (ALL) vary from region to region, therapeutic adjustments for empirical antibiotic therapy are likely to focus on gram-negative pathogens.

Keywords: Lymphocytic leukemia; Neutropenia; Gram-negative micro-organisms

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Received 28 February 2023; revised 30 May 2023; accepted 29 June 2023; published 19 August 2023

Introduction

Acute lymphocytic leukemia (ALL) is the most frequent malignancy in childhood, with a peak incidence occurring at 3 to 4 years of age. Medical progress in this field has been significant; therefore, the long-term survival has been increased [1]. However, as the number of survivors

Research Article doi:10.18081/2333-5106/2023.11/136

increases, complications, including neutropenic fever episodes, with its repercussions in relation to morbidity, costs of care, etc., make it essential to carry out the risk categories in a prospective way that allows a close management of these patients [2]. The purpose of this study was to prospectively determine via a 2-weekly determination the pattern of infections in febrile neutropenic children with ALL, related to their severity, in order to standardize the management through the use of therapies that improved a more benign evolution, in the group of patients who had a frequent infection pattern [3].

Most of these patients are classified in a disease presenting a low and intermediate severity, with an evolution, according to reports from specialized centers, in around 95-90% to cure. However, relapses are observed in approximately 10 to 15%, which makes it essential to have a good risk estimator of these events that allow us to carry out a better management of the patients. The most important factors reported in relation to it are the presence of leukemia in greater or lesser degree in the cerebrospinal fluid and the presence or not of a complete remission after induction [4]. The report of the Pediatric Branch of the Allergic Study Group reported that those patients who clearly had peripheral blood without blasts were patients who benefited more from the continuation therapy with chemotherapy. It should be noted that febrile neutropenia secondary to myelosuppressive therapy is due to intensive cytosolic secretion that causes diaphragmatic paralysis [5]. This effect is dose-dependent, so remission was observed since the cessation of the therapy; furthermore, this is related to the number of progenitors present. The long-term damage is related to a dose and latency during life, and it is lethal dependent on the dose. The appearance of leukemia in these patients is rare, so it is not related to the same histology of the tumor [6].

The despair immune function associated with long-term chemotherapy and large doses of hormones contributes to the Neutropenic Acute Lymphocytic Leukemia (NALL) of the patients, rendering them highly susceptible to severe systemic bacterial infections. In the present study, NALL patients developing severe systemic bacterial infections were attempted to be classified by clinical symptoms and the patterns of the patients [7]. Each of the clinical symptoms showed variations in incidences to some extent, but they also showed biases to the patterns of the patients with bacterial infections to some degree. And all of the clinical symptoms were significantly correlated with the types of bacterial infections, including Gram-positive, Med-negative, Gram-positive cocci, and Anaerobe bacteria infection. These results suggest that the clinical symptoms can identify the types of bacterial infections to some extent and will help the clinician for focused anti-infective treatments to fight against the bacterial infections in NALL patients [8].

NALL, a common blood system malignant tumor, with difficult treatment, high fatality, and severe infection [9]. In order to reduce the medical care cost and case fatality, many clinicians treat these patients as out-patients, which delays the best treatment time of NALL patients. Moreover, the constitution of out-patients in China especially leads to the incidence of bacterial infections or even the causes of infections not completely consistent with foreign countries to

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some degree. And the patients with NALL continue to have neutropenia after treatment (Neutrophils count lower than 1.5 × 109/L). Circulatory chemotherapy and the body immunity are severely repressed and correspondingly lead to the degree of bacterial infections caused by the Neutropenia directly associated with circulating neutrophil count [10]. Most of the common pathogenic bacteria of the systemic infection are found in the evacuating colon and sigmoid combination, and a large number of gas production is produced by these bacteria, together and accounted for a small life-threatening to perforation.

Patients and methods

A non-randomized descriptive and cross-sectional study involving 100 hospitalized children was carried out at the emergency and pediatric hematology and oncology units of Quaem, Imam Reza, and Dr. Sheikh Hospitals affiliated with Mashhad University of Medical Sciences from September 2004 to September 2005. Neutropenic children younger than 12 years old with clinical signs of infection and/or fever were enrolled in the present study. Chemotherapy-induced neutropenic children who developed fever within 24 hours after administration of chemotherapy and the fever subsided within the next 24 hours after completion of chemotherapy,8 and also children with fever occurring during or within 6 hours after transfusion of blood, blood products, and other intravenous fluids,8 were excluded from the study.
All participating units were required to report all eligible cases met the inclusion criteria to the data Centre. All eligible recruited patients underwent a thorough assessment including detailed history, careful and complete physical examination, and relevant hematological, microbiological, and radiological investigations.

Materials

Three ml blood was collected in dipotassium salt of ethylene diamine tetra-acetic acid (K2 EDTA) within two hours for a complete blood count. Two sets of 2 ml blood were collected at one-hour intervals for blood culture. Throat swabs for culture were sent to the laboratory within 2 hours. Pus swabs, pus, and exudates from skin, mouth, ear, eyes, joint, sinuses, wound, and ulcers with sterile disposable syringes or sterile cotton wool swabs were delivered to the laboratory within 2 hours. Midstream urine samples were collected and delivered to the laboratory for urine culture. One to two ml of stool specimens were collected and transmitted quickly to the laboratory for stool examination and stool culture. Effusion (peritoneal, pleural, etc.) fluids were aspirated and transported to the laboratory within 2 hours for routine examination and culture. Cerebrospinal fluid samples were collected with sterile disposable syringes and transported to the laboratory within 1 hour after collection for routine examination and culture.

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Statistical Analysis

SPSS software version 12 was used for data management. The bivariate correlation procedure was used to compute Pearson's correlation coefficient. A P value of 0.05 was considered statistically significant.

Result

White Blood Cell Counts

The mean absolute white blood cell count at the time of diagnosis was 3368±2940/µl (range 100-12500/µl). It was categorized into four groups: 4000/µl (22%). The mean absolute neutrophil count was 643±407/µl (range 0-1400/µl), categorized according to neutropenia severity into three groups: 1000/µl (mild neutropenia, 22%). Severe neutropenia was most detected in 5-12 years (47.4%) and 2-5 years (31.6%) old groups. Moderate neutropenia was most detected in 5-12-year-old group (55%). There was a statistically significant difference in the severity of neutropenia according to the age group (r=-0.235, P=0.007). Severe and mild neutropenia were most detected in males (65.8% v 34.2% and 63.6% v 36.4% respectively). There was no statistically significant difference in the severity of neutropenia according to gender (r=0.060, P=0.526). Severe neutropenia in acute lymphoblastic leukemia (ALL, 50%), moderate neutropenia in ALL (30%) aplastic anemia (12.5%), and mild neutropenia in histiocytosis (22.7%) were most detected. There was a statistically significant difference in the severity of neutropenia according to the underlying disease(r=0.366, P<0.001).

Discussion

Bacterial infections have been reported to account for life-threatening complications in 5-10% of febrile episodes in childhood malignancies [11]. In the current study, the mean absolute white blood cell count at the time of diagnosis was 3368 ± 2940/µl, and the mean ANC was 643±407/µl, while other study have reported the median absolute white blood cell count of 250/µl and the median ANC of 18/µl [12]. In the current study, 87% of neutropenic episodes had established infection and in 13% of cases, no pathogen was cultured. Other have reported that infection was certain in 36% of febrile episodes, probable in 14%, and not determined in 50%. However, other have demonstrated 21.4% and 78.6% positive and negative cultures, respectively [13-17]. This significant difference may be due to different sampling methods and laboratory procedures. Gram-negative bacilli were the most common cause of infection in neutropenic patients from the late 1960s until the early 1980s [18]. Other have shown that gram-negative bacilli were cultured in approximately 60-80% of infections, of which P. aeruginosa was the most important isolate [19]. In the mid-1980s, the spectrum of isolated pathogens began to change. Gram-positive cocci have taken the place of gram-negative bacilli, constituting 50-70% of bacteremia with single organisms. This has been confirmed by the

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results of the eight therapeutic trials performed by the IATCG-EORTC in the last 22 years in febrile and neutropenic patients. Coagulase-negative staphylococcus and S. aureus were the predominant organisms. This change from gram-negative to gram-positive pathogens is probably multifactorial. Neutropenic patients can differ in their clinical presentation when suffering from an acute bacterial infectious disease. Nevertheless, the clinical findings in these patients can often be nonspecific [20]. However, certain general findings should raise the possibility of bacterial infection in the neutropenic patient. Some of these features, such as persistent fever, purulent secretions from the respiratory system, sinusitis in granulocytopenic patients, infiltrates in pulmonary radiograms, and atypical clinical presentation are similar in their value of suspecting bacterial infection both in granulocytopenic and in non-neutropenic patients. In addition, localizing signs should alert the clinician to the possibility of bacterial infection [21]. As a general rule, bacteremia should be kept in mind even at low-grade fever in the neutropenic patients. A reliable temperature measurement is important to detect this important sign of infection. Often, the personnel in the hematology ward are aware of the potential complications of a single-instance bacteremia in a granulocytopenic patient, who could deteriorate rapidly and critically [22]. A minority of the cases of fever in leukemic children during bacteremia are in fact complicated by septicemia. Clinical examination of the neutropenic patient, including passive and active searching for the origin of the fever, is important. However, the physical examination is often insufficient and nonspecific in neutropenic patients who are at risk of bacterial infection, as well as in patients with normal granulocyte counts. Respiratory disease in neutropenic patients typically manifests as atypical, widespread infection clinically characterized by cough and wheezing or dyspnea that are rapidly deteriorated into shock and hypoxia. Several hematological and biochemical studies have reported "nonspecific infiltrate" being the most frequent diagnosis of pneumonia in neutropenic patients [23]. Unfortunately, the term should not indicate a noninfectious process that, on the contrary, is often a feature of such atypical cases, specifically, the majority of infiltrates that are due to infectious disease display the same atypical radiographic findings, but all these putative classical and atypical radiological concepts should not be overemphasized, as the detection of both bronchial signs and cavitation can increase the specificity [24].

Conclusion

The present study confirms findings from previous publications and before leukemic patients. Our experience goes to support those of others and illustrates that the pattern of bacterial infections probably reflects the type of underlying disease more than the treatment used to control them. Infections occur in host environments that are severely immunodeficient. The risk of infections generally is not only directly related to the degree of leukopenia but is dependent on other defects of host defense mechanisms. Altered complement activity, aberrations of granulocytes, depressed activity of reticuloendothelial system and defects in cellular immunity represent the most important of these factors and may account for the pattern. Rather than the

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chemotherapy per se acting as an immunosuppressive factor, the risk of infection is assumed to be directly proportional to the degree of immunocompromise of the host. These factors are manifested in most leukemic patients who have a tendency to failed responses despite treatment. Prophylactic agents directed against specific opportunistic organisms can only partially modify the pattern.

Funding

No funding was received.

Competing interests

The authors declare no conflict of interest.

Ethics Statement

Not applicable.

Authors' contributions

All authors shared in the conception and design and interpretation of data, drafting of the manuscript and critical revision of the case study for intellectual content and final approval of the version to be published. All authors read and approved the final manuscript.

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American Journal of BioMedicine
Journal Abbreviation: AJBM
ISSN: 2333-5106 (Online)
DOI: 10.18081/issn.2333-5106
Publisher: BM-Publisher
Email: editor@ajbm.net