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A Fulminant Case of Febrile Neutropenia with Bacteremia Detected by Peripheral Smear in ALK Negative Anaplastic Large Cell Lymphoma

Deepthi B*, N. Rukmangadha, B. Swathi and A. Sreelekha

Department of Pathology, Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India

Abstract

Febrile neutropenia is a frequent complication in cancer patients and affects nearly 80% with hematological malignancies and 10%-50% with solid malignancies occurring most frequently during the first chemotherapy cycle. Bacterial Bloodstream Infections (BSIs) accounts for 10% to 25% of all febrile episodes and is considered the most common among the infectious complications in febrile neutropenic patients due to the lack of adequate inflammatory response and makes sepsis a significant cause of mortality in this particular setting.

Keywords: Febrile neutropenia • Bloodstream infections • Patients • Chemotherapy

Introduction

The occurrence of severe sepsis and septic shock in the setting of febrile neutropenia have been estimated to be 20%-30% and 5%-10% respectively. Febrile neutropenia should be suspected and considered a medical emergency with prompt administration of empirical antibiotic therapy to reduce the mortality. Peripheral smear examination plays a key role in the diagnostic work up of many blood borne infections like malaria, filaria, borrelia, babesia etc, and it is not a routine clinical scenario to identify other blood stream bacterial infections even with respect to buffy coat examination [1]. It is a very rare reported scenario of identification of bacteremia in peripheral smear and it may provide an important clue in the initial diagnostic process as it enables a rapid diagnosis of blood stream infections in comparison to considerable time for blood cultures to become positive [2].

Herein we elucidate a similar rare scenario of a fulminant febrile neutropenia post first cycle of CHEOP chemotherapy regimen for ALK negative Analapstic Large Cell Lymphom (ALCL) with bacteremia diagnosed by a meticulous peripheral smear examination even before blood cultures were requested [3].

Case Presentation

A fifty one year old male was initially evaluated for swelling in the chest wall of one month duration. PET scan showed multiple soft tissue density lesions in anterior and superior mediastinum, bilateral supraclavicular lymph nodes, bilateral axillary lymphnodes, bilateral lung parenchymal and pleural nodules [4]. Biopsy from the chest wall lesion diagnosed as ALK negative anaplastic large cell lymphoma with clinical stage IV E. The patient was planned for 6 cycles of CHEOP regimen. The patient was admitted for two days to receive the first cycle with CHEOP regimen Inj cyclophosphamide 1350 mg/msq, tab. prednisolone 100 mg D1-D5, tab. etoposide 180 mg, injection adriamycin 90 mg, injection vincristine 2 mg on 6/11/2022 [5]. The complete blood count prior chemotherapy showed mild neutrophilic leucocytosis and thrombocytosis-Hb-10.8 g/dl, total leucocyte count-13100/cumm with differentials of 78% neutrophils and 11% lymphocytes, platelets-5.59/cumm [6].

After 7 days post first cycle chemotherapy, the patient presented to emergency department on 15/11/2022 with low grade fever associated with chills and rigor, altered sensorium and generalised weakness. On examination the patient was found to be in shock with basal crepts, blood pressure 90/50 mmhg, spo_2: 90% on room air and metabolic acidosis [7].

The patient was started on supportive therapy with intravenous fluids, oxygen support, ionotropes and sodium bicarbonate. The patient had sudden cardiac arrest and was put on mechanical ventilator and ionotrope support. The patient had progressive course and was declared dead on the same day of admission with possible immediate cause of death being septic shock and antecedent cause of febrile neutropenia due to chemotherapy for ALCL stage IV E [8]. The blood counts during the brief second admission revealed a dramatic fall in counts with pancytopenia-HB: 6.5 g.dl, total leucocyte count-160 cells/cumm with

***Address for Correspondence:** Deepthi B, Department of Pathology, Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India, Tel: 9963168822; E-mail: drbdeepthi@gmail.com*

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nil neutrophils and platelets-0.8/cumm.

The peripheral smear examination which was requested as a part of initial work up revealed marked leucopenia with meticulous search revealing medium size, stout bacilli in pairs, short chains and groups seen predominantly extracellulary (Figure 1) [9]. There were absolutely no neutrophils in the entire markedly leucopenic smear to comment on the presence of intracellular bacilli. An index of cross contamination was suspected by the pathologist and a repeat smear also confirmed the presence of bacteremia in the peripheral smears [10]. Upon a detailed elicitation of clinical history of high grade lymphoma post CHEOP regimen, the diagnosis of bacteremia with severe pancytopenia was confirmed on peripheral smear. Owing to the rapid downhill course of the disease, the patient succumbed before initiation of antibiotic regimen [11].

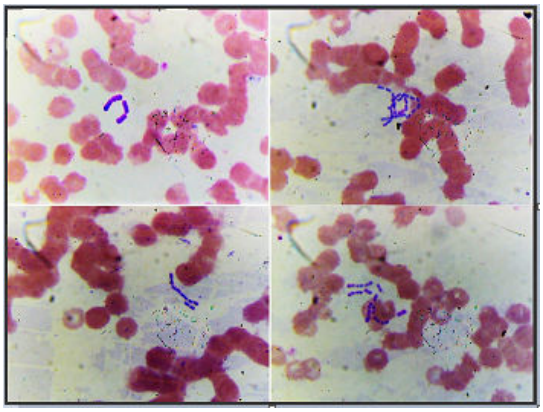

Figure 1. Peripheral smear showing stout rod shaped bacilli in Paris, short chains and clusters, Leishman stain × 1000.

Results and Discussion

The introduction of multi agent chemotherapy has radically improved the prognosis of patients with high-grade malignant non-Hodgkin's lymphoma [12]. Among the drugs which are effective in the treatment of aggressive NHL, etoposide, together with doxorubicin and cyclophosphamide, has become the most firmly established [13]. In general, neutropenia with infection is the major side effect of this regimen while other toxicities are modest [14]. Other severe toxicities include stomatitis (2%), diarrhoea (4%) neurotoxicity (2%) and liver toxicity. The mortality in this scenario is mostly due to therapy related deaths or septicemia following neutropenia [15]. Limited information is available on the significance of the visualization of bacteria in peripheral blood smears but the general prognosis of patients with peripheral bacteremia is extremely grave [16].

A rapid and definitive diagnosis is essential in the prompt management of septicemia which is characterized by systemic signs of fever, shock and systemic organ failure and can be a life saving intervention [17]. Blood cultures are the considered the corner stone of diagnostic workup of febrile neutropenia, as they help in pathogen identification along with susceptibility pattern. However their sensitivity is significantly lowered with initiation of antibiotic therapy and they should be performed immediately when infection during neutropenia is suspected clinically [18]. Blood cultures require incubation time and do not play a crucial role in the initial treatment decision. A microscopic examination of peripheral Page 2 of 3blood can be of great help to hasten the confirmation of bacteremia, thereby enabling doctors to initiate empirical antibiotic therapy, which can be a crucial step towars recovery. However, the presence of bacteria in peripheral smear is found only in settimg of overwhelming sepiticemia [19]. To be able to detect by peripheral smear, a microorganism with the centration of 10^5 CFU/mL or greater is required. Even more a peripheral smear examination or a buffy coat examination are not routinely used for dectecting bacteremia as the sensivity is very less and the organisms cannot be identified to the species level [20].

The detection in peripheral smear requires a meticulous examination with adequate training and sensitisation of the examiner and serves as simple, cost effective, rapid procedure in providing a preliminary diagnosis as well as assess the type of inflammatory response to the agent [21]. The bacteria may be located free between the blood cells or within the cytoplasm of erythrocytes, neutrophil granulocytes or monocytes [22]. They are obsererverable on standard Leishman or May-Grunwald-Giemsa (MGG)-stained slides, but special stains are necessary for further characterization. The mortality rate is considered to be very high when bacteria are visualized on a patient's peripheral blood smear [23].

Conclusion

Finding microorganisms on peripheral blood smears is unusual and if bacteria are spotted, it must be as certained that the observation is not an artefact or contamination. Finding bacteria within the leucocytes is considered true bacteremia and a gram stain is done to validate the results. In our scenario owing to marked leupenia, only occasional lymphoctes were identified on the peripheral smear to comment of presence of intracellular bacteria, but with the adequate clinical background, the diagnoisis was made. This case highlights the simple, inexpensive, safe and meticulous peripheral examination be more widely used especially when overwhelming bacteremia is suspected in conditions like hyposplenism, AIDS, neonatal sepsis, post chemotherapy. PBS is not a routine procedure for detecting bacteremia, in specific scenario, it can prove to be an important tool to provide rapid preliminary diagnosis, thereby allowing clinicians to act promptly and expedite antibiotic therapy to reduced fatality.

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