

Insight into Leukemia-like Presentations in Tuberculosis Patients

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Abstract

Tuberculosis (TB) continues to pose a considerable public health concern, characterized by elevated prevalence rates and varied clinical manifestations. Tuberculosis can induce hematological abnormalities resembling leukemia, posing diagnostic challenges in resource-constrained settings. This brief review delves into the leukemia-like features of tuberculosis patients, an issue of considerable interest and importance to medical practitioners, researchers, and public health authorities. We explore fundamental principles, diagnostic methods, and clinical implications, highlighting the critical need for heightened awareness and enhanced diagnostic tools to distinguish tuberculosis from hematological malignancies. Furthermore, the outcomes of this review may improve diagnostic methods in resource-limited settings, which should particularly interest medical professionals, researchers, and public health officials focused on tuberculosis and hematology. Case studies, including acute lymphoblastic leukemia-like, chronic myeloid leukemia-like, and other presentations, improve the literature and provide practical insights.

Keywords: tuberculosis; leukemia; leukemia-like presentation; hematological abnormalities

Introduction

Tuberculosis (TB) is a significant worldwide health issue, especially in high-burden nations, where the incidence was 10.8 million people (95% UI: 10.1–11.7 million) in 2023 [1]. Although tuberculosis predominantly impacts the lungs, 20-30% of cases are extrapulmonary [2]. Tuberculosis can lead to notable hematological abnormalities, such as leukocytosis, monocytosis, lymphocytosis, and pancytopenia, which may closely mimic leukemia [3]. The epidemiology of tuberculosis (TB) globally indicates that it is endemic, characterized by elevated prevalence and burden of both pulmonary and extrapulmonary forms of the disease [4]. Contributors to the significant load include poverty, starvation, overcrowding, and restricted access to healthcare [5]. Hematological abnormalities are prevalent in tuberculosis patients, with anemia being the most commonly documented condition. Leukocytosis, monocytosis, lymphocytosis, and pancytopenia have been noted, frequently resulting in diagnostic ambiguity with leukemia [6].

Pathophysiology of Hematological Alterations in Tuberculosis

1. Inflammatory Cytokines: Tuberculosis induces the secretion of pro-inflammatory cytokines (e.g., interleukin (IL-6) and tumor necrosis factor (TNF- α),

which inhibit bone marrow activity and modify hematopoiesis.

2. Bone Marrow Infiltration: Disseminated tuberculosis may affect the bone marrow, developing granuloma, caseous necrosis, and dysplastic alterations.

3. Nutritional Deficiencies: Malnutrition, prevalent among tuberculosis patients, aggravates anemia and other cytopenias.

4. Immune Dysregulation: Tuberculosis can induce immune-mediated death of blood cells, especially in instances of hemophagocytic lymphohistiocytosis (HLH) [8].

Leukemia-Like Presentations of TB Patients

Chronic tuberculosis may induce leukocytosis and monocytosis, mimicking chronic myelomonocytic leukemia (CMML) [9]. Reactive lymphocytosis in TB may resemble chronic lymphocytic leukemia (CLL) [10]. Disseminated tuberculosis can result in pancytopenia, imitating bone marrow failure or acute leukemia [11]. Chronic neutrophilic leukemia-like is a prevalent kind that may occur in conjunction with tuberculosis [12]. Additionally, an acute myeloid leukemia-like condition may be detected in cases of severe pulmonary or extrapulmonary tuberculosis [13]. Further, acute lymphoblastic leukemia-like conditions are frequently observed in children and may be related to miliary tuberculosis [14].

Diagnostic Challenges in Limited Resource Countries

1. **Insufficient Diagnostic Resources:** In low-income countries, sophisticated diagnostic instruments for hematological malignancies (e.g., flow cytometry and cytogenetics) are often inaccessible. As a result, clinicians must rely on clinical judgment, basic laboratory tests, and TB-specific diagnostics (e.g., Sputum AFB smear) to make an accurate diagnosis.

2. **Intersection with Malaria and Other Infections:** Malaria, prevalent in some nations, may induce hematological anomalies, complicating the diagnostic procedure. For example, a study by Fauchald et al. [16] reported a case of a 10-year-old girl with fever, hepatosplenomegaly, and cytopenias who was initially suspected of having hemophagocytic lymphohistiocytosis (HLH) but was later diagnosed with TB based on bone marrow findings and positive TB smear.

3. **Significant Burden of TB:** The elevated incidence of TB heightens the probability of observing leukemia-like manifestations, requiring a heightened level of suspicion [15].

Diagnostic Approach

1. **Clinical Evaluation:** A comprehensive history and physical examination are crucial for identifying tuberculosis risk factors (e.g., persistent cough, nocturnal diaphoresis, weight reduction).

2. **Laboratory Tests:** Complete blood count (CBC) and peripheral blood smear to evaluate for reactive alterations. Tuberculosis-specific assays (e.g., sputum acid-fast bacilli smear, polymerase chain reaction, culture, interferon-gamma release assays).

3. **Bone Marrow Examination:** A bone marrow biopsy may identify granulomas or caseous necrosis in tuberculosis, differentiating it from leukemia.

4. **Exclude Alternative illnesses:** Conduct tests for malaria, HIV, and other endemic diseases that may induce comparable hematological anomalies.

Implications for Clinical Practice

In resource-limited settings, where advanced diagnostic tools for hematological malignancies are often unavailable, distinguishing TB from leukemia is critical to avoid misdiagnosis and ensure appropriate treatment [18]. Misdiagnosis can result in unwarranted chemotherapy or postponement of anti-TB therapy, both of which may have dire repercussions [19]. Furthermore, including TB-specific tests (PCR and interferon-gamma release assays) in the diagnostic workup of patients with

unexplained hematological abnormalities can help reduce misdiagnosis and ensure timely initiation of anti-TB therapy [20]. This study seeks to elucidate the hematological manifestations of tuberculosis patients, emphasizing leukemia-like appearances while addressing the diagnostic challenges in this context.

Case Studies from Around the World

Case 1: ALL-like presentation in a child [21]

Presentation: A 6-year-old male exhibited fever, tiredness, and widespread lymphadenopathy. Preliminary blood tests indicated leukocytosis accompanied by lymphocytosis and thrombocytopenia.

Initial suspicion: Acute lymphoblastic leukemia (ALL).

Diagnostic workup: The peripheral blood smear displayed reactive cells alongside many blasts. A bone marrow biopsy indicated the presence of granuloma, and the TB PCR test returned positive.

Outcome: The child commenced anti-TB therapy and showed substantial improvement within two months.

Case 2: CML-like presentation [22]

Presentation: A 37-year-old male exhibited tiredness, nocturnal sweats, and splenomegaly. Blood tests indicated leukocytosis with a left shift, signifying an elevation in immature cells.

Initial suspicion: Chronic myeloid leukemia (CML).

Diagnostic workup: The peripheral blood film showed no basophilia and eosinophilia. A bone marrow biopsy indicated the presence of granuloma, and the TB PCR test returned positive.

Outcome: The patients had favorable responses to anti-TB medication, resulting in normalized blood counts and the elimination of splenomegaly.

Case 3: HLH-like Presentation [23]

Presentation: A 17-year-old male exhibited high fever, hepatosplenomegaly, and cytopenias. Blood tests demonstrated elevated ferritin, triglycerides, and hypofibrinogenemia.

Initial suspicion: Hemophagocytic lymphohistiocytosis (HLH).

Diagnostic workup: The bone marrow biopsy indicated the presence of hemophagocytosis and granuloma, and the TB PCR was positive.

Outcome: The patient received anti-TB medicine and corticosteroids, resulting in symptom remission.

Case 4: Pancytopenia Mimicking bone marrow failure [24]

Presentation: A 74-year-old male presented with fever, pallor, and bleeding tendencies. Blood tests demonstrated pancytopenia.

Initial suspicion: Acquired aplastic anemia.

Diagnostic workup: The bone marrow biopsy indicated the presence of caseous necrosis and granuloma, and the TB PCR was positive.

Outcome: The patient received anti-TB medicine and showed gradual improvement in blood counts.

Discussion

This research explores the hematological consequences linked to tuberculosis (TB) patients, focusing specifically on leukemia-like manifestations. Tuberculosis is recognized to influence multiple hematological parameters. The study identified substantial changes in hemoglobin concentrations, red blood cell counts, and packed cell volume relative to healthy controls in tuberculosis patients. Indeed, tuberculosis patients demonstrated reduced values of these markers, signifying anemia. Furthermore, there was a significant elevation in total and absolute leukocyte count, indicating leukocytosis and monocytosis [6]. These findings are of utmost significance since they suggest the likelihood of anemia, leukocytosis, and monocytosis in individuals with tuberculosis.

The phenomenon of leukemia-like manifestations in TB patients is a challenging and fascinating subject of investigation. These presentations exhibit hematological abnormalities analogous to those observed in leukemia patients, including severe neutrophilia, lymphocytosis, and thrombocytosis. This overlap can result in diagnostic difficulties, as clinicians may initially suspect leukemia instead of tuberculosis [25]. The exact processes causing these leukemia-like manifestations in tuberculosis patients remain incompletely elucidated. Nonetheless, other hypotheses have been put forward. One idea posits that the persistent inflammatory response triggered by tuberculosis infection may cause modifications in hematopoiesis, leading to irregular white blood cell levels. Another concept is that immunological dysregulation induced by tuberculosis may contribute to the emergence of these hematological abnormalities [26].

A tuberculous infection should always be considered when determining the cause of hematological abnormalities. Tuberculosis can induce various abnormalities, such as leukocytosis, leukopenia, monocytosis, and pancytopenia. These alterations are often reactive and influenced by the systemic inflammatory response to *Mycobacterium tuberculosis*

[27]. In certain instances, the hematological profile may closely mimic leukemia, especially chronic myelomonocytic leukemia (CMML) or acute leukemia [13, 28].

Ali BM et al. [4] emphasized the risk of misdiagnosis in tuberculosis cases. It was determined that 30% of tuberculosis patients exhibiting monocytosis were initially misdiagnosed with chronic myelomonocytic leukemia, highlighting the critical nature of the problem. Pancytopenia in disseminated tuberculosis might resemble bone marrow failure, as demonstrated in a study reported by Achi et al. [11]; pancytopenia was observed as suspected of having acute leukemia. Then, it was subsequently confirmed with miliary tuberculosis following a bone marrow investigation, highlighting the risk of misdiagnosis.

Padhi et al. documented a case involving a 17-year-old girl presenting with fever, hepatosplenomegaly, and cytopenias, first suspected of having hemophagocytic lymphohistiocytosis (HLH). Subsequently, they confirmed tuberculosis (TB) based on bone marrow analysis and positive TB PCR results [23]. This example is significant as it illustrates the necessity of thorough testing to achieve an accurate diagnosis, particularly when symptoms may coincide with other illnesses.

Numerous case studies and research publications have recorded leukemia-like manifestations in tuberculosis patients, such as a report released by the American Society of Hematology stating the diagnosis delay in tuberculosis patients with acute myeloid leukemia (AML), stressing the necessity for increased clinical vigilance [18]. A separate study examined the correlation between tuberculosis (TB) and patients with chronic myeloid leukemia (CML), highlighting the heightened vulnerability of these individuals to TB as a result of their immunocompromised condition [22].

The strength of this review approach is that it facilitates extensive knowledge of tuberculosis's hematological findings (leukemia-like presentation). The research highlights patients profoundly affected by tuberculosis, providing relevant and context-specific insights. The study highlights the presence of leukemia-like hematological abnormalities in tuberculosis patients, an important finding that could significantly influence differential diagnosis and treatment approaches, thereby enhancing patient outcomes. This study's limitations restricted the findings' applicability to broader populations. They also restricted the heterogeneity of the patient cohort,

thereby impacting the external validity of the findings. The study may not consider all possible confounding variables, such as concurrent infections or pre-existing health issues, which could affect the hematological parameters.

Conclusion

In conclusion, the study of leukemia-like events in tuberculosis patients is a challenging and insufficiently explored area of hematology. Understanding the etiologies and clinical implications of diverse manifestations is essential for enhancing the diagnosis and treatment of tuberculosis, especially in areas with elevated TB prevalence. The significance of continuous research and your clinical acumen cannot be exaggerated. Your attentiveness and accountability are essential to our joint endeavors in elucidating the complex association between TB and hematological well-being.

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