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The Diagnostic Value of Absolute Neutrophil Count, Band Count and Morphologic Changes of Neutrophils in Predicting Bacterial Infections

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Key Words

White blood cell count · Absolute neutrophil count · Band count · Neutrophil morphologic changes

Abstract

Objectives: To evaluate the value of neutrophil left shift parameters and neutrophil morphologic changes in diagnosing acute bacterial infections. Materials and Methods: Peripheral blood samples were obtained from 105 patients who had a positive culture for bacteria. Automated complete white blood cell count was performed as well as peripheral blood smear preparation. Absolute neutrophil count (ANC) and neutrophil band count were determined and the neutrophils were evaluated for morphologic changes, namely toxic granulation, vacuolation and Döhle bodies. **Results:** Band count was less sensitive than ANC and white blood cell count in predicting bacterial infections except in the elderly and infant population. Toxic granulation in neutrophils appeared to be as sensitive as ANC in predicting bacterial infection. Conclusion: ANC and toxic granulation appear to be more sensitive than band count in predicting bacterial infections. However, band count has a greater sensitivity in infants and elderly patients. Copyright © 2007 S. Karger AG, Basel

Introduction

Bacterial infections may be acute and life-threatening or chronic and relapsing. They may elicit noninflammatory, pyogenic, granulomatous or lymphohistocytic reactions. The most common tissue response, however, in acute inflammation is dominated by neutrophils. Although studies of other indicators of infection such as sedimentation rate and C-reactive protein have been conducted, they are less helpful than the total leukocyte count (WBC) in the acute care setting of the emergency department. In addition, the volume of blood required for these tests and the delay in obtaining results make these tests impractical. The WBC is presently the most readily available marker.

The relationship between acute infectious diseases and WBC, absolute neutrophil count (ANC) and increased number of band neutrophils has been recognized for many years. However, the efficacy of manual band count in predicting bacterial infections compared to the WBC and ANC is controversial. Some authors suggest that WBC and ANC are more reliable for the diagnosis of infection than a manual differential count [1–6], while others [7–9] found that the presence of a left shift shows a strong correlation with infection. The determination of band count is labor-intensive and the reproducibility is

highly dependent on the technique and training of the examiner.

This investigation was undertaken to better define the diagnostic values of ANC and total WBC for acute bacterial infections and whether or not the manual differential count (band cell count) is necessary. In addition, the value of neutrophil morphologic changes in diagnosing acute bacterial infection was evaluated.

Subjects and Methods

One hundred and five patients, 55 males and 50 females ranging in age from 2 days to 93 years, mean age of 34 years, with bacterial infections documented by culture, were studied. The patients were seen in King Khalid University Hospital, Riyadh, Saudi Arabia, and had one or more positive cultures for bacteria. Cases of severe neutropenia $<1.0\times10^9/l$ or acute leukemia were excluded.

Hematologic evaluation: peripheral blood samples were obtained within 24 h of the positive cultures. Samples were drawn into vacutainer tubes containing EDTA (1.2 mg/ml anticoagulant). WBC, neutrophil and 5-part differential count were obtained using automated analyzer (Coulter LH 755). The cut-off points for leukocytosis and neutrophilia were based on normal international institutional values adjusted for age. The cut-off for leukocytosis was $>9.6 \times 10^9$ /l. Peripheral blood smears were made and stained with Wright Giemsa stain for each specimen. Examination of white blood cells was performed by a magnification of 1,000. Two hundred white blood cells were counted and the band count estimated according to the criteria of the College of American Pathologists Survey Manual [10]. A cell was considered a band if there was a visible distinction between chromatin and parachromatin in the narrowest segment of the nucleus. A band count of 20% was considered an elevated count. The presence of reactive morphologic changes in neutrophils such as toxic granules, Döhle bodies and cytoplasmic vacuoles was also determined.

Results

Of the 105 patients, 22 were infants (<1 year) and 20 were elderly (>70 years). The total WBC count range was 2.9×10^9 /l to 50×10^9 /l with a mean of 11.4×10^9 /l. Cultures from various sites were positive for neutrophilevoking bacterial organisms (table 1).

The sensitivity for predicting a bacterial infection was best for ANC and neutrophil toxic granules followed by WBC, band cells, and Döhle bodies. Neutrophil vacuoles seem to be the least sensitive. However, in elderly patients, the band count seemed to be the most sensitive compared to WBC and ANC (tables 2–4).

Table 1. Source of infections and organisms cultured

Source	Positive cultures	Organisms with number of cases
Body fluids	23	Staphylococcus aureus: 2 Pseudomonas aeruginosa: 4 Klebsiella pneumoniae: 5 Streptococcus species: 1 Escherichia coli: 7 Enterobacter species: 1 Viridans streptococci: 1 Aeromonas species: 1 Streptococcus group D: 1
Blood	27	Bacteroides fragilis: 11 Staphylococcus aureus: 5 Pseudomonas aeruginosa: 3 Viridans streptococci: 1 Streptococcus group B: 1 Acinobacter species: 1 Streptococcus milleri: 1 Haemophilus influenzae: 1 Bacillus species: 1 Citrobacter species: 1 Enterobacter species: 1
Exudate	20	Staphylococcus aureus: 10 Pseudomonas aeruginosa: 3 Klebsiella pneumoniae: 1 Escherichia coli: 3 Acinobacter species: 1 Serratia species: 1 Streptococcus group A: 1
Respiratory	43	Staphylococcus aureus: 17 Pseudomonas aeruginosa: 13 Klebsiella pneumoniae: 3 Escherichia coli: 1 Enterobacter cloacae: 1 Stenotrophomonas maltophilia: 2 Acinobacter species: 1 Streptococcus group A: 1 Streptococcus pneumoniae: 1 Haemophilus influenzae: 2 Klebsiella pneumoniae: 1
Stool	1	Salmonella species: 1
Tissue	3	Staphylococcus aureus: 2 Klebsiella pneumoniae: 1
Throat	7	Staphylococcus aureus: 1 Pseudomonas aeruginosa: 1 Streptococcus group B: 2 Streptococcus group A: 2 Aeromonas species: 1

Table 2. Sensitivity of WBC, ANC, and band cells as predictors of bacterial infections

Parameter	Sensitivity, %			
	all patients	elderly patients	infants	severe infections
ANC >8.0 × 10^9 /l WBC count >9.6 × 10^9 /l Band cells >20%	48 36 32	45 35 50	55 41 50	67 56 52

Table 3. Sensitivity of morphologic changes in neutrophils as predictors of bacterial infections

Parameter	Sensitivity, %				
	all patients	elderly patients	infants	severe infections	
Toxic granulation	48	55	50	78	
Döhle bodies	32	50	10	50	
Vacuoles	22	20	27	37	

Table 4. Sensitivity of combined parameters in predicting bacterial infections

Parameters	Sensitivity, %
Elevated WBC + elevated ANC	49
Elevated WBC + elevated ANC + elevated band count	62
Elevated WBC + elevated ANC	
+ elevated band count + morphologic changes	80

Discussion

The relationships between acute bacterial infection, WBC, and ANC and increased number of band neutrophils have been recognized for many years. However, the diagnostic value of these WBC quantitative parameters, including elevated levels of bands as well as of qualitative parameters as indicators of acute bacterial infection are the subject of an ongoing debate. In the United States, some groups have even concluded that manual band counts are worthless in predicting bacterial infections [1–6]. The determination of band count

is labor-intensive and the reproducibility is highly dependent on the technique and training of the examiner. Some studies have recommended that total WBC and ANC should be monitored instead of the band count because these parameters yield more reproducible information [10, 11]. On the other hand, despite the technical difficulties associated with the neutrophil count, many laboratories and clinicians, especially in Europe, still continue to use peripheral blood smears as a diagnostic tool for evaluating acute bacterial infection [7–9].

Todd [11] has suggested that band count or ANC is more accurate than total WBC in predicting bacteremia. These findings were supported by Sabah et al. [12], who indicated that an elevated band count was of a higher diagnostic value in detecting acute bacterial infection than either total WBC or ANC. Ardan et al. [13] analyzed the clinical value of band cell count as a correlate to infection in patients who had culture-proved acute bacterial infection and normal WBC, and they found that an elevated band count had a sensitivity of 49%. Marchand et al. [14] also suggested that ANC and band cell count were more accurate than the total WBC in predicting bacteremia. However, Gombos et al. [15] demonstrated that band count is a poor indicator of occult bacteremia and does not add any predictive value, and that WBC and ANC are better indicators of bacteremia.

Our findings indicated that ANC was far more sensitive than WBC, while the latter showed similar sensitivity to that of band count (table 2). However, band cell count was more sensitive in the more vulnerable patient groups, namely infants and elderly patients, superseding WBC in these groups.

The utility of morphologic changes in neutrophils has also been debated. Liu et al. [16] described the usefulness of morphologic changes such as vacuolation and toxic granulation of neutrophils as a screening test for bacteremia in a febrile patient. In their study, the presence of toxic granulation and vacuolation was more predictive of bacteremia than WBC.

Sabah et al. [12] suggested that toxic signs in neutrophils were highly sensitive. Jafri and Cass [17] also demonstrated a high correlation between vacuolated neutrophils and culture-positive infections. Adams et al. [18] disagreed, demonstrating in their study that vacuolation of neutrophils was not sensitive for sepsis. Gombos et al. [15] supported the findings of Adams et al. [18], finding minimal vacuolation and toxic granulations in specimens from patients who had bacteremia.

Our findings indicated that the presence of toxic granulation in neutrophils is sensitive in detecting acute bacterial infection, especially in severe infections with 78% sensitivity, while vacuolation is not sensitive, and actually the presence of Döhle bodies is more sensitive than vacuolation.

Conclusion

Our findings indicate that ANC is more sensitive than band count in predicting acute bacterial infection and that the band count as a single parameter is of a limited diagnostic value. Morphologic changes in neutrophils were helpful, especially toxic granulation. However, a combination of more than one parameter helps increase the sensitivity of predicting acute bacterial infection.

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