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Original Research

Evaluation of 52 cases of children with neutropenia

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ABSTRACT:

Background: Neutrophils have an important role in host defense and acute inflammation. An absolute neutrophil count (ANC) below the normal level by age and race is defined as neutropenia. Neutropenia is not uncommon in childhood. The present study evaluated cases of neutropenia and fever in children. **Materials & Methods:** Fifty two consecutive children with neutropenia were enrolled in this study. Clinical and laboratory features were analyzed. **Results:** Age group 10-12 years had 7 boys and 4 girls, 12-14 years had 10 boys and 5 girls and 14-16 years had 15 boys and 6 girls. The main cause of neutropenia was bacterial in 27, viral in 10, fungal in 8, drugs in 4 and autoimmune in 3 cases. The difference was significant (P< 0.05). Out of 104 patients, 46 survived and 8 died. The difference was significant (P< 0.05). **Conclusion:** There is great etiological heterogeneity of neutropenia in children. Authors found that maximum cases were seen in boys and age group 14-16 years. Neutropenia remains a disease of concern to pediatricians, requiring several laboratory investigations, prolonged follow-up, and, in few cases, advanced molecular methods.

Key words: Acute neutropenia, children, fever.

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INTRODUCTION

Neutropenia, defined by an absolute neutrophil count (ANC) <1 9 109/l in infants and <1.5 9 109/l thereafter, is not uncommon in pediatric patients.[1] Among black populations, lower cutoff values must be considered, because their circulating neutrophils are physiologically reduced.[2,3] Neutropenia can be defined as acute or chronic depending on its duration, lower or higher than 3 or 6 months according to different authors. The severity of neutropenia depends on the ANC: For patients older than 1 yr of age, neutropenia is defined mild with an ANC between 1 and 1.5 9 109/l, moderate with an ANC between 0.5 and 1 9 109/l, and severe when ANC is below 0.5 9 109/l. It is widely accepted that infective diathesis, in terms of frequency and severity of infections, is proportional to the degree of neutropenia. Nevertheless, a lot of children with moderate–severe isolated neutropenia have a benign course, meaning that other factors may influence susceptibility to infection, such as the speed of onset and the duration of neutropenia, the bone marrow myeloid reserves, the absolute circulating monocyte count, and the functional status of phagocytes Despite a considerable reduction over the past decades in infection-related mortality in patients with cancers who present with fever and neutropenia (FN), infections remain a major cause of morbidity and mortality in this susceptible population. The strategy of using empiric antibiotics has greatly influenced the outcome of fever in a neutropenic host.[3]

It is important to note that blood neutrophil counts are not as stable as other blood cell counts or many other physiological measurements. Counts may vary considerably over short periods of time, associated with activity, exercise, eating or just the time of day. Counts vary even more with serious infections, inflammatory disorders, corticosteroid therapy or extreme anxiety.[4] It is always important in the evaluation of blood neutrophil counts to consider the conditions when the blood sample was obtained and to have several measurements when defining the severity of acute or chronic neutropenia. Neutropenia can be described as transient (or “acute”) or chronic (or “persistent”); extrinsic or intrinsic; by descriptive names (e.g., neonatal isoimmune neutropenia of infancy, cyclic neutropenia, severe congenital neutropenia) and as syndromes (e.g., Kostmann,

Shwachman-Diamond, and Barth syndromes). The discovery of the diverse causes for the congenital neutropenias now permits genetic diagnosis in many cases.[5] The present study evaluated cases of neutropenia and fever in children.

MATERIALS & METHODS

The present study comprised of 52 children confirmed case of fever and neutropenia of both genders. Fever was defined as a single oral temperature of ≥ 38.3 °C or an oral temperature of ≥ 38.0 °C that persists for over one hour. Neutropenia was defined as an ANC ≤ 500 cells/mm3. All were included in the study after obtaining their written consent.

Data such as name, age, gender etc. was recorded. A thorough clinical examination was performed. Duration of fever, days of hospitalization and mortality rate was recorded. Results of the study was compiled and entered in MS sheet for statistical analysis. Chi- square test and Mann Whitney U test was used for analysis. P value less than 0.05 was considered significant.

RESULTS

Table I Distribution of patients

Age group (Years)	Boys	Girls
10-12	7	4
12-14	10	5
14-16	15	6

Table I shows that age group 10-12 years had 7 boys and 4 girls, 12-14 years had 10 boys and 5 girls and 14-16 years had 15 boys and 6 girls.

Table II Causes of neutropenia in children

Causes	Number	P value
Bacterial	27	0.025
Viral	10	
Fungal	8	
Drugs	4	
Autoimmune	3	

Table II, shows that main cause of neutropenia was bacterial in 27, viral in 10, fungal in 8, drugs in 4 and autoimmune in 3 cases. The difference was significant (P< 0.05).

Table III Outcome of cases

Outcome	Number	P value
Live	46	0.02
Death	8	

Table III shows that out of 52 patients, 46 survived and 8 died. The difference was significant (P< 0.05).

DISCUSSION

The widespread use of routine biochemical assay has led to increased findings of neutropenia in pediatric practice. A special feature is that neutropenia is in fact a laboratory data, before representing a disease itself, and its origin and significance are extremely variable. Neutropenia may represent a predisposing factor to severe and life-threatening infections, as it is well known for patients with malignancies, but it can even be diagnosed incidentally in asymptomatic children, as complete blood count (CBC) is widely performed in outpatient settings.

The differential diagnosis for a fever of unknown origin is expansive, but it can be classified into 4 major categories related to underlying etiology: 1) infection; 2) autoimmune/ connective tissue disease; 3) malignancy; and 4) allergic/reactive. Other and less common etiologies including granulomatous and congenital diseases can also be considered.[6] Infections represent the most common causes of fever, although the likelihood of a specific agent varies across geographic location, exposure history, and inherent patient characteristics including age, gender, and race. Autoimmune and connective tissue diseases such as systemic lupus erythematous and vasculitis are also commonly encountered causes of fever. Among the malignancies, lymphoma, in particular non-Hodgkin lymphoma.[7] The present study evaluated cases of neutropenia and fever in children.

In present study, age group 10-12 years had 7 boys and 4 girls, 12-14 years had 10 boys and 5 girls and 14-16 years had 15 boys and 6 girls. Dubey et al[8] in their study out of 56 patients, males were 30 and females were 26. Etiology of fever was bacteremia in 25, viral URI in 13, GI infection in 4, pneumonia in 7, fungal infection in 4 and others in 3. The difference was significant (P< 0.05). The mean duration of fever in males was 1.5 days and in females was 1.8 days, duration of hospitalization in males was 4.2 days and in females was 3.7 days, mortality within 2 weeks in males was 5 and in females was 2. The difference was significant (P< 0.05).

We observed that main cause of neutropenia was bacterial in 27, viral in 10, fungal in 8, drugs in 4 and

autoimmune in 3 cases. Out of 52 patients, 46 survived and 8 died. Ren et al[9] reported a case in a 22-year-old African-American male with chief complaint of episodic fever. Patient has experienced episodic fevers regularly for the past 6 months. Initially, the fevers occurred 4-6 weeks apart but have been increasing in frequency in the past 2 months. Each episode reportedly lasts about 3 days, with the fever peaking around 103°F. The fever is accompanied by muscle pain and occasionally sore throat, chills, and night sweats. There is no associated nausea, vomiting, or lymphadenopathy. During the previous 3 weeks, the patient reported a decreased appetite and an unintended weight loss of 10-20 pounds. The fevers typically resolved with acetaminophen, and the patient recently completed several courses of amoxicillin.

As suggested by the consensus guidelines on diagnosis from the Neutropenia Committee of the Marrow Failure Syndrome Group of the AIEOP, considering that chronic idiopathic neutropenia is an disorder of granulopoiesis characterized by prolonged neutropenia in the absence of any apparent underlying etiology, CIN patients should be placed on a monitoring program, and a diagnostic revaluation should be performed in case new elements suggestive of other diagnosis arise. In the future, the differential diagnosis of chronic idiopathic neutropenia will include a broad spectrum of genes, including recently identified genes. New approaches based on next-generation sequencing will eventually be adopted on a wider basis to facilitate the diagnosis of these patients. This will require an extensive validation of these new techniques and careful evaluation of the cost-benefit of this approach.

Chronic autoimmune neutropenia of infancy and early childhood is a relatively common disorder and virtually always runs a benign course, despite very low ANCs. It usually resolves spontaneously by age 3–5 years, with a mean duration of 17 months. In most cases, neutropenia is detected during the occurrence of an acute febrile illness.[10] With follow-up, the neutropenia persists after resolution of the illness that led to testing. Systematic studies indicate that many, but not all, of these children have autoantibodies directed against surface antigens of neutrophils. From a clinical perspective the value of testing for autoantibodies in patients with moderate to severe neutropenia without evidence of recurrent fevers or infections is debatable.[11] Testing is not widely available and, if done, it is best performed by a reference laboratory performing these assays frequently. Serial testing may give inconsistent results and patients with genetic as well as acquired neutropenia may have false positive test results.[12]

Griffin et al[13] found that out of 337 FN episodes, infection was proven in 86 (25%) and probable in 75 (22%). 177 episodes (53%) were judged fever of unknown origin (FUO). Bacteremia accounted for most (41) of the proven bacterial episodes, with viridans streptococci (13), Pseudomonas spp (6) and E. coli (6) the most frequently isolated organisms. The median time to positivity of blood cultures was 12 hrs (range 5.4 – 143.7) with 93% positive within 24 hours of incubation. Viral pathogens were identified in 29 (34%) episodes. Compared to other patients, those with FUO had shorter median duration of fever.

In older children, chronic autoimmune neutropenia or multiple immune cytopenias should raise suspicion of a congenital immunological disorder such as autoimmune lymphoproliferative syndrome or common variable immunodeficiency.[14] Screening for these disorders can be performed by measurement of circulating T cell receptor alpha/beta positive, CD4/CD8 double negative T cells or of serum immunoglobulins, respectively. Definitive diagnosis of these conditions requires specialized immunological testing.[15]

CONCLUSION

There is great etiological heterogeneity of neutropenia in children. Authors found that maximum cases were seen in boys and age group 14-16 years. Neutropenia remains a disease of concern to pediatricians, requiring several laboratory investigations, prolonged follow-up, and, in few cases, advanced molecular methods.

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