

Chronic granulomatous disease in Sohag university hospital: Case series

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Abstract

Introduction: Chronic granulomatous disease (CGD) is a rare inherited immunodeficiency disorder with an incidence of 4-5 per 1 million individuals. It is caused by mutation in 5 genes, *CYBA*, *CYBB*, *NCF1*, *NCF2*, or *NCF4* genes, *CYBB* inherited as X-linked while other 4 genes inherited as autosomal recessive. CGD is characterized by neutrophils and monocytes capable of normal chemotaxis, ingestion and degranulation, but unable to kill catalase-positive microorganisms due to defects in one of the 5 major subunits of NADPH oxidase.

Method: The medical records of patients diagnosed with CGD within 1 year from August 2017 to July 2018 were reviewed and analyzed with respect to demographic data, age at presentation and diagnosis, clinical features, laboratory investigations, organisms isolated and treatment & prophylaxis given.

Aim: Increase awareness of pediatric physicians in Sohag government about CGD for early diagnosis and early management.

Results: 15 patients were diagnosed with CGD in the period of the study with failure to thrive and lymphadenopathy were the common presentation of them.

Introduction

Chronic Granulomatous Disease (CGD) was described for the first time by both B.H. Landis and R.A. Good in 1957 (1). CGD comprises a rare group of genetically determined changes affecting the immune system characterized by the inability of the body's phagocytic cells (neutrophil and monocyte/granulocytes) to kill certain phagocytosed microorganisms (2). This phagocytic cell defect is caused by mutations in the gene coding for the NADPH oxidase enzyme essential for the microbicidal activity of phagocytic cells (2). The disease affects an average of one in every 250,000 live births. Affected children are subject to frequent severe bacterial and fungal infections with the granulomatous hallmark of inflammatory lesions in histological specimens from which the name CGD derives. Patients with CGD

usually present in infancy or childhood with repeated, severe bacterial and/or fungal infections. However, delayed diagnosis in adulthood is also possible (3). The most common manifestations include infection, granulomatous disease, inflammation, and failure to thrive (nutritional effects of chronic infection and inflammation). The disease is heterogeneous in its manifestations, related to the subtypes, and severity of the associated macrophage defect (4). In the majority of patients, the production of superoxides is undetectable and the manifestations are therefore early and predictable to a great extent. In others, low level respiratory burst activity may delay manifestations or diagnosis into early adulthood (5). Most patients present with infectious illness, which include sinopulmonary disease,

abscesses, or lymphadenitis. Other manifestations are related more to inflammatory consequences and/or structural disease and resultant organ dysfunction. As there is a paucity of

data on CGD from developing countries, we aim to study the clinical profile, microbiological spectrum in children diagnosed with CGD in a tertiary care hospital over a span of 1years(6).

Results

Our study had 9 males and 6 females with 11(73.3%) having history of consanguinity. Their mean age at presentation and diagnosis was 2.25 years and 3.89 years respectively. Failure to thrive was present in 9 cases (60%), lymphadenopathy in 9 cases (60 %) followed by hepatomegaly 6 cases (40 %) and splenomegaly in 4 cases (26.6 %). Multiple infections were present in the same patient with the commonest infection was abscesses 11 cases (73.3%) involving lungs, liver, subcutaneous tissue and brain followed by pneumonia 8 cases (53.3 %) followed by lymphadenitis in 7 cases (46.6 %) , and osteomyelitis 6 cases (40 %)

Organisms isolated from blood, stool and pus of infected lesions included **bacteria**- Staphylococci 6 cases (40 %), Mycobacterium tuberculosis 3 cases (20 %), Klebsiella 1 case (6.6%) and atypical mycobacterium 1 case (6.6 %) and **fungi**- Aspergillus 3 cases (20 %), Candida 1(6.6 %). Diagnosis was based on reduced nitroblue tetrazolium test (NBT) between 0-5 % in all patients and confirmed by dihydrorhodamine (DHR) assay in 100 % patients. Complete blood count in all patients showed leucocytosis with marked neutrophilia. Also we excluded other common types of primary immune deficiency in all our cases by normal immunoglobulin levels and normal CD markers for T and B lymphocytes. All patients received the needed treatment of the current infection but no one received gamma interferon as it is not available in Egypt, 3 cases are under preparation for BM transplantation and all received antifungal and antibacterial prophylaxis. 4 patients are lost to follow-up. Genetic mutation analysis has been done in the 3 patients prepared for BMT

Conclusion

CGD is one of the primary immune deficiency disorders caused by defect in phagocytic function common present in Upper Egypt due to high consanguineous rate. The commonest mode of presentation was skin and subcutaneous abscesses, Pneumonia, lymphadenitis and osteomyelitis. Staphylococcus Aureus, Mycobacteria TB, Klebsiella, Atypical mycobacterium were the commonest bacteria with Aspergillus and candida were the commonest isolated fungi in our series. All cases showed leucocytosis and positive NBT test and DHR test. All children with

CGD should be given routine chemoprophylaxis with trimethoprim-sulfamethoxazole and Itraconazole. Families should be screened and counseled during future conceptions.

References

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