Case Study

Chronic Granulomatous Disease presenting first time in newborn period as neonatal sepsis due to Staphylococcus Aureus infection: A rare presentation.

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ABSTRACT

Chronic Granulomatous Disease is characterized by defective intracellular bacterial and fungal killing in neutrophils and monocytes. It is caused by defects in NADPH oxidase, the enzyme complex responsible for generating the phagocyte respiratory burst. Catalase positive organisms can cause severe deep-seated infections. The most common types of infections are skin abscesses, pneumonia, lymphadenitis, liver abscess, and osteomyelitis. We report a newborn with CGD, who presented with recurrent staph aureus infections. The case reminds the importance of early suspicion of immunodeficiency in a newborn with recurrent staph infections.

Key words: Chronic Granulomatous Disease, Phagocyte, Skin pustules

INTRODUCTION

Chronic granulomatous disease (CGD) is an inherited and genetically heterogeneous immunodeficiency disorder resulting from defects of one of the subunits of the nicotinamide adenine dinucleotide phosphate (NADPH) oxidase enzyme complex in phagocytic cells [1]. It is a rare disease affecting between 1 in 2, 00,000 and 1 in 2, 50,000 live births [1]. The NADPH oxidase complex catalyzes the conversion of molecular oxygen O2 to superoxide anion (O2-) and other reactive oxygen intermediates. Therefore, defects in any of the components of the NADPH oxidase complex results in impaired killing of intracellular microorganisms and renders patients with CGD susceptible to recurrent and often life threatening infections with bacteria and fungi.

CASE REPORT:

21 days old male baby, first in birth order born to non-consanguineous parents by institutional NVD with birth weight of 2.8 kg. There was no significant antenatal history. He was exclusively breast fed with no significant postnatal history. He was admitted with multiple boils over the body since 8 days, low grade fever since 7 days, and decreased oral feed since 1 day. There was no history of any persisting vomiting, jaundice and abnormal body movements. At admission, baby was febrile, 102°F with signs of respiratory distress RR= 64/min. On general physical examination there were multiple pustular lesions present over face , trunk and back and ruptured pustule over lower back, with pus discharge **[Figure 1]**. The respiratory system examination had bilateral crepitations,rest of the systemic examination did not reveal any abnormal finding. At admission his Hb was 13.7, ,TLC 21300 (75% polymorphs, 16% Lymphocytes, monocytes 4, eosinophil 3, basophils 2), Platelet 4.05 s. CRP was positive and other investigations including renal, liver function tests and electrolytes were normal. Blood and pus cultures grewstaph aureus with sensitivity to Amoxiclavulanicacid and amikacin. Provisional diagnosis of neonatal sepsis with pneumonia multiple abscesses was kept to rule out immunodeficiency. The baby was started on IV antibiotics Amoxiclavulanic acid and amikacin. His CSF examination was normal. After treatment oral acceptance and activity improved and skin lesions started healing. On D6 of admission- new abscesses developed over back and scalp and fever reappeared. Repeat blood Culture grown methicillin sensitive staph aureus , Sensitive to cefotaxime, vancomycin and antibiotics changed accordingly. Fever spikes decreased and became afebrile from day 8 of admission. He received total 3 weeks ofIV antibiotics and finally discharged. Maternal retroviral status was non-reactive. Primary immunodeficiency work-up planned and was discharged. His second admission was at 2 months of age with c/o cough, fever and

lethargy since 2 days. He had evidence of respiratory distress and bilateral crepitations in chest . Investigations revealed Hb 9.1 gm/dl, TLC14200 (P50/L45, m5), Platelets 6lacs ESR 35.CXR showed Lt sided pneumatocele. He was treated in lines of sepsis with bronchopneumonia with left sided pneumatocele**.** Blood culture grown staph aureus and was started on IV antibiotics piperacillin-tazobactam/ vancomycin as per sensitivity. Received parenteral antibiotics for 3weeks was discharged on oral antibiotics. Immunodeficiency work up was done in view of recurrent staph infections, which revealed normal Immunoglobulin level normal for age, normal T- cell markers and Neutrophil oxidative index by dihyrorhodamine was reduced as compared to control which led us to the diagnosis of chronic granulomatous disease. Child was started on daily oral trimethoprim-sulphmethoxazole and itraconazole prophylaxis. Baby is on regular follow-up and doing well. Genetic study for X linked gene CYBB gene was planned.

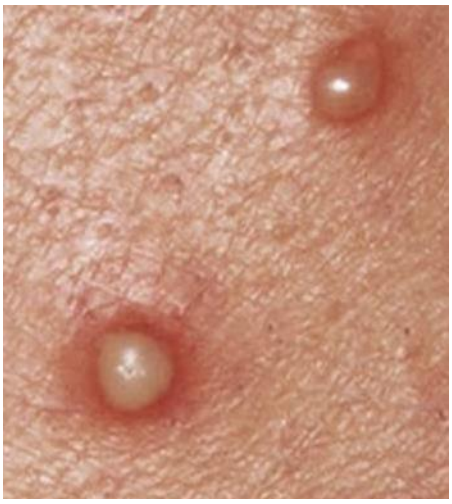

FIGURE 1: Showing multiple pustules over skin

DISCUSSION:

Chronic granulomatous disease is caused by inherited defect in the immune system involving phagocytosis. It is a genetically heterogeneous disease due to defects in one of the five major subunits of the nicotinamide adenine dinucleotide phosphate (NADPH) oxidase complex. An abnormal granulocyte oxidative burst evaluated by either Nitroblue Tetrazolium (NBT) test or flow cytometry based Dihyrorhodamine 123 assay is used for diagnosis of CGD. Genetic mutation analysis is used for confirming the molecular diagnosis. The actual incidence is likely to be higher due to underdiagnosis of patients presenting with milder disease phenotype. CGD was initially described in 1954 [2] and 1957 [3], but it was not well characterized as a distinct clinical entity until 1959 [4]. The defects in any of the components of the NADPH oxidase complex results in impaired killing of intracellular microorganisms and make the patients with CGD susceptible to recurrent and often life threatening infections with bacteria and fungi. X-linked recessive form of the disease due to mutations in the CYBB gene encoding for gp91phox accounts for approximately 65 % of the patients with CGD [5]. Mutations in the NCF1 gene encoding for the p47phox account for 30%of the cases whereas CYBA andNCF2 mutations are detected in <5% patients each. Only one patient with mutation in NCF4 has been reported thus far [5]. The risk of mortality in CGD is estimated to be 1–5 % annually and is likely dependent on the mode of inheritance i.e. X-linked or AR[6]. There is a paucity of data on chronic granulomatous disease from developing countries although large series have been published from Europe and USA [6–9]. All the presently known mutations in the CYBB gene have been reported in a large series recently [10]. All patients are managed on cotrimoxazole and itraconazole prophylaxis along with management of breakthrough infections. Severity of infection is higher in developing world probably because of increased exposure to infectious agents leading to higher incidence of infections with increased severity. So the higher frequency as well as increased severity of breakthrough infections compared to developed world could have contributed to the increased mortality. Delay in initiating therapy for intercurrent infections due to the parents having to travel long distances to reach medical facilities and poor economic conditions are likely to have contributed significantly to this higher mortality. The index of

suspicion for diagnosis of primary immunodeficiency should be kept in a newborn with sepsis with recurrent staph infections. Our case was different from existing reports because patient presented early in neonatal period and skin lesions led to the diagnosis. So multiple pustules in a new-born with sepsis with documented evidence of staph infection should prompt the work –up for chronic granulomatous disease.

In conclusion, it is possible to provide a reasonable quality of life to patients with prophylactic antimicrobials even in a developing country with all its constraints.

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