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Case Study

A Case Report on X-Linked Chronic Granulomatous Disease (CGD)

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ABSTRACT

The Chronic Granulomatous Disease is a rare primary immunodeficiency disease, principally attacking white blood cells, characterized by an increased susceptibility to the recurrent bacterial and fungal infections along with the genesis of granulomas in tissue. Staphylococcus and aspergillosis are the main pathogens responsible for majority of infections in CGD. Here we report a case of 5yrs old boy who came with the complaints of fever, cough, and multiple abscess over the right leg, right ankle and left hand with puss discharge. DHR test was performed and have shown the positive results for chronic granulomatous disease.

1. Introduction

Chronic granulomatous disease (CGD) is a genetic disorder of immune system that fails to destroy certain invading bacteria and fungi due to the defect in phagocytic cells to produce reactive oxygen species. The pathology under phagocytic cell defect is mutations in any one of the four genes encoding for the phagocyte NADPH oxidase, the enzyme that generates oxygen radicals which is essential for microcidal activity[1].

Mutation in the CYBB gene which encodes for gp 91-phox component is responsible for x-linked CGD[2]. Mutations in the CYBA, NCF1 and NCF2 which encodes for p22-phox, p47-phox, p67-phox respectively is responsible for autosomal recessive CGD[3]. There is a male to female ratio of seven to one reflecting the predominance of X-linked CGD over autosomal recessive CGD[4].

The hallmarks of CGD are recurrent infections at epithelial surfaces such as skin, lungs and gut as well as formation of granulomas in tissues[5].

Diagnosis of CGD can be confirmed by establishing the impaired granulocyte activity by using any one of the following tests like Nitro blue tetrazolium test under normal conditions NBT is reduced to formazan, a dark blue insoluble reagent precipitated in phagocytic cells. In CGD patients NBT is not reduced to formazan due to inability of superoxide formation.

Flow cytometric analysis, in these tests DHR is used as fluorescence marker to know the activity of NADPH. Most of times these tests have replaced NBT as it is very sensitive method and its ability to distinguish X-linked CGD from autosomal recessive CGD.

Cytochrome C, when these are reduced, a different light absorbance spectrum can be obtained which can be measured spectrophotometrically. These types of reduction can't be seen in CGD.

Genetic testing is important to know the presence of specific mutations[6].

The mainstay of treatment in CGD involves the prophylactic therapy with antibacterials and antifungals. Daily doses of sulfa-methoxazole and itracanazole are recommended. Interferon gamma, which is natural product of immune system, three times weekly is recommended to boost immunity. For the stable remission of CGD, Stem cell transplantation is recommended[4].

2. Case Presentation

A 5 years boy was brought to Clinic, with the complaints of fever, cough, and multiple abscesses over the right leg, right ankle, and left hand with pus discharge. Similar complaints were seen at 3 years of his age. The child was

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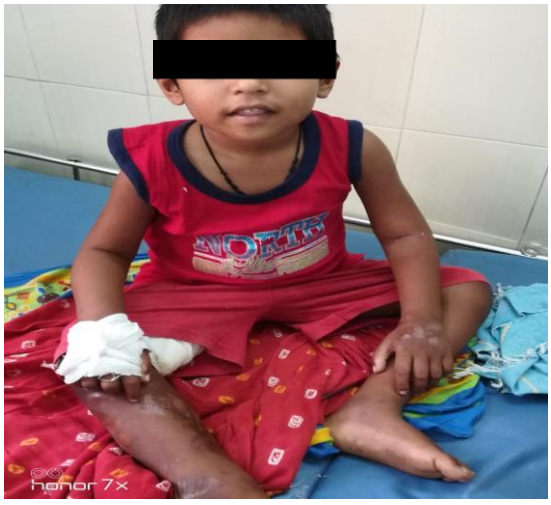
asymptomatic till 3 months of life, then developed pneumonia for which he was ventilated for 5 days. Child has recurrent episodes of LRTI for which IV antibiotics were prescribed. There were no similar complaints in family relating to immune deficiency. Child was immunized as per age profile but has delayed milestones. Immunological studies show normal concentrations of IgA-192 (100-490), IgM-90 (50-320) with mild decrease of IgG-797 (800-1700). Complete blood picture reveals microcytic hypochromic anaemia. Antibiotic sensitivity test was done, and child was found to be sensitive to levofloxacin, imipenem and meropenem.



Erythrocyte sedimentation rate is high in the 1st hour-48 mm and 2nd hour-90 mm. Lymphocyte subset assay was performed and found that all values were within normal range of CD4+T Helpercells-37.1 % (28-47 %), CD3+Tcells-58.3 % (56-75%), CD19+Bcells-33.2 % (14-33 %), CD16& CD56+(NKcells)-6.6 % (4-18 %) except CD8+ Tsupressor-10.7 % (16-30 %), CD4+CD8 ratio-3.47 (1.26-2.90). DHR assay was performed and the results was abnormal indicating low stimulation index (SI)-2.35 (180). But further genetic studies are needed to confirm the type of CGD. Genetic testing was done and found mutations in CYBB gene and confirmed the diagnosis of X-linked CGD. Treatment given was Inj Metrogyl 25 ml IV TID, Inj Meropenem 250 mg IV TID, Inj Vancomycin 210 mg in 100 ml NS TID for 21 days and Inj Augmentin 700 mg IV BD for 4 days.

3. Results and Discussion

Chronic granulomatous disease was first described in 1957 as recurrent infections occurring in setting of hypogamma-globulinemia[7]. Chronic granulomatous disease is characterized by severe, recurrent and often fatal infections which results from defects in NADPH oxidase system to produce superoxide in patient phagocytes[8].The common infections in CGD are pneumonia, lymphadenitis, liverabsess, osteomyelitis, skin abscesses, granulomas typically involving genitourinary system and gastrointestinal system[9]. In CGD as most mutations takes place in X-linked gene, affected individuals are mostly male. Pneumonia is most common type of infection encountered in CGD[10]. In our case child has reported pneumonia at 3 months of age. Cytochrome reduction assay & Nitro blue tetrazolium test measures superoxide activity whereas DHR123 assay and amplex red assay test measures hydrogen peroxide[11]. In our case diagnosis was confirmed by DHR123. Prophylactic use of antibiotics, antifungals, interferon gamma has improved prognosis but still CGD is associated with increased morbidity and mortality from life threatening infections. Haematopoietic stem cell transplantation remains prominent cure of disease, but difficulty in finding suitable donors and associated risks with the procedure have limited its use[12]. In recent years gene therapy has been proposed as alternative to stem cell transplantation for CGD patients .Use of regulated SIN-lentiviral vectors targeting gp91 (phox) in in myeloid cells to increase safety and efficacy of GT protocols has proposed but still research need to be done[13].

4. Conclusion

Sound knowledge about primary immune-deficiencies should be present among health care practitioners for differential diagnosis of chronic granulomatous disease and application of test at proper time would help in timely diagnosis of disease.

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Conflict of Interest

The author(s) confirm that this article content has no conflict of interest.

References

1. Heyworth PG, Curnutte JT (2003). Chronic granulomatous disease. Curr. Opin. Immunol. 15(5): 578-84.
2. Rae J, Newburger PE, Dinaver MC, Noack D, Hopkins PJ, Kuruto R (1998). X-linked Chronic granulomatous disease: mutations in the CYBB gene encoding the gp91-phox component of respiratory-burst Oxidase. Am. J. Hum. Genet. 62(6): 1320-31.
3. Noack D, Rae J, Cross AR, Ellis BA, Newburger PE, Curnutte JT (2001). Autosomal recessive Chronic granulomatous disease caused by defect in NCF-1, the gene coding the phagocyte p4phox:mutations not arising in the NCF-1 pseudogenes. Blood. 97(1): 305-11.
4. Newburger PE, Cohen HJ, Rothchild SB, Hobbing JC (1979). Prenatal Diagnosis of Chronic Granulomatous Disease. N. Engl. J. Med. 300: 178-81.
5. Gold blatt D, Thrasher AJ (2000). Chronic granulomatous disease. Clin. Exp. Immunol. 122(1): 1-9.
6. Holland SM (2013). Chronic Granulomatous Disease. Hematol. Oncol. Clin. N. Am. 27: 89-99.
7. Segal AW (1996). The NADPH oxidase and chronic granulomatous disease. Mol. Medicine Today. 2(3): 129-35.
8. Bortolttu P, Lyman K, Katz BZ (2015). Chronic granulomatous disease. Paed.. Infect. Dis. J. 34(10): 1110-4.
9. Yu JE, Azar AE, Chong HJ, Jongco AM, Prince BT (2018). Considerations in the Diagnosis of Chronic Granulomatous Disease. J. Paed. Inf. Dis. Soc. 7: 6-11.

10. Dirk Ross (2016). Chronic granulomatous disease. British Medical Bulletin. 118:53-66
11. Kume A, Dinaver MC (2000). Gene therapy for chronic granulomatous disease. J. Lab. Clin. Lab. 135(2): 122-28.
12. Chiriaco M (2016). CGD clinical, molecular and therapeutics aspects. Pediatr. Allergy Immunol. 27(3): 242-53
13. Togha M, Sahraian MA, Hosseini SJ, Haddadi A (2012). Brain tuberculoma: Report of a case presented with prolonged nonspecific symptoms and multiple brain tuberculoma. Iranian journal of neurology. 11(1): 34.
14. Saleh M, Saeedi AA, Pooran AA (2014). Brain tuberculomas: a case report. Jundishapur J. Microbiol. 7(7).
15. Rali P, Arshad H, Bihler E (2016). A case of tuberculous meningitis with tuberculoma in nonimmune-compromised immigrant. Case reports in pulmonology..
16. Pinto DS, Joseph T, George A, Hoisala RV (2016). A case report of racemose pattern of intracranial tuberculoma with brain stem and hypophyseal involvement developing paradoxically during treatment. BJR case reports. 1:20160034.
17. Dubey S, BIndira D, Jawalkar VK, Bhat DI (2002). Tuberculoma en plaque: a case report. Neurol. India. 50(4): 497.
18. Udani PM, Parekh UC, Dastur DK (1971). Neurological and related syndromes in CNS tuberculosis clinical features and pathogenesis. Journal of the neurological sciences. 14(3):341-57.