International Journal of Contemporary Pediatrics
*Sahoo MR et al. Int J Contemp Pediatr. 2021 May;8(5):946-949*
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20211694

**Case Report**

# A chronic granulomatous disease masked by tuberculosis in an young infant

**Manas Ranjan Sahoo*, Sunil Nath Jondhale, Anil Kumar Goel**

Department of Pediatrics, All India Institute of Medical Sciences, Raipur, Chhattisgarh, India

**Received:** 03 March 2021
**Accepted:** 31 March 2021

***Correspondence:**
Dr. Manas Ranjan Sahoo,
E-mail: drmrsahoo@gmail.com



## ABSTRACT

Chronic granulomatous disorder is a rare primary immunodeficiency disorder with phagocytic defect resulting in recurrent bacterial infections. Here we report a 2-year 2-month old male child, who presented with recurrent lymphadenitis and recurrent pneumonia since early infancy. In recent episode he presented with right cervical lymphadenopathy. Biopsy of lymph node revealed confluent necrotizing epithelioid cell granulomas and occasional giant cells but without evidence of tuberculosis and atypical organisms. His dihydrorhodamine 1,2,3 assay (DHR) was positive. Later he responded to prolonged parenteral antibiotics and discharged on itraconazole and trimethoprim-sulhamethaxazole prophylaxis. Here we are going to report a rare case of chronic granulomatous disease whose diagnosis was masked by tuberculosis

**Keywords:** Chronic granulomatous disease, Dihydrorhodamine assay, Recurrent pneumonia

## INTRODUCTION

Chronic Granulomatous Disease (CGD) is a congenital primary immunodeficiency disorder causing recurrent bacterial and fungal infection with inflammation and granuloma formation.[1,2] Basically it occurs due to inability of phagocytic NADPH oxidase system to produce superoxide resulting in failure of phagocytic killing of catalase positive organisms and accumulation of intracellular debris. Mostly this disease is diagnosed at early infancy and most common presentation is pneumonia.It is a rare X-linked or autosomal recessive disorder with male preponderance. The laboratory diagnosis of this disorder is by Dihydrorhodamine assay and genetic test. We report a 2-year 2-months old child with this rare disorder.

## CASE REPORT

This is a 2year 2month old male child with history of multiple admission in the past since 1year age. He was 3rd order male child born out of non-sanguineous marriage and developmentally normal child. His 2nd order brother died at age of 13 months due to pneumonia. His eldest sister is healthy. Tracing back to his history, he was diagnosed to have tubercular lymphadenopathy over right submandibular region at 1 year of age. After initiation of anti-tubercular treatment, the swelling subsided gradually. Following 3 months of treatment of tubercular lymphadenopathy, child admitted with non-resolving pneumonia for which he underwent CECT which was suggestive of consolidation involving right upper lobe, superior segment of lower lobe and apico-posterior segment of upper lobe. There were multiple well defined variable sized centrilobular and subpleural nodules scattered both lung parenchyma, some of these were showing tree in bud pattern. CECT guided biopsy was suggestive of necrotising granulomatous inflammation

consistent with Tuberculosis. Urine examination showed growth of hyphae. He was diagnosed to be progressive pulmonary tuberculosis with fungal Urinary tract

infection. He received prolonged parenteral antibiotics like ceftriaxone, meropenem, clindamycin, anti-tubercular treatment and antifungal amphotericin B during hospital stay of one month. After 3 months, child required hospital admission for mainly fever and oral ulcer. In view of persistent radiological findings, he was put on extension of continuation phase of ATT of 3 months. After 14 days he was once again admitted with pneumonia, so he was investigated for recurrent pneumonia. Repeat CECT suggested of multiple variable sized randomly scattered nodules in bilateral lung parenchyma with mediastinal lymphadenopathy with patchy areas of consolidation in bilateral upper lobe, right middle lobe and lower lobe. In this admission immunodeficiency, HIV, MDR TB, Asperigilloma, cystic fibrosis, malignancy possibilities were kept. His HIV test was negative.

Repeat TB work up by CBNAAT of BAL came negative. Allergen test for aspergillus fumigatus was negative. Immunodeficiency was suspected and Ig level-IgA-1.97, IgG-27.6, IgM-1.86, IgE-42(normal), flowcytometry for NK cells, T cells, B cells done. Flow-cytometry was reported asNK cells (CD3-/CD 16 +56): 3% (141-absolute) decreased, B-cells (CD19) and T-cells (CD3, CD4, CD8): normal. Peripheral Blood Smear was done for blast cells and it came to be normal. Child received piperacillin-tazobactam and ampiclox for 10 days and discharged in afebrile state with diagnosis of immunodeficiency cystic fibrosis.

Once again in his latest presentation, he presented with fever and left submandibular lymphadenopathy for 15 days, on examination it was around 3×4 cm, firm consistency, non-tender, no erythema, no local rise of temperature. His vitals were stable. His weight was 8.6 kg, height: 82 cm (between -2 to -3 SD), his MUAC: was 11.5 cm, so he was having moderate acute malnutrition. On system examination it was within normal limit. This time his blood investigations were as Hb 7.4, MCV 74.4, MCH 23.6, MCHC 31.8, RDW 15.2, TLC 16.7 DLC- neutrophil 60, lymphocyte 37, monocytes 3, eosinophil 0, basophil 00, absolute leukocyte count-8500, absolute neutrophil count 8.8, absolute lymphocyte count 6200, platelet count 540, ESR 150 and blood c/s was sterile. Histological examination of submandibular lymph node showed confluent necrotizing epitheloid cell granulomas and occasional giant cells noted which was consistent with necrotizing granulomatous lymphadenitis and CBNAAT of biopsy specimen was negative. USG abdomen was normal. Serum calcium and ACE levels were normal, which ruled out sarcoidosis. Brucella Ig M antibody (2.79) and IgG antibody (2.8) were normal. Dihydrorhodamine 1 2 3 assay was done which showed decreased expression of b558 on gated neutrophils compared to control, consistent with CGD. Final diagnosis of Chronic granulomatous disease was made. Child responded to prolonged iv antibiotics meropenem and vancomycin. He was discharged on trimethoprim-suphamethoxazole, and itraconazole prophylaxis.

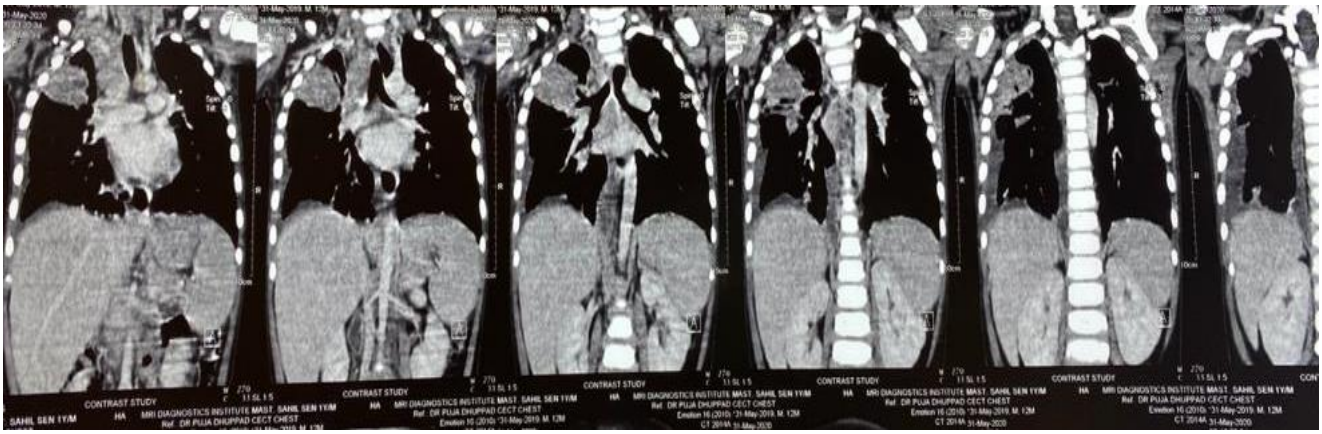

**Figure 1: CT scan showing consolidation involving right upper lobe, superior segment of lower lobe. multiple well defined variable sized centrilobular and subpleural nodules scattered both lung parenchyma, some of these are showing tree in bud pattern and apicoposterior segment of upper lobe.**

**Table 1: Expression of b558 on gated granulocytes.**

| Gated population | Control | Patient |
|---|---|---|
| **MFI unstained** | 30.86 | 32.05 |
| **MFI stained** | 54.08 | 30.87 |
| **Stain Index** | 1.75 | 01.25 |
| **% positive** | 21.29% | 0.02% |

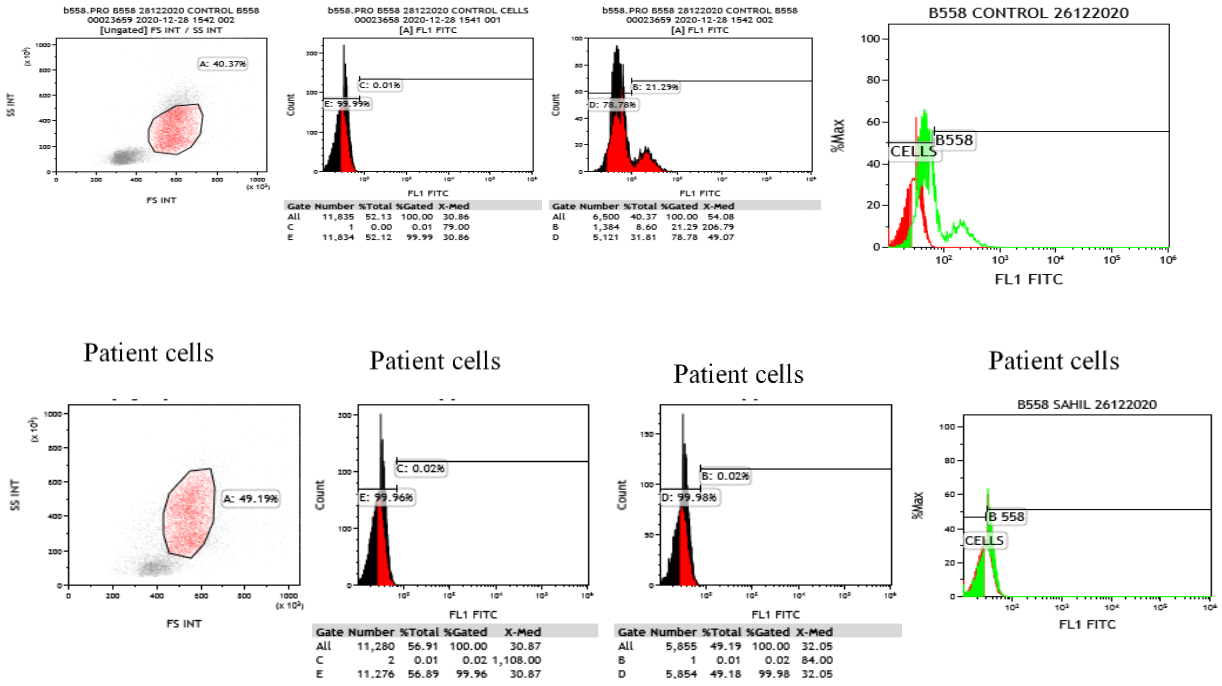


**Figure 2: Decreased expression of b558 on gated neutrophils compared to control. Consistent with X-linked CGD with CYBB gene defect.**

## DISCUSSION

CGD is a fatal immunodeficiency disorder mainly due to phagocytic defect due to defective superoxide generating system resulting in recurrent bacterial and fungal infection. Though neutrophils and macrophages are able tophagocytose pathogens properly but there is defect in killing of pathogens due to lack of generation of superoxide by NADPH oxidase complex. Due to this defect, there is persistent of inflammation and tissue granuloma formation which forms the characteristic feature of CGD.[1] Its incidence is very rare 1 in 200,00population. It has 2 types of inheritance, X-linked recessive comprising of 70% cases and autosomal recessive form accounting for remaining 30% cases.[2] Majority of cases are diagnosed in early infancy and particularly below 5 yearsage.[3,4] They present with lymphadenitis, pneumonia, cutaneous and liver abscess and granulomatous inflammation. They get infection by catalase producing organisms like staphylococcus, tuberculosis, aspergillous, candia. The X-linked form of diseases have earlier and more severe presentation including higher rates of infection and death in comparison to autosomal recessive forms which are diagnosed in the older age and have a better outcome.

We have to keep a high index of suspicion to diagnose primary immunodeficiency disorder while dealing with recurrent infection or infection with unusual organism. In our case child presented with recurrent infection mainly pneumonia and cervical lymphadenitis requiring multiple hospitalization and prolonged admission. He had tubercular infection and candida infection also. Earlier for screening NBT test was used more frequently but now a days, DHR flowcytometry test has become method of choice as it is more sensitive and inexpensive.[5,6] his diagnosis was confirmed by dihydrorhodamine 1,2,3 assay positive result. He was discharged with tmp-sulfamethoxazole and itraconazole prophylaxis.

## CONCLUSION

Always high index of suspicion should be there for diagnosis of primary immunodeficiency disorder in cases presenting with persistent or recurrent infection. Serial and methodical approach very often helps in clinching diagnosis. Early and prompt diagnosis can be of great help to patients for prognosis and giving them chance for future therapies.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: Not required*

## REFERENCES

1. Seger RA. Chronic granulomatous disease: recent advances in pathophysiology and treatment. Neth J Med. 2010;68(11):334-40.
2. Segal BH, Veys P, Malech H, Cowan MJ. Chronic granulomatous disease: lessons from a rare disorder.

Biol Blood Marrow Transplant. 2011;17(1 Suppl):123-31.
3. Holland SM. Chronic granulomatous disease. Clin Rev Allergy Immunol. 2010;38(1):3-10.
4. Winkelstein JA, Marino MC, Johnston RB Jr, Boyle J, Curnutte J, Gallin JI, Malech HL, et al. Chronic granulomatous disease. Report on a national registry of 368 patients. Medicine (Baltimore). 2000;79(3):155-69.
5. Vowells SJ, Fleisher TA, Malech HL. Testing for chronic granulomatous disease. Lancet. 1996;347(9007):1048-9.
6. Jirapongsananuruk O, Malech HL, Kuhns DB, Niemela JE, Brown MR, Anderson-Cohen M, et al. Diagnostic paradigm for evaluation of male patients with chronic granulomatous disease, based on the dihydrorhodamine 123 assay. J Allergy Clin Immunol. 2003;111(2):374-9.
7. Gallin JI, Alling DW, Malech HL, Wesley R, Koziol D, Marciano B, et al. Itraconazole to prevent fungal infections in chronic granulomatous disease. N Engl J Med. 2003;348(24):2416-22.
8. Beauté J, Obenga G, Le Mignot L, Mahlaoui N, Bougnoux ME, Mouy R, et al. Epidemiology and outcome of invasive fungal diseases in patients with chronic granulomatous disease: a multicenter study in France. Pediatr Infect Dis J. 2011;30(1):57-62.
9. Mouy R, Veber F, Blanche S, Donadieu J, Brauner R, Levron JC, et al. Long-term itraconazole prophylaxis against Aspergillus infections in thirty-two patients with chronic granulomatous disease. J Pediatr. 1994;125(6 Pt 1):998-1003.

**Cite this article as:** Sahoo MR, Jondhale SN, Goel AK. A chronic granulomatous disease masked by tuberculosis in an young infant. Int J Contemp Pediatr 2021;8:946-9.