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Case Report

Paediatrics Section

Chronic Granulomatous Disease

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ABSTRACT

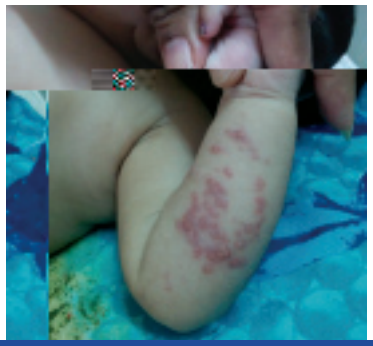
Chronic Granulomatous Disease (CGD) is an inherited immunodeficiency disorder characterized by defective functioning of NADPH oxidase enzyme in the phagocytes. This leads to recurrent infections by catalase positive organisms and later, granuloma formation in multiple organs. This condition usually presents in the age group of 2-5 y and is uncommon in neonates. In this case report, we describe a rare case of CGD in a 40-day-old male child who initially presented with a history of erythematous pustular rash on left forearm and refusal to feeds. He remained unresponsive to regular antibiotics. CT chest and abdomen revealed multiple ill-defined lesions suggestive of granulomas or developing abscesses. Immunodeficiency workup showed negative Nitroblue Tetrazolium test and positive Dihydrorhodamine test (flow cytometry). A diagnosis of CGD was then made and treated accordingly. The aim of this report is to highlight the fact that although it is rare for CGD to present at such an early age, but in a neonate with multiple granulomas or abscesses, it should be considered as a differential and worked up accordingly. Early diagnosis and treatment can significantly improve the prognosis.

Keywords: Immunodeficiency disorders, Multiple granulomas, NADPH oxidase deficiency, Neonates

CASE REPORT

A 40-days-old male child presented to our tertiary care hospital, Dr Yewale's Multispeciality Hospital for Children, Navi Mumbai, India, with the complaints of an erythematous rash on forearm since five days and fever and decreased feeding since one day. Child initially had generalised pustular eruptions five days back and was treated with intravenous cefotaxime, amikacin and augmentin at another hospital. These eruptions resolved over a period of four days but there was no change in the size of the eruptions on left forearm.

On examination, child was febrile but active, nontoxic looking pink baby. He was at 50th percentile for weight and height for the age. There was a localised cluster of erythematous pustular rash on left forearm [Table/Fig-1]. Systemic examination was normal. All blood [Table/Fig-2] and urine investigations were carried out and their results indicated anaemia and high WBC count and increased CRP and they all pointed towards infection. Blood culture was negative. He was started on intravenous augmentin. But child had persistent fever and refusal of feeding and in this view, lumbar puncture was done to rule out meningitis. CSF Findings [Table/Fig-3] were normal and even CSF culture did not show any growth. Antibiotics were stepped up to meropenem on 4th day. During the course of illness, baby started appearing more lethargic, toxic, enlargement of bilateral preauricular and inguinal lymph nodes were noticed. There was gradual development of hepatosplenomegaly. USG Abdomen revealed hepatosplenomegaly and hypoechoic lesions on liver and spleen suggestive of granulomas [Table/Fig-4]. CT Chest and Abdomen revealed multiple pulmonary nodules with perilesional consolidation, hepatosplenomegaly with ill defined lesions suggestive of granulomas or developing abcesses. In view of persistent fever and deteriorating condition, immunodeficiency work up was done. Immunoglobulins levels were found to be normal with IgG- 300 mg/dl, IgM- 42 mg/dl and IgA- 10 mg/dl.All other tests were also normal except that Nitroblue Tetrazolium reduction was 0% and Dihydrorhodamine test (flow cytometry) was positive. Based on the negative NBT test and positive DHR Test, diagnosis of Chronic Granulomatous Disease (CGD) was made. Parents were



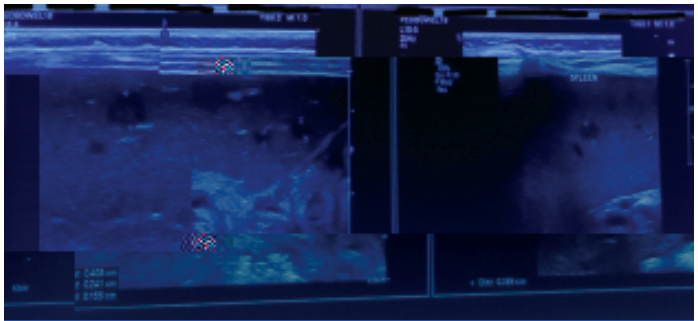
[Table/Fig-1]: Initial skin lesion on child's forearm

TEST	RESULT	COMMENT
RBC	3.6 million/cumm	-
Haemoglobin	10.3 g/dl	Decreased
WBC Count	14,500 cells/cumm	Increased
Platelets	1.92 Lakhs/ cumm	-
Differential Count:		
Neutrophils	72%	-
Lymphocytes	28%	-
Eosinophils	00	-
Monocytes	00	-
Basophils	00	-
Smear study	Hypochromasia+, microcytosis+, macrocytosis+, poikilocytosis+	
CRP	110	Increased

[Table/Fig-2]: Initial blood test reports

TEST	RESULT	COMMENT
Colour	Clear	-
Sugar	33 mg%	Decreased
Protein	5%	Decreased
Any cells	2 lymphocytes	-

[Table/Fig-3]: CSF analysis



[Table/Fig-4]: USG findings of the patient showing multiple ill-defined lesions in the spleen indicative of granulomas or developing abscesses

counselled and told about the modality of treatment. Patient was started on a prophylactic therapy of Trimethoprim-Sulfmethoxazole and Itraconazole and Stem Cell Transplantation was planned as the ultimate treatment after HLA matching the sibling.

DISCUSSION

CGD is a primary immunodeficiency disorder characterised by inability to generate superoxide free radicals by the phagocytes resulting in recurrent infections. Its diagnosis requires a high degree of suspicion and the confirmation of diagnosis by NitroblueTetrazolium Test and flow cytometry should be followed by long term antibiotic therapy [1,2].

In our patient, the presence of multiple granulomatous lesions, persistent fever and dermatitis not responding to usual antibiotics; absence of fungi, bacilli and atypical mycobacteria along with the finding of no atypical lymphocytes pointed towards the diagnosis of CGD and it was then confirmed with Nitroblue Tetrazolium test and Dihydrorhodamine test. Normally the percentage of blue-stained neutrophils in NBT test is close to 100, but in CGD patients, this percentage is close to 0 as was seen in this case [3].

Majoratively infections are caused by catalase positive organisms which include *Staphylococcus aureus, Serratia, Burkholderia, Pseudomonas* among the bacteria and *Aspergillus* and *Candida* among the fungi [4]. It appears to occur because of the failure to clear the microorganisms by neutrophils' NADPH Oxidase enzyme. Also, the defect in phagocytes' oxidant production causes a prolonged inflammatory response ultimately leading to granuloma formation [5]. But in this patient, cultures remained negative for any microorganism.

The pattern of presentation may differ from patient to patient. Our patient presented with skin infection and developing abscesses in liver. Other common manifestations could be in the form of pneumonia, pulmonary abscess, lymphadenitis, osteomyelitis and even subcutaneous abscess [6].

Treatment for this condition includes prophylactic antibiotic therapy and aggressive treatment of acute infections. Hematopoietic stem cell transplantation is considered curative in CGD [7]. Human leukocyte antigen (HLA)-identical BMT or peripheral blood stem cell transplantation has been successfully performed with granulocyte colony stimulating factor (G-CSF)-mobilized granulocyte transfusions. A therapeutic alternative for patients with no HLA-identical donors is the genetic modification of autologous hematopoietic stem cells (HSC) [8]. In this case, child has an elder sibling who will be tested for HLA matching and if suitable, then stem cell transplantation will be done.

CONCLUSION

This case is presented here for the rarity of Chronic Granulomatous Disease presenting at such an early age and to emphasize the need to consider it as a differential diagnosis in a child with multiple granulomas or abscess throughout the body.

REFERENCES

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