Non-resolving hepatic and lung abscess in a child: a case report from Pakistan

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Abstract

Chronic granulomatous disease (CGD) is a rare, primary immunodeficiency disorder that occurs due to a defective NADPH (Nicotinamide Adenine Dinucleotide Phosphate) oxidase system. Due to the varying clinical presentation and symptom overlap with other conditions, CGD can often pose as a challenge for paediatricians. This case report describes the approach to diagnosis and management of an infant affected by CGD, with liver abscess.

Keywords: Immunodeficiency; Chronic granulomatous disease; Liver abscess.

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Introduction

Chronic granulomatous disease (CGD) is a rare, heritable immunodeficiency of the phagocytic system, with persistent bacterial and fungal infections, mostly affecting males.[1] Although the clinical presentation is highly variable, infections, dermatitis, gastrointestinal complications, and faltering growth are frequent symptoms that aid in the diagnosis.[2] Because of the atypical clinical picture, CGD can easily be ignored or mistaken for pyloric stenosis, food or milk allergy, or iron deficiency anaemia.[2] Herein, we present a case study of this rare condition for which informed consent statement was obtained.

Case Report

A six-year-old unvaccinated male child, issue of consanguineous marriage, with growth parameters <5th centile was brought in ER of Ziauddin University Hospital, Karachi, on August 15, 2021, with high-grade fever and cough for the last two months. Fever was continuous and associated with rigors and chills, which were relieved temporarily by antipyretics. Cough was productive, in bouts without post-tussive vomiting. On examination, the temperature was 103°F with a respiratory rate of 58/min, pulse of 142/min, blood pressure of 110/70 mmHg, and SaO2 of 85% in room air. He was sick-looking and lethargic. He was oriented to time, place, and person with a GCS (Glasgow Coma Scale) of 15/15 with a normal neurological examination. Chest examination revealed bilateral crepitation with harsh breathing. He had an audible S1 and S2 with no added sound. Abdominal examination revealed a soft abdomen with tenderness in the right upper quadrant. The liver was palpable 6cm below the costal margins with a span of 13cm. The laboratory investigations revealed, Haemoglobin: 9.2 g/dl, Total Leucocyte Count: 12 x 10E9/L (Neutrophils: 85, Lymphocytes: 13), Platelets: 511 x 10E9/L, Urea: 20mg/dl, Creatinine: 0.50mg/dl, Sodium: 130 Meq/l, Potassium: 4.3Meq/l, Chloride: 95Meq/l, Bicarbonate: 23Meq/l, Total Bilirubin: 0.40mg/dl, Direct Bilirubin: 0.10mg/dl, Alanine Aminotransferase: 39 IU/L, Alkaline Phosphatase: 959 IU/L, Gamma-Glutamyl Transferase: 60IU/L, CRP (C-Reactive Protein): 64 mg/L, and Erythrocyte Sedimentation Rate: 18 mm/hr. Blood culture showed no growth, while gene expert from gastric lavage was also negative. Ultrasound of the abdomen showed abscess in segment 6 of the right lower lobe of the liver with a single cavity of 4.5cm. Chest X-ray (Figure 1) and HRCT (High-

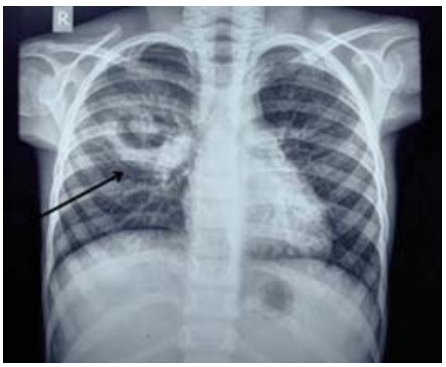

Figure-1: Chest X-ray, frontal view revealing non-homogenous opacity in the right middle zone, around radiolucent area with defined margin suggestive of lung cavitation.

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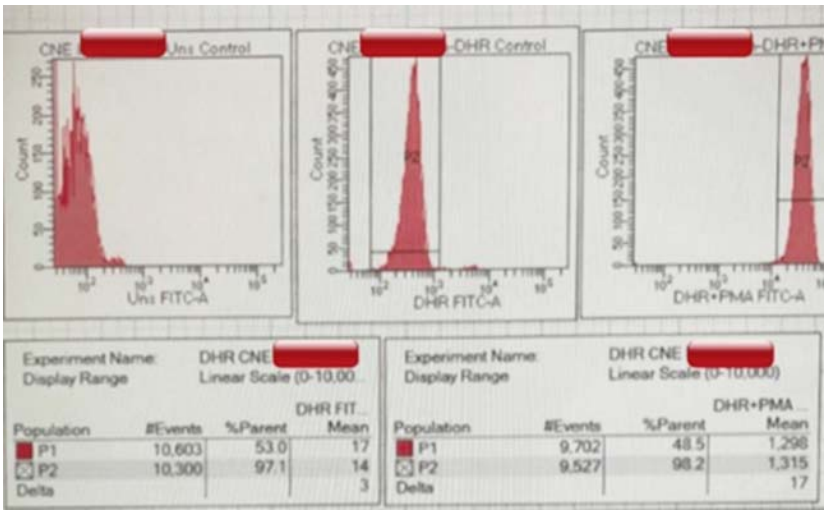

Figure-2: Suggestive of decreased Dihydrorhodamine reduction to Rhodamine in patient's phagocytic cell as compared to control

resolution Computed Tomography) were suggestive of ARDS (Acute Respiratory Distress Syndrome) and cavitation in the right mid-zone on sequential series. The patient was kept on bubble CPAP (Continuous Positive Airway Pressure) support as a Non-Invasive Ventilation Mode. During the hospital course of 20 days, the patient received multiple antibiotics including Meropenem, Vancomycin, Metronidazole, Teicoplanin, Sulzone, and Fluconazole. He was discharged on antibiotics initially parenteral as well as oral and was called for follow-up regularly with CBC (Complete Blood Count), CRP, Chest X-ray (Tuberculosis (TB) workup was done showing negative Mantoux test, negative sputum for gene expert, there is no history of the child's exposure to TB, and ultrasound of the abdomen. Even after two follow-ups, each after one week, the patient was not completely cured which gave the suspicion of an underlying primary immunodeficiency disorder. Immunodeficiency panel revealed absolute count of CD3+ total T- lymphocyte of 3,735 (normal: 1,500-2,900), absolute count of CD4+ total T- Helper lymphocyte of 2,004 (normal: 1,000-2,100), absolute count of CD8+total T- regulatory lymphocyte of 1,491 (normal: 500-1,200), and absolute count of CD56+ Natural killer cells of 686 (normal: 300-600). Ultimately DHR (Dihydrorhodamine test) was done, and the result proved that the patient had CGD (Figure 2). The diagnostic laboratory assessment for CGD includes evaluation of NADPH oxidase function in neutrophils, using historically the nitroblue tetrazolium test or currently the more analytically sensitive DHR test. Activation of neutrophils with phorbol myristate acetate (PMA) results in oxidation of DHR to a fluorescent compound, rhodamine, which can be measured by flow cytometry. Flow cytometry can distinguish between the different genetic forms of CGD. Complete myeloperoxidase (MPO) deficiency can cause a false-positive result for CGD in the DHR flow cytometric assay; however, there is a difference between the percent DHR+ neutrophils and the mean fluorescence intensity after PMA stimulation that allows discrimination between true X-linked CGD and complete MPO deficiency. Further, the addition of recombinant human MPO enhances the DHR signal in MPO-deficient neutrophils but not in CGD neutrophils.[3]

The case was referred to immunodeficiency clinic and kept on prophylactic antibiotics and regular follow-up.

Discussion

CGD manifests itself when the genes responsible to produce NADPH (Nicotinamide Adenine Dinucleotide Phosphate) oxidase are defective. This results in an inability to produce superoxide radicals necessary for the elimination of ingested catalase-positive microbes.[1] Local studies have shown that CGD is one of the main causes of PID (Primary Immunodeficiency Disorder) in Pakistan because of the high rates of consanguineous marriages (almost 70%); however, due to unavailability of genetic testing, diagnosis is often compromised.[4, 5]

In our patient, the infections were being treated in isolation without realisation of the underlying immunocompromised condition. The development of multiple, severe infections which did not respond well to treatment became red flags. As highlighted by previous studies, there are 10 warning signs of primary immunodeficiency disease, among which the need for prolonged antibiotics or Intravenous (IV) antibiotics, failure to thrive, and positive family history are deemed to be the most sensitive.[6] While our patient did not have a family history of CGD, the other two factors were present.

The most common early manifestation of CGD is the involvement of the skin, which was not seen in this patient whereas he developed lung cavitation and liver abscess. In Western studies, lung involvement is seen in as many as ~80% of CGD patients and liver abscesses in as many as ~26% of the patients.[7] Contrarily, in India 68 patients of CGD were studied wherein only 7 (about 10%) were noted to have developed liver abscess, thus establishing that it is a relatively uncommon presentation of the disease in this region.[8]

Diagnostic tests for CGD available worldwide are NTB (nitro blue tetrazolium test), DHR, and genetic testing. DHR is considered to be the more accurate screening test for CGD and was done on the current patient as well. The PMA-stimulated positive cells were higher in flow cytometry than the NBT. Although there was poor correlation between the two methods, a good agreement between flow cytometry assay and NBT test results was observed in terms of positive and negative results in simulated and unstimulated cells. Moreover, in flow cytometry, >95% of stimulated cells suggest the higher sensitivity. All samples with negative NBT showed negative DHR, reflecting high degree of agreement between these two methods and eliminating possible false negative result in flow cytometry.[3] Low incidence of CGD and a large number of unique mutations preclude standardised genetic testing.

While previously the disease was fatal in childhood, today most patients survive into adulthood. This dramatic improvement in survival should be attributed to the use of modern management techniques such as allogeneic haematopoietic cell transplantation (HCT) and gene therapy.[9] Surgical intervention, while effective, is often deferred due to the high risk of surgical morbidity. Therefore, most clinicians prefer medical management. Studies have shown that a combination of high-dose corticosteroids along with IV antibiotics is highly effective, especially for hepatic abscess.[10]

Conclusion

CGD can present as a diagnostic challenge for paediatricians, largely due to the non-specific nature of presentation at the outset. However, with prompt diagnosis and initiation of management, mortality from CGD can be significantly reduced.

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