

## Case Report

# Anterior chest wall protrusion as initial presentation of chronic granulomatous disease: a case report

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Chronic granulomatous disease (CGD) is a rare primary immunodeficiency disease characterized by recurrent life-threatening bacterial and fungal infections. We report a 4-month-old girl with CGD, who was firstly presented with an anterior chest wall protrusion because of an aspergillosis mass.

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Chronic granulomatous disease (CGD) is a rare inherited primary immunodeficiency disorder in which phagocytes are unable to generate reactive oxygen intermediates, such as superoxide, because of defects in gene coding for one of several components of the nicotinamide dinucleotide phosphate (NADPH) oxidase. The leukocytes of the CGD patients cannot produce adequate amount of superoxide and other oxygen metabolites that are toxic to microorganisms. As a result, the phagocytes fail to kill the ingested microorganisms, especially those with catalase activity. This leads to recurrent life-threatening bacterial and fungal infections (1–5). The most common fungal infections are caused by *Aspergillus* species (4–7). Typically, CGD patients suffer from recurrent pyogenic infections starting from the first year of life (3). Affected patients have recurrent infections from infancy, usually involving the skin, lymph nodes, lungs, liver, and gastrointestinal tract (1–3). CGD is also characterized by abnormally exuberant inflammatory responses leading to granuloma formation, such as granulomatous enteritis, genitourinary

obstruction, poor wound healing, and dehiscence (2, 7). The prevalence of CGD has already been estimated as approximately about 1 per 1,200,000 individuals (3).

In the present study, a case of CGD with atypical presentation is reported.

## Case report

A 4-month-old female child born of consanguineous marriage, with difficult breathing, tachypnea, and anterior chest wall protrusion was admitted to the Children Medical Center hospital of Tehran university in May 2003.

One week before admission, her cries sounded to be hoarse and 4 days later, the parents found an anterior protrusion in her thoracic cavity associated with tachypnea.

She was born by normal vaginal delivery with appropriate apgar score and the weight of birth was about 3200 g. Pregnancy and delivery were uneventful, and she had received her vaccines according to national vaccination program. Her growth parameters were weight: 5 kg (10–25%),

length: 60 cm (<5%), head circumference: 42 (75–90%) by National Center for Health Statistics (NCHS) growth curve for infant from birth to 36 months.

The family history had no remarkable point, expect her elder sister had a history of febrile seizure, treated with phenobarbital. At admission time her examination revealed: pulse rate: 140/min, respiratory rate: 75/min, and temperature: 36.5°C. Posterior fontanel was closed and anterior one was 2 × 2.5 cm. No lymphadenopathy was detected in her neck.

A 6 × 5 cm non-tender bulging was seen next to the right upper sternal border with rubbery consistency, without any warmth or redness. Diffuse rales and bilateral inspiratory and expiratory crackles were auscultated. Abdominal respiration was visible. The scar of *Bacillus Calmette-Guerin* (BCG) vaccination was seen on right arm with some lymph nodes (probably BCG adenitis) in right axillary's cavity. Other clinical examinations were normal.

Laboratory evaluations revealed WBC: 21,700/mm<sup>3</sup> (P 57, L 35, monocyte 7, eosinophil 1), hemoglobin (Hb): 9.5 g/dl, PLT, PT and PTT: normal. Erythrocyte sedimentation rate (ESR) was 50 mm in the first hour. Chest X-ray of the patient showed some opacity in both apical segments and right cardiophrenic angle while a retrosternal mass with right side deviation had made a protrusion in anterior chest wall. Chest computerized tomography (CT) scan, done with contrast, showed a large mediastinal mass with cystic appearance and necrotic areas within it without any pulmonary involvement (Fig. 1).

We thought first that the mass was due to disseminated BCG because she had a scar of BCG adenitis in her axillary region at the same side of BCG vaccination. A needle biopsy was done under ultrasound guide. The frozen section examination suggested an erroneous diagnosis of rhabdomyosarcoma because of a few cells resembling rhabdomyoblasts, but permanent sections of the biopsy revealed proliferation of spindle cells. No significant inflammatory cell infiltrate, neither fungal hyphae were seen.

The bone marrow aspiration was reported as normal and hematopoietic stem cell malignancies or lymphoproliferate disorders were ruled out. The 24-h urine Vanilmandelic Acid (VMA) concentration was within normal range that excluded neuroblastoma.

The partial excision of the mass was performed because it could not be removed entirely due to the adhesion to the chest wall. It revealed a cold abscess with fungal hyphae (acute angle

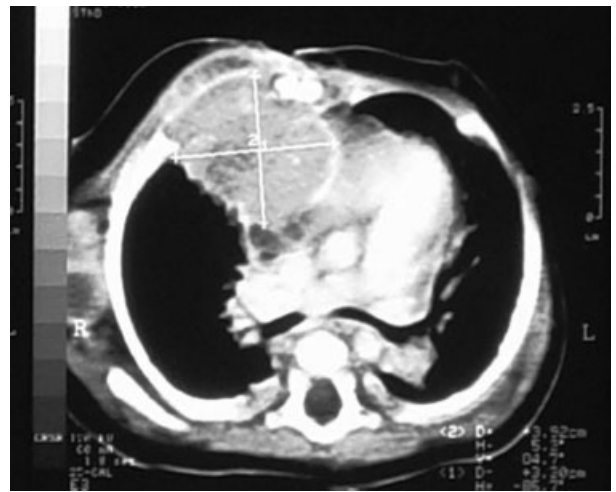


Fig. 1. Chest computerized tomography (CT) scan showing a cystic mediastinal mass with necrotic areas within the mass without pulmonary involvement.

septations, most possibly *Aspergillus* species). No acid fast bacilli were detected by special staining. In this way, BCG infection was ruled out. A specific fungal culture of the drain secretion was positive for *Aspergillus* sp. Fungal mass raised a suspicion of immunodeficiency disorder so the immune system was evaluated and the nitroblue-tetrazolium (NBT) dye reaction test showed 0% activity. Diagnosis of CGD with poor prognosis was made for her and intensive antifungal treatment and  $\gamma$ -interferon were started promptly.

Cardiopulmonary arrest occurred a month after admission and attempts to resuscitate the patient was unsuccessful; the patient did not response to medical and surgical treatment and she died because of respiratory obstruction because of the mass compression.

## Discussion

The hallmark of the clinical presentation of CGD is recurrent infections in specific anatomic sites and at epithelial surfaces in direct contact with the environment such as the skin, lungs, and gut (5, 8). Even in the setting of life-threatening infections, CGD patients may be asymptomatic or have mild non-specific symptoms (7). *Aspergillus* is one of the most important causes of morbidity and mortality in CGD (9, 10). In a review of aspergillosis in CGD patients at the National Institutes of Health (NIH), one-thirds of patients were asymptomatic at diagnosis and only approximately 20% were febrile (4). In many of these patients, a pulmonary infiltrate on routine screening chest

X-ray or CT scan was the first presentation of an infection. Therefore, a high level of vigilance in searching for infection is necessary in caring for CGD patients. Frequent radiographic evaluation (for example, chest radiographs during routine clinic visits and CT scans in patients with fever or focal signs) is critical for making early diagnoses (2).

In fact in our case, CGD was first presented with an anterior mediastinal mass because of aspergillosis and what makes this interesting is that she had the mass in the absence of pulmonary involvement as the first presentation of CGD.

The patient had no typical manifestations of CGD but her laboratory findings including neutrophil leukocytosis and elevated ESR could reflected an infection. When infection is suspected, aggressive effort to obtain culture material is required (2) that in this case showed *Aspergillus* sp.

In conclusion, diagnosis of CGD should be kept in mind when encountering an atypical aspergillosis particularly during the first year of life. Evaluation of phagocytic system is highly suggested and the diagnosis must be confirmed by means of necessary tests. Rapid institution of treatment is warranted.

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