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## Pericardial effusions in two boys with chronic granulomatous disease

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**Abstract** Pericardial involvement in chronic granulomatous disease (CGD) is very rare. We present two children with known CGD and pericardial effusions in whom no microbial cause for the effusions was found.

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### Introduction

Chronic granulomatous disease of childhood (CGD) is a rare congenital abnormality of phagocytic function first described by Berendes et al. in 1957 [1]. The X-linked form of the disease accounts for up to 66% of cases; hence boys are predominantly affected. CGD is now known to be a group of genetic disorders each affecting a particular component of the reduced nicotinamide adenine dinucleotide phosphate (NADPH) oxidase system. The disease is characterised by the inability of phagocytic cells to kill catalase-positive bacteria and fungi and results in recurrent suppurative infections primarily involving the skin, lymph nodes, lungs, liver, bones and gut. Granulomatous reaction to infection is typical. Improved understanding and management of the disease have considerably reduced the early mortality. Pericardial involvement is very rare. We present two children with known CGD and pericardial effusions in whom no microbial cause for the effusions was found.

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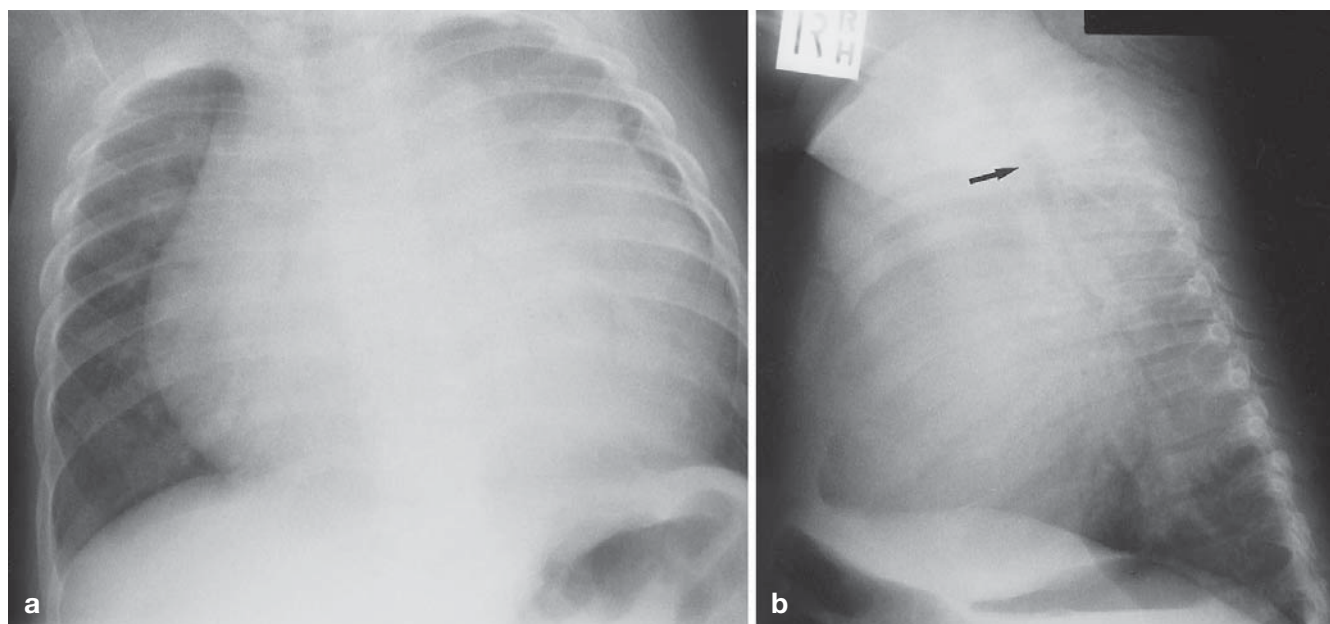
### Case reports

#### Patient 1

A 10 and 1/2-month-old boy, in whom the diagnosis of CGD had been made postnatally, was admitted with a history of fever, cough and difficulty in breathing. He had been unwell for the previous 10 days, and his family practitioner had diagnosed possible ear infection and prescribed amoxycillin. There had been no real clinical improvement.

On examination, he was febrile, tachypnoeic and tachycardic. He had a maculopapular rash on his skin, unremarkable abdominal examination and no signs of dehydration. The throat was normal and his ears could not be examined because of wax. Some wheezing was noted at the right lung base. Haematological investigations revealed: haemoglobin  $9.9 \text{ g dl}^{-1}$ , white-cell count  $13.9 \times 10^9 \text{ l}^{-1}$ , neutrophils  $6.2 \times 10^9 \text{ l}^{-1}$ , lymphocytes  $6.7 \times 10^9 \text{ l}^{-1}$  and platelets  $571 \times 10^3$ . Urea, electrolytes, clotting and liver-function tests were normal.

The provisional diagnosis was lower respiratory tract infection, and a chest X-ray was obtained which showed an enlarged cardiac shadow with a possible mediastinal mass (Fig. 1a). There appeared to be some AP compression of the trachea on a lateral radiograph (Fig. 1b). There were no signs of lung consolidation. CT was unsuc-



**Fig. 1a,b** Patient 1. Chest X-ray showing **a** an enlarged cardiothymic shadow and **b** some posterior displacement of the trachea (arrow)

cessful because the child was agitated. Chest ultrasound showed no evidence of a mediastinal mass, a normal thymus and a large pericardial effusion with 20–30 mm depth of fluid around the heart (Fig. 2). There was right atrial and right ventricular diastolic collapse throughout, but cardiac function was otherwise normal. The effusion was drained under general anaesthesia and 260 ml of straw-coloured proteinaceous fluid (an exudate) was obtained from the pericardial space. The patient was placed on broad-spectrum antibiotic cover with flucloxacillin, ciprofloxacin and amikacin. Prednisolone was also commenced. His condition rapidly improved and he was discharged from hospital 6 days after admission. Microbiological culture for viruses, fungi and mycobacteria were negative.

#### Patient 2

A 4-year-and-11-month-old boy with known CGD diagnosed early in life was admitted with tachypnoea and fever. Five days prior to admission he had developed a sore throat. He had been to the GP who had treated him with an oral cephalosporin. His condition worsened the next day and despite altering the antibiotics to erythromycin, there was no real clinical response.

On admission, he was febrile, but his physical examination was unremarkable. The blood counts showed: haemoglobin 8.8 g dl<sup>-1</sup>, white-cell count  $25.5 \times 10^9$  l<sup>-1</sup>, neutrophils  $18.6 \times 10^9$  l<sup>-1</sup>, lymphocytes  $3.47 \times 10^9$  l<sup>-1</sup> and platelets  $678 \times 10^3$ . Urea and electrolytes were normal.

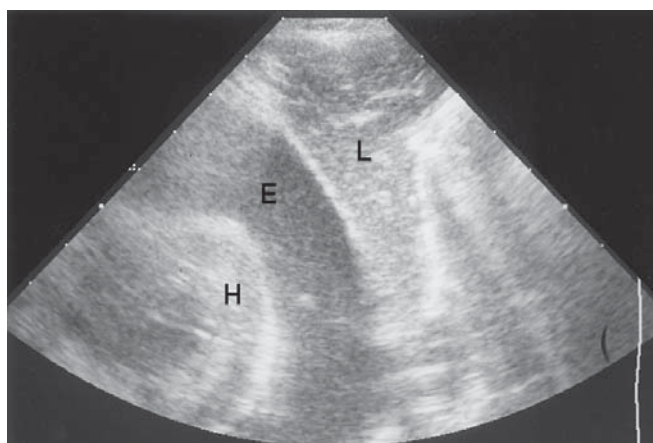
A chest X-ray was performed which showed a large heart shadow. There were no signs of lung consolidation or pleural effusion. An echocardiogram showed a moderately large pericardial effusion (17 mm adjacent to the mitral valve, 3 mm anteriorly). The heart was structurally normal and there was no evidence of tam-

ponade. He was commenced on intravenous amikacin and vancomycin and continued on erythromycin because of the possibility of *Mycoplasma* infection. After 5 days of IV antibiotics, he was changed to amoxicillin and clavulanic acid. The effusion rapidly resolved and his clinical condition improved. He was discharged 8 days after admission with no obvious cause for the pericardial effusion. A further 8 days after discharge the symptoms of tachypnoea and chest discomfort returned. He was readmitted and an echocardiogram was repeated, which showed that his pericardial effusion had reaccumulated. A total of 180 ml of straw-coloured fluid was aspirated. Bacterial, fungal and viral cultures of blood and pericardial fluid showed no growth. *Aspergillus* and *Candida* serum antigens were negative. He was commenced on intravenous piptazobactam, amikacin and amphotericin and his effusion and clinical status improved. Again, no microbial cause for the pericardial effusion was found.

#### Discussion

CGD is a rare inherited disorder resulting in abnormal phagocytic function. Normal oxidative responses are necessary for efficient intracellular killing of bacteria and fungi by human phagocytic cells [2]. Affected children have abnormalities of NADPH oxidase leading to failure of cells to generate superoxide, other reactive oxygen species and hydrogen peroxide in the phagolysosome after phagocytosis. Although microbiological cultures do not always yield positive culture, the organisms most commonly cultured from sites of infection are the catalase-positive bacteria such as *Staphylococcus aureus* and enteric gram-negative rods such as *Klebsiella pneumoniae*, *Salmonella* species and various species of *Aspergillus*, *Candida* and *Nocardia*.

The characteristic histopathological changes found in CGD consist of extensive granuloma formation in sever-



**Fig. 2** Patient 1. Longitudinal US image showing a large pericardial effusion (H heart, E pericardial effusion, L liver)

al tissues. Most patients develop signs and symptoms during the first 2 years of life. Milder forms of the disease have been described with onset in adolescence and even adulthood [3]. CGD patients often present with fever of unknown origin, and in such cases thorough fever work-up including comprehensive imaging

may be necessary. Hilar lymphadenopathy is often present and pleural effusion is frequent. Hepatosplenomegaly and liver abscesses are relatively common. Calcification in a granuloma may occur in many locations. Other gastrointestinal manifestations include oesophageal dysmotility or strictures, gastric antral narrowing, diarrhoea secondary to small and large bowel inflammation and perianal fistulas. Osteomyelitis is also well recognised.

Cardiac and pericardial manifestations are exceptional. To our knowledge, only two previous children with CGD have been reported with similar complications, including constrictive pericarditis and granulomatous infiltration of the epicardium and myocardium [4, 5]. We report two cases of large pericardial effusions in boys with known CGD in whom no infectious cause for the effusion was identified. Pericardial effusion should therefore be considered in the differential diagnosis of CGD patients presenting with fever, cough, tachypnoea, or symptoms of a possible lower respiratory tract infection. The cultures and pericardial fluid in both children were negative, although both had been on broad-spectrum antibiotics. No organisms were seen on microscopy, however, suggesting the effusions may represent a serositis-like response to non-specific inflammation.

## References

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