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CASE REPORT

Persistent pulmonary mass-like lung consolidations and chest wall extension in a newborn diagnosed with chronic granulomatous disease

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Introduction

Chronic granulomatous disease is a primary immune deficiency disorder characterised by recurrent infections that particularly affect the lungs. Patients are usually diagnosed during infancy at around 2–3 years of age.

A newborn or infant with persistent lung consolidations involving the chest wall should raise the suspicion of immunodeficiency syndromes, particularly chronic granulomatous disease. Ultrasound of the chest is preferred for further characterisation following chest X-ray when consolidations are seen in the pleura. Doppler ultrasound may be better than X-rays or unenhanced chest computed tomography at showing extension beyond the lungs.

A persistent mass-like lung consolidation involving the chest wall in a child should lead to consideration of a possible diagnosis of chronic granulomatous disease.

Case report

A 23-day-old boy, born to non-consanguineous parents, was admitted to another hospital owing to difficulty with sucking and was diagnosed with late-onset sepsis. Abundant leukocytes were detected on lumbar puncture, so vancomycin and meropenem were initiated. The chest X-ray revealed infiltration in both lungs. Oseltamivir, clarithromycin and fluconazole were added to the initial antibiotics on the eighth day as the patient had ongoing fever and increased C-reactive protein levels. Computed tomography of the chest showed pleura-based lung masses in the right upper and left lower lobes. He was referred to the authors' hospital on the 45th postnatal day with a preliminary diagnosis of thoracic neuroblastoma and sequestration.

On admission, his vital signs were within normal limits. The sole pathological finding was crepitations in the right middle zone of the lung by auscultation. Laboratory tests showed an increased white blood cell count of 25 450/µl with neutrophil predominance (70%), C-reactive protein level 124.37 mg/litre and procalcitonin level 0.69 µg/litre. Microbiological culture results were all negative except for *Staphylococcus hominis* isolated from the catheter tip. All previously initiated treatments were continued.

The chest X-ray revealed pleura-based mass-like lung consolidations in the right upper and left lower lobes. Subsequent chest ultrasound showed two pleura-based consolidations in the right upper and left lower lobes with intense vascularisation on Doppler ultrasound extending beyond the lungs (**Figures 1a** and **b**). Magnetic resonance imaging with gadolinium-based contrast medium was performed to further characterise the lesions and allow comparison with previous chest computed tomography scans. On magnetic resonance imaging, the consolidations were stable in size, they had homogenous signal and the pleura was involved in both hemithoraces. Contrast enhancement extended through the chest wall adjacent to the consolidations (**Figures 2a** and **b**). There was no accompanying osteomyelitis of the ribs. Since they were not located at the posterior mediastinum and had no feeding vessels, neuroblastoma and sequestration were ruled out.

On further work up, the tuberculin skin test was negative, tumour markers were normal and there were increased levels of all immunoglobulins. Quantitative oxidative burst activity ('Phagoburst' kit, Glycotope, Biotechnology) was abnormal (Peptide formyl-methionyl-leucly-phenylalanine 7.8%, phorbol myristate acetate 15.8% and O.E. Coli 16.2%; normal values 1–10%, 98–100% and 97–100% respectively). He was diagnosed as having chronic granulomatous disease, which was later confirmed with molecular analysis revealing a hemizygous X-linked c.972C>A (p.Tyr324Ter) mutation in the gp91phox CYBB gene.

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Case report (continued)

Follow up chest computed tomography showed complete regression of the pulmonary consolidations 3 months after the initial presentation, leaving fibroatelectatic changes.

The mass-like lung consolidations were assumed to represent the lung infection and associated granulomatous reaction. Allogeneic haematopoietic stem cell transplantation was performed from an HLA-matched unrelated donor at 10 months of age. Complete chimera was obtained 6 months after transplantation and graft vs host disease did not develop.

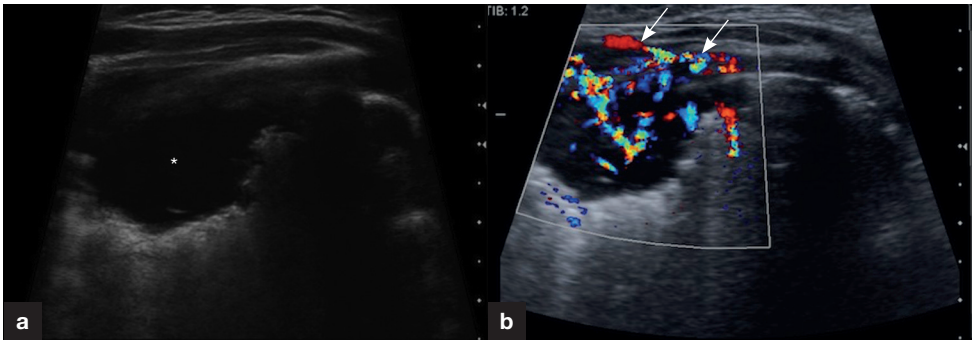

Figure 1. a. B mode and (b) colour Doppler images of lung consolidation (asterisk) located in the right upper lobe revealing extension beyond lungs through chest wall (arrows).

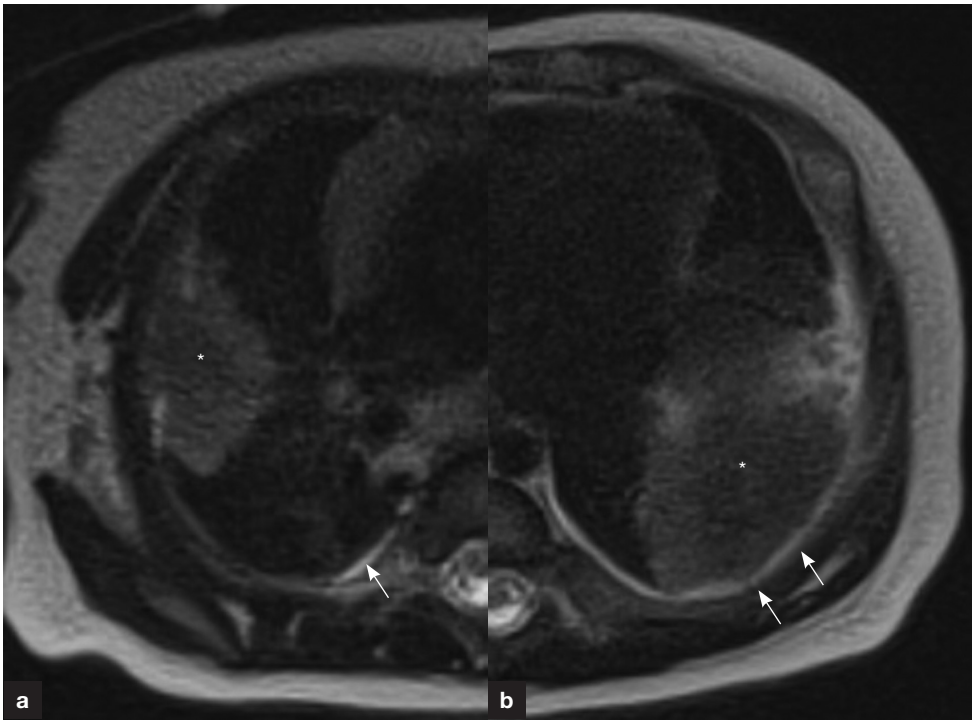

Figure 2. T2-weighted magnetic resonance images revealing peripherally located lung consolidations (asterisk) of (a) right upper and (b) left lower lobes. Pleural involvement is also apparent on both hemithoraces (arrows).

Discussion

Chronic granulomatous disease is characterised by defective production of oxygen radicals by phagocytes. This impairs the action of the nicotinamide adenine dinucleotide phosphate oxidase complex, which prevents phagocytes being able to engulf microorganisms (Winkelstein et al, 2000; Martire et al, 2008; Mahdaviani et al, 2013). The lung is most commonly involved, so pneumonia may be the presenting symptom before chronic granulomatous disease has been diagnosed (Winkelstein et al, 2000). There is a

Learning points

- When persistent mass-like lung consolidations are encountered in neonates, immune deficiency syndromes should be considered in the differential diagnosis.
- Persistent, peripherally located mass-like lung consolidations should raise suspicion of chronic granulomatous disease when the chest wall is involved.
- Colour Doppler ultrasound may help detect chest wall involvement of lung infection before it is seen on computed tomography and magnetic resonance imaging of the chest.
- Owing to concerns about radiation exposure, particularly in children, peripherally located persistent lung consolidations should be evaluated with ultrasound or colour Doppler ultrasound following chest X-ray rather than computed tomography.

predisposition to infections with microorganisms such as *Aspergillus and Staphylococcus* spp. (Liese et al, 2000; Towbin and Chaves, 2010; Arnold and Heimall, 2017).

Pulmonary infection may manifest as focal areas of consolidation, ground glass opacities or small nodules (Khanna et al, 2005). In one-third of patients, the lung infection extends directly to the chest wall and may cause osteomyelitis of the ribs (Liese et al, 2000; Khanna et al, 2005; Chiriaco et al, 2016; Arnold and Heimall, 2017). In the present case, the mass-like consolidations of the lungs emerged in the neonatal period and persisted until the third month. Chest wall extension was first seen on colour Doppler ultrasound, and magnetic resonance imaging revealed accompanying involvement of the pleura. Aspergillus is the most common causative agent (Kawashima et al, 1991) of lung infection extending through the chest wall in patients with chronic granulomatous disease, but neither blood cultures nor serology were positive for Aspergillus in this case.

In an infant presenting with persistent mass-like lung consolidation with involvement of pleura and chest wall, immune deficiency syndromes should be kept in mind. Chest ultrasound should be used to evaluate peripherally located consolidations, following chest X-ray. Extension of the chest wall may be detected with ultrasound before it is seen on computed tomography and magnetic resonance imaging. Since magnetic resonance imaging was sufficient to reveal the consolidations, pleural and chest wall involvement, this may be a preferred radiation-free imaging modality for follow up rather than computed tomography.

The gold standard diagnostic test for chronic granulomatous disease is oxidative burst activity. Since the X-linked form of the disease is associated with a more worrisome course, genetic sequencing will help identify patients who might benefit from haematopoietic stem cell transplantation (Connelly et al, 2018).

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