Pulmonary aspergillosis appearing as chronic nodular disease in chronic granulomatous disease

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Abstract. Chronic nodular pneumonia is unusual in children. Three children are described who presented with diffuse nodular pulmonary disease and in whom lung biopsy demonstrated Aspergillus infection. One child was known to have chronic granulomatous disease of childhood (CGD) and further investigation demonstrated CGD in the other two patients as well. These cases indicate that Aspergillus infection and CGD should be considered in the differential diagnosis in children who present with chronic diffuse nodular pneumonia.

The development of chronic nodular pneumonias in children is unusual. The conditions most commonly associated with such a pattern on the chest radiograph include malignancies and certain kinds of disseminated infection such as miliary tuberculosis [1]. We recently encountered three children who demonstrated diffuse nodular pulmonary disease. One of these children was known prior to the development of his pneumonia to have chronic granulomatous disease of childhood (CGD), a genetic defect of polymorphonuclear leukocyte (PMN) metabolism and function associated with frequent severe infections. The other two children in whom a

Fig. 1. a and b Chest radiograph obtained on a 8-year-old male 2 weeks after development of a cough and low grade fever. The PA projection shows small nodules disseminated throughout the lung without consolidation, adenopathy, or fluid. The lateral projection likewise confirms the diffuse pulmonary nodules due to the Aspergillus infection
The phagocytes from patients with CGD are able to move and ingest microorganisms normally, but lack the normal postphagocytic respiratory oxidative burst which allows the elaboration of antimicrobial agents such as superoxide, hydrogen peroxide and hydroxyl radical, critical for the killing of certain microorganisms [2, 3]. Children with CGD often develop infections early in life, sometimes within the first weeks after birth. Common clinical findings in CGD include hepatosplenomegaly, generalized lymphadenopathy, anemia and hypergammaglobulinemia.

Fungal infections are often encountered in patients with CGD, but bacterial infections are much more common. The usual pathogenic organisms are catalase-positive microorganisms including *Staphylococcus aureus*, *Klebsiella*, *Escherichia coli*, *Serratia marcescens*, *Proteus*, and *Salmonella* [4]. Organisms which produce hydrogen peroxide but are catalase-negative (such as streptococci, pneumococci, or lactobacilli) are not major pathogens since these organisms are killed normally by CGD phagocytes [2, 3]. Fungal infections are documented in approximately 20% of children with CGD. The most common pathogens are *Aspergillus* strains followed by *Candida albicans* and *Torulopsis glabrata* [3].

The lungs represent the most common site of infection in CGD. Bacterial pneumonias in patients with CGD may be lobar or subsegmental and patchy. “Encapsulated” round pneumonias have also been described [5]. *Staphylococcus aureus* is the most commonly isolated organism. *Streptococcus pneumoniae*, a catalase-negative organism, while a cause of pneumonia in patients with CGD, is not a species with increased virulence in this patient population, and thus, pneumonias caused by this organism lack any characteristic radiographic pattern that would alert the clinician or radiologist to the underlying problem of CGD.

### Discussion

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Fungal pneumonia in CGD is most commonly due to one of the *Aspergillus* strains [6, 7]. The radiographic findings in *Aspergillus* pneumonia are quite varied. Segmental or lobar consolidation similar to bacterial pneumonia may occur. Cavitation sometimes occurs within an area of consolidation. Pulmonary involvement may be unilateral or bilateral. Multiple subsegmental ill-defined densities may occur. Miliary nodules similar in appearance to miliary tuberculosis may occur, as demonstrated in our cases [8]. The aggressive nature of *Aspergillus* infection is indicated by the occurrence of extension through tissue planes, with invasion of the thoracic wall and ribs [7, 9].

In the patients with CGD that we saw, the initial presenting chest radiograph demonstrated a purely nodular pattern of disease in the lungs. This pattern is an uncommon presentation in an otherwise well child. It is probably best epitomized by that seen in hematogenous infections such as miliary tuberculosis. However, this pattern is not specific (Table 1).