Propionibacterium acnes Chest Infections in Patients with Chronic Granulomatous Disease: Case Reports

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Antibiotic prophylaxis in patients with chronic granulomatous disease (CGD) has decreased the prevalence of infections, but uncommon microorganisms are being observed more frequently. Propionibacterium acnes, a saprophyte of the skin, is generally not involved in infections other than acne. Two cases of P. acnes extracutaneous infections in teenagers with CGD are reported.

Chronic granulomatous disease (CGD) is an inherited primary immunodeficiency resulting from an inability of phagocytic cells to kill microorganisms, particularly fungi or bacteria. One of the manifestations of CGD is abnormally low nicotinamide adenine dinucleotide phosphate (NADPH)–oxidase activity, and this exposes patients to severe and repeated infections, especially with intracellular catalase-positive organisms. Propionibacterium acnes, a saprophyte of the skin, has not previously been reported to infect patients with CGD. We report 2 cases of P. acnes chest infections in pediatric patients with CGD.

Patient 1. Patient 1, a 10-year-old boy, was the fourth child of nonconsanguinous healthy parents. CGD had been diagnosed in 1 brother and 1 sister who experienced recurrent bacterial and aspergillar infections that led to the death of both children. In patient 1, CGD was diagnosed at birth by use of the nitroblue tetrazolium test. In addition, a homozygous mutation in the gene encoding gp91-phox, a subunit of NADPH, was detected (C676T in exon 7, resulting in a stop codon R226X). The child had received prophylactic therapy with trimethoprim-sulfamethoxazole (TMP-SMZ; 20 mg/kg and 4 mg/kg per day, respectively) and itraconazole (10–20 mg/kg per day), but, in accordance with local guidelines, the patient did not receive IFN-γ [1]. Bone marrow transplantation was not considered in the absence of a human leukocyte antigen–identical sibling.

The patient presented with cutaneous abscess associated with Serratia marcescens at 3 years of age and common pneumonia at 5 years of age. Results of serologic testing for Aspergillus species became positive at the age of 3 years, but there was no clinical or radiological evidence of active aspergillosis at any time. At the age of 10 years, he developed persistent cough and mild fever. Analysis of chest radiographs revealed a mediastinal mass. The WBC count, hemoglobin level, and erythrocyte sedimentation rate were normal. A CT scan and an ultrasonograph revealed a liquid mass in the superior mediastinum. A diagnostic aspiration was performed. Direct bacterial examination showed many gram-positive bacilli that were identified as P. acnes. The isolates were resistant to cotrimoxazole and metronidazole and susceptible to penicillin, doxycycline, rifampicin, erythromycin, and vancomycin. The results of repeated investigations for Aspergillus species and other fungal or bacterial microorganisms were consistently negative. A combination of penicillin V and doxycycline was administered for 3 weeks. All symptoms disappeared rapidly at the end of the treatment, and the findings of chest tomodensitometry were normal. The child did not display any signs of acne during the infection.

Patient 2. Patient 2 was the fifth child of nonconsanguinous healthy parents. CGD had previously been diagnosed or suspected in 1 brother and 3 sisters (2 of whom died of severe bacterial infections within the first months of life, before diagnosis). In this patient, CGD was diagnosed soon after birth, and she received prophylaxis involving TMP-SMZ (20 mg/kg and 4 mg/kg per day, respectively) and itraconazole (10–20 mg/kg per day). Bone marrow transplantation was not considered in the absence of a human leukocyte antigen–identical sibling.

At the age of 6 weeks, she developed cutaneous abscess associated with Propionibacterium acnes. At 3 years of age, Serratia marcescens was isolated, but, in accordance with local guidelines, the patient did not receive IFN-γ [1]. Bone marrow transplantation was not considered in the absence of a human leukocyte antigen–identical sibling. At the age of 6 weeks, she developed Aspergillus fumigatus pneumonia, which was successfully treated with amphotericin B for 12 months. At the age of 6 years, she developed facial cellulitis, and at 8 years, perirectal abscess. No microorganism was identified, but symptoms resolved while the patient received prolonged empirical antibiotic therapy. At the age of 10 years, chest pain, cough, and fever developed. Clinical examination disclosed pleural rubbing and atypical acne; this was treated with locally administered erythromycin.

Analysis of chest radiographs revealed alveolar pneumonia of the middle lobe. The WBC count was 14.7 × 10³ cells/L and...
the neutrophil count was \(11.2 \times 10^7\) neutrophils/L. The erythrocyte sedimentation rate was 120 mm/h, the fibrinogen level was 6.8 g/L, and the C-reactive protein level was 55 mg/L. The results of serologic testing for *Aspergillus* species were negative. Empirical antibiotic treatment consisted of imipenem, ciprofloxacin, and amikacin. An analysis of a sample of the lung, guided by tomodensitometry, definitely ruled out *Aspergillus* infection. Anatomocpathologic examination revealed a fibrous pleurisy and chronic inflammatory lesions of the lung, but the results of Gram, Grocott, and Ziehl staining were all negative. Bacterial cultures were positive for *P. acnes* after 10 days. The isolate was resistant to cotrimoxazole and susceptible to penicillin, doxycycline, erythromycin, vancomycin, and rifampicin. Treatment was changed to orally administered rifampicin (20 mg/kg per day) and amoxicillin (100 mg/kg per day) administered for 6 weeks. Complete clinical and biological remission was achieved within 3 weeks. The findings of chest radiographs were normal at the end of treatment and at the last follow-up visit 3 years later.

**Discussion.** The microorganisms that most frequently infect patients with CGD are *Staphylococcus aureus*; gram-negative bacteria, such as *Pseudomonas, Klebsiella, Serratia*, and *Nocardia* species; mycobacteria; and *Aspergillus* species [2]. Chest infections are common in patients with CGD. Many cases of pneumonia have been described, and the organisms usually involved are *Aspergillus fumigatus* and *Nocardia* and *Pseudomonas* species. None of these microorganisms were found in any of the cultures for either of our patients, despite use of multiple staining techniques and adequate culture conditions.

*P. acnes* infections have already been described in patients without CGD at several sites other than the skin. Most of these infections occurred after surgery and were related to the presence of foreign material. The major clinical features are osteomyelitis [3] or CNS infections [4]. Some chest infections have also been reported, including chronic endocarditis [5] and bronchopneumonia [6, 7]. *P. acnes* infections have also been described in patients treated with chemotherapy [7] or corticosteroids (reviewed in [3]) and in 1 neutropenic patient [8]. This is consistent with a general disturbance of phagocytic cell function that favors these infections. To our knowledge, the 2 pediatric cases we report here are the first cases of *P. acnes* visceral infection ever reported in patients with CGD. Various authors have emphasized the difficulties of identifying anaerobic species, such as *P. acnes* [1], and positive cultures may be a consequence of contamination from the skin. In the 2 patients we studied, the rigorous surgical conditions observed during the puncture procedure make contamination of the sample unlikely.

*P. acnes* is a gram-positive, non-spore-forming anaerobic catalase-positive bacillus. Catalase reduces \(H_2O_2\) to \(H_2O + O_2\), and it has been suggested that this allows microorganisms to evade the host microbicidal \(H_2O_2\)-derived oxidants. Catalase production may thus be a microbial pathogenicity factor in CGD. However, this view has been questioned [9]. Colonization by *P. acnes* develops just before puberty, when the sebaceous glands enlarge. The bacteria proliferate optimally in the closed comedones that are characteristic of early adolescence. Moreover, the pathogenic role of *P. acnes* in acne has been established [10]. Only 1 of our patients presented with acne at the time of infection, but both children were pubescent. Acne, the effect of which was like surgical skin incision, may have been the origin of the invasive *P. acnes* infections, as has been reported elsewhere [3]. The extreme susceptibility to catalase-positive organisms just before and at the age of development of acne may well favor *P. acnes* infections in patients with CGD.

Of interest, the infections developed while the patients were receiving prophylactic treatment that included TMP-SMZ, to which *P. acnes* was resistant. This illustrates one of the problems of the emergence of drug-resistant microorganisms in immunodeficient patients receiving prolonged prophylactic antibiotic therapy [11].

*P. acnes* infection should be considered when teenagers with CGD experience infections, even in the absence of acne, and microbiological analyses should be conducted carefully. Even aggressive investigations, such as lung biopsy, may be justified in some cases, because only appropriate antibiotic treatment may allow complete remission, as we report here.

**References**