Letter to the Editor

Skin ulcers and disseminated abscesses are characteristic of *Serratia marcescens* infection in older patients with chronic granulomatous disease

To the Editor:

Chronic granulomatous disease (CGD) is a primary immune deficiency resulting from mutations in any of 4 subunits of phagocytic cell NADPH oxidase. Patients with CGD are at risk for infections with catalase-positive bacteria and fungi.[1-3] *Serratia marcescens* infection of bone and soft tissue is a common presentation of CGD in infancy.[4-6] In older children and adults with CGD, infection with *Staphylococcus aureus*, *Burkholderia cepacia*, and *Nocardia* species or fungi such as *Aspergillus* make up the majority of infections.[3,4] Our experience indicates *S marcescens* remains a significant cause of infection in older children and adults with CGD. These infections have a pattern different from that seen in infants with CGD. Osteomyelitis is less common, skin infections form poorly healing ulcers,[7] and infections frequently occur at multiple sites.

We describe 16 episodes of *S marcescens* infections in 15 patients 8 to 39 years of age with CGD followed between 1999 and 2008 at the National Institutes of Health (Table I). Only patients with culture documented *S marcescens* were included in this report. All patients were participants in an Institutional Review Board–approved study of the natural history of CGD. Written informed consent specifically allowed study of infections and other complications of CGD.

Three patients had additional documented *S marcescens* infection at some time before the index period under review for this report. One of these 3 patients had a history of 2 previous *S marcescens* lung infections. Each of these previous infections antedate the index review period by at least 4 years. We did not include these older episodes of infection because detailed information about those infections was deemed less reliable.

During the review period, some patients had 1 or more infections characteristic of CGD with organisms other than *S marcescens*. Only 1 (patient 13, Table I) developed 2 episodes of infection with *S marcescens*. We concluded that they were distinct *Serratia* infections and not relapse of the first infection, because those 2 infections were 3 years apart. This assumption was consistent with a previous report noting that for most infections in CGD, reinfection is more common than persistent infection.[8]

Sites of infection included lung parenchyma (6), vertebrae (1), lymph nodes (3), deep intra-abdominal or pelvic abscess (4), deep soft tissue abscess of limb (6), and superficial infection of skin (2). Seven patients were found to have metastatic infection at multiple sites (Table I).

None of the 6 patients presenting with pneumonia had clinically apparent secondary sites of *S marcescens* infection. Conversely, 7 of the 10 episodes of *S marcescens* infection that did not involve pneumonia presented with widely metastatic dissemination. The characteristics of this dissemination included more than 1 noncontiguous site of skin abscess, deep muscle abscess in limbs, and/or abscess in internal organs. A particularly informative example was patient 9 (Table I), who presented with skin and soft tissue abscesses (Fig 1). Epididymitis, apparent on physical examination, prompted pelvic magnetic resonance imaging that revealed a prostate abscess (Fig 2).

Mixed infection in the same biopsy sample (*S aureus* or *Streptococcus anginosis* in addition to the *Serratia*) was identified in 4 patients, but in all cases, the predominant organism by colony count appeared to be *S marcescens*. Although the significance and relative impact of these additional organisms on the clinical course was unknown, antibiotic coverage was adjusted as necessary to include coverage for treatment of these additional

TABLE I. CGD mutation, age at diagnosis of infection, clinical sites of infection, and length of antibiotic therapy in patients presenting with *S marcescens* infections

Patient no.	CGD defect	Age at infection (y)	Sites of infection†	Approximate length of treatment (d)
1	gp91^{phox}	30	Lung	36
2	p47^{phox}	9	Lung	180
3	gp91^{phox}	15	Lung	31
4	gp91^{phox}	19	Deep calf and arm abscesses	97
5	p47^{phox}	13	Lung	50
6	gp91^{phox}	19	Arm abscess	14
7	gp91^{phox}	8	Axillary lymph node abscess	14
8	gp91^{phox}	27	Lung	14
9	gp91^{phox}	20	Arm, leg and scrotal abscesses, epididymitis, prostatic abscess	180
10	p47^{phox}	24	Face and arm abscesses	55
11A*	gp91^{phox}	26	Lung	140
11B*	gp91^{phox}	29	Arm abscess	55
12	gp91^{phox}	20	Submental abscess, nares	14
13	gp91^{phox}	20	Peripancreatic abscess and periaortic lymph node	104
14	gp91^{phox}	24	Multiple paraspinal abscesses, gluteal abscess, hip osteomyelitis	90
15	gp91^{phox}	39	Cervical lymph node	21

The gp91^{phox} refers to deficiency of this glycoprotein subunit of the phagocyte oxidase that is the cause of the X-linked form CGD. The p47^{phox} refers to deficiency of this protein subunit of the phagocyte oxidase that is the cause of the most common autosomal-recessive form of CGD.

Phox, Phagocyte oxidase.

*Patient 11 had 2 documented episodes of *S marcescens* during the review period.

†Patients 4, 7, 9, 10, 12, 13, and 14 had multiple sites of infection, whereas, each of the other patients had a single anatomic site of infection.

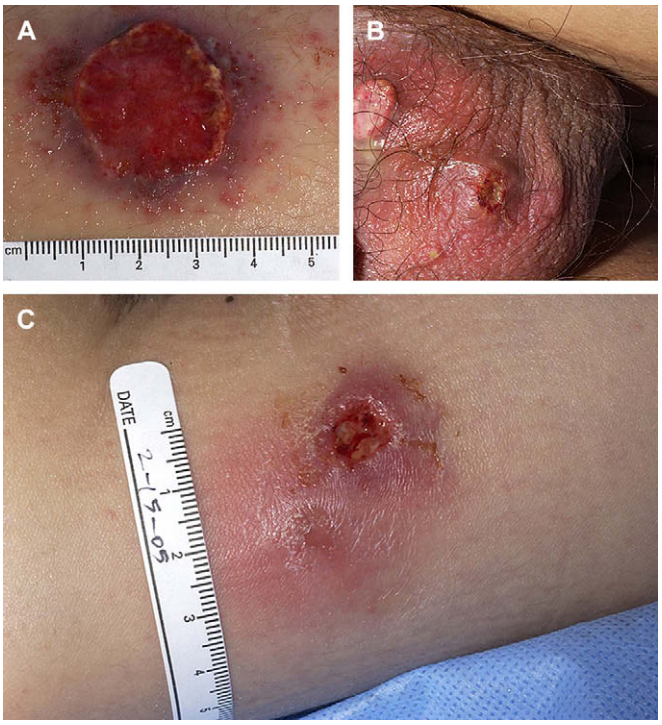

FIG 1. Photograph of skin ulcers resulting from *S. marcescens* infection in patient 9. **A,** Ulcerating lesion on the inner right thigh. **B,** Ulcerating lesions on the left scrotum. **C,** Lesions on the inner aspect of the right upper arm. Note that the upper lesion has ulcerated, whereas at the time of this photograph the lower area of infection has not yet ulcerated, but also went on to ulcerate.

organisms. In all cases, the *S marcescens* isolate was sensitive to a broad range of antibiotic classes including carbapenems, quinolones, cephalosporins, aminoglycosides, extended-spectrum β-lactams, and trimethoprim-sulfamethoxazole. There was a tendency to include or use a quinolone as primary treatment in most cases. If a second antibiotic was used, it tended to be either an intravenous carbapenem or intravenous high-dose trimethoprim-sulfamethoxazole. In all of the cases, these *Serratia* infections occurred in a setting where standard long-term infection prophylaxis had included trimethoprim-sulfamethoxazole. Compliance with this long-term prophylaxis was variable. Notably, 10 of 16 of the *Serratia* isolates were sensitive to this agent. The majority of patients received intravenous antibiotic therapy with 2 agents for at least a portion of the treatment period. One patient was treated with 3 intravenous antibiotics, and 1 patient was treated with only 1 intravenous antibiotic (levofloxacin). Two patients received oral quinolone (ciprofloxacin or levofloxacin) therapy only (lymph node infection in 1 case and superficial abscess in the other, both without metastatic infection). Duration of therapy varied according to severity of the infection (range, 14-180 days; mean, 81 days; median, 55 days). All infections were successfully eradicated, and all patients survived the infection.

Our current report represents the largest aggregate detailed description of *Serratia* infections in older children and adults with CGD. Previous reports describe either single patients or small case series,[4-7] primarily in infants and young children. In other publications, the incidence of *Serratia* infection is reported incidental to an overall report of a registry of patients with CGD without detailed description of the characteristics of the *Serratia*

FIG 2. Magnetic resonance image of the pelvis of patient 9. The 2 bright, confluent, round objects in the center of this image represent a large abscess in the prostate.

infections.[3] The important findings of our study reporting the details of 16 episodes of *S marcescens* infections in 15 older children and adults with CGD are the following: (1) *Serratia* osteomyelitis was uncommon compared with that reported in infants with CGD; (2) *Serratia* infections of skin form large, poorly healing ulcers; (3) *Serratia* pneumonia in our series was not associated with clinically apparent infection of extrapulmonary sites; (4) 7 of the 10 (70%) nonpulmonary infections with *Serratia* in our series were associated with metastatic spread of infection to multiple sites. As clinically indicated by history, examination, or laboratory findings, this group of patients often may require additional imaging studies (computed tomography, magnetic resonance imaging, or PET scan) to demonstrate the presence of cryptic sites of infection. Finally, we note that all the infections in our series were eventually eradicated, indicating that full recovery from *Serratia* infection in CGD is an expected outcome with recognition of the variable presentation of this disease and with proper management.

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