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***Rothia aeria* Neck Abscess in A Patient with Chronic Granulomatous Disease: Case Report and Brief Review of the Literature**

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Abstract

Rothia aeria caused a necrotic lymphadenitis and neck abscess in a patient with CGD. This infection was aggressive, crossed tissue planes, required two surgeries, as well as prolonged antibiotics for complete resolution. *Rothia aeria* is a rare pathogen that can be added to the spectrum of agents causing disease in CGD, a finding that further reinforces the importance of microbiologic identification of infections in this patient population.

Keywords

Chronic granulomatous disease; *Rothia aeria*; neck abscess; lymphadenitis

Introduction

Chronic granulomatous disease (CGD) is a phagocyte defect characterized by recurrent life-threatening bacterial and fungal infections due to defective NADPH oxidase activity leading to impaired superoxide and downstream hydrogen peroxide (H₂O₂) production. This defect can be inherited as an X-linked trait, affecting the NADPH oxidase gp91^{phox} subunit (*CYBB* [cytochrome b-245, alpha polypeptide]), or as an autosomal recessive trait, affecting the NADPH oxidase subunits p22^{phox} (*CYBA* [cytochrome b-245, beta polypeptide]), p47^{phox} (*NCF1* [neutrophil cytosolic factor 1]), p67^{phox} (*NCF2* [neutrophil cytosolic factor 2]), and p40^{phox} (*NCF4* [neutrophil cytosolic factor 4]) [1]. These recurrent infections primarily

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affect the lung, skin, lymph nodes and liver, and are typically due to a rather narrow spectrum of bacteria and fungi, including *Staphylococcus aureus*, *Serratia marcescens*, *Burkholderia cepacia* complex, *Nocardia* species and *Aspergillus* species. The mechanisms behind these pathogen susceptibility patterns remain to be fully elucidated and are likely complex [2]. Emerging pathogens (e.g. *Granulibacter bethesdensis*) [3], previously misidentified pathogens (e.g. *Neosartorya udagawae*) [4] and common pathogens (e.g. streptococci) [5] have also been identified in CGD.

We report necrotic cervical lymphadenitis due to *Rothia aeria* in a patient with CGD. This infection was aggressive, crossed tissue planes, and required two surgical interventions, as well as a prolonged course of antibiotics for complete resolution.

Case Presentation

A 19 year-old Caucasian man from Ohio presented with an eight-week history of a right-sided neck mass while being maintained on prophylactic trimethoprim-sulfamethoxazole, moxifloxacin and posaconazole. The mass began as a small bump that waxed and waned. After 2 weeks, it became fluctuant, erythematous, and tender measuring approximately eight centimeters in diameter. A prednisone taper was without clinical response. He denied any fevers, chills or sweats, but did have a ventriculoperitoneal shunt catheter tracking posterior to the mass.

The patient was diagnosed with X-linked CGD at birth due to a largeintragenicdeletion in *CYBB* but sparing Xk based on a positive family history. At 5 months of age, a ventriculoperitoneal shunt was placed for hydrocephalus. This was complicated by fungal meningitis, resulting in its removal and subsequent replacement at 16 months of age. At 11 years he had sepsis of unclear etiology and later developed *Aspergillus fumigatus* pneumonia. By 15 years he developed a lower gastro-intestinal bleed, which was diagnosed as CGD proctitis, treated with pramoxine-hydrocortisonefoam for 1 year. He had no history of infectious contacts, foreign travel, recent dental or surgical procedures and had been clinically well for 3 years prior to his current presentation with the exception of one episode of left neck lymphadenitis of unknown etiology.

He was afebrile with an 8 cm fluctuant mass overlying the right sternocleidomastoid muscle. Oro-pharynx was clear with no evidence of poor dentition or dental abscesses. His C-reactive protein was 24 mg/L and his erythrocyte sedimentation rate 7 mm/h. Complete blood count was normal. Computed axial tomography (CT) of the neck with intravenous contrast showed a 6×3×1.5 cm fluid density with enhancing periphery that was partially ventral to the right sternocleidomastoid muscle compatible with a subcutaneous soft tissue abscess and two subcentimeter foci deep to the sternocleidomastoid muscle (Fig. 1a). Ultrasound confirmed the mass surrounding the ventriculoperitoneal shunt catheter.

Incision and drainage released frank pus; a drain was placed. Gram stain showed few neutrophils and no organisms. Cultures in liquid media only grew a branching gram-positive rod identified as *Rothia* species by MALDI-TOF MS (see below). The patient received amoxicillin-clavulanate for 14 days. Two months later he returned with 2 days of right neck swelling and tenderness with a pustule at his previous incision. CTscan of the neck showed

interval resolution of the previous abscess overlying the right sternocleidomastoid. However, necrotic nodes deep to the sternocleidomastoid muscle (Fig. 1b) led to a right neck dissection of a granulomatous lymphadenitis and intramuscular sternocleidomastoid abscess. Gram stain again showed few neutrophils without organisms. Culture of the abscess fluid grew a gram-positive organism. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) using a MALDI-TOF MicroFlex LT mass spectrometer (Bruker Daltonics, Billerica, MA) identified it as *Rothia* species with best match to *R. aeria* (highest score 0.20). Full 16S rRNA gene sequencing (~1,500 bp) confirmed the species level identification with 99.8 % match to *R. aeria* type strain. Antibiotic susceptibility testing performed by the Microscan microdilution method using the Streptococcus panel showed the following minimal inhibitory concentrations [MIC] in µg/ml: penicillin (MIC0.06), clindamycin (MIC0.5), azithromycin (MIC<0.25), levofloxacin (MIC>4) and meropenem (MIC>0.5).

Meropenem was switched to high dose penicillin based on in vitro sensitivities. He was discharged on amoxicillin 1 g and probenidol 500 mg, each orally three times daily. After 2 weeks a right neck hematoma was drained. The patient continued to improve clinically. His inflammatory markers returned to normal, and follow up CT scan 2 months later showed no lymphadenopathy, masses or abscesses (Fig. 1c and d).

Discussion

R. aeria belongs to the genus *Rothia*, family *Micrococcaceae*. The genus *Rothia* was proposed in 1967 with *R. dentocariosa* as the type species (first isolated from dental caries). Only in 2000 was the second species, *R. nasimurium*, added, followed by *R. mucilaginoso*, and *R. amarae*. *R. aeria* was first identified in 2004, and like most *Rothia* species, is an oral colonizer. However, it owes its name to its first isolation from air and condensation water samples from the Russian space laboratory, Mir. *Rothia* species are aerobic, Gram-positive, mostly catalase-positive, non-acid-fast, non-spore-forming, non-hemolytic, and non-motile bacteria that may appear coccoid, cocco-bacillary or filamentous [6].

In the general population, infections with *Rothia* species are rare. Most reported cases are due to infections with *R. dentocariosa*, followed by infections with *R. mucilaginoso*. *R. dentocariosa* has been associated with severe diseases such as endocarditis [7] and bacteremia [8], peritonitis (especially in the peritoneal dialysis population) [9], pneumonia [10], septic arthritis [11], and ocular infections such as corneal ulcers [12] and endophthalmitis [13]. *R. mucilaginoso* is less commonly reported, but has been associated with bacteremia [14], peritonitis [15], meningitis [16], pneumonia [17], and septic arthritis [18]. Only four infections due to *R. aeria* have been reported including sepsis, septic arthritis, acute bronchitis and pneumonia (Table I). In three out of four cases, the patients were on immunosuppressive medications, and two cases were associated with dental pathology. All patients survived antibiotic therapy.

Patients with CGD are generally prone to infections by catalase-producing organisms, which are thought to degrade both microbial and host-derived H₂O₂. *R. aeria* is a catalase-positive organism and an oral colonizer. Our patient's risk factors for infection with *R. aeria* included

his underlying immunodeficiency with CGD and low dose intermittent steroids for CGD colitis. He did not, however, have poor dentition. *R. aeria* is typically resistant to both levofloxacin and meropenem.

This unusual and fastidious pathogen caused recurrent, extensive, persistent disease in a patient with CGD, a rare genetic phagocyte disorder. *R. aeria* should be suspected and pursued diagnostically in the CGD population, especially when conventional microbiological methods are unrevealing. *Rothia aeria* is a rare pathogen that can be added to the spectrum of agents causing disease in CGD, a finding that further reinforces the importance of microbiologic identification and susceptibility testing in infections in this patient population. This is the first reported case of necrotizing cervical lymphadenitis due to *R. aeria* in a patient with CGD, and to date the only soft tissue infection caused by this organism reported in the literature.

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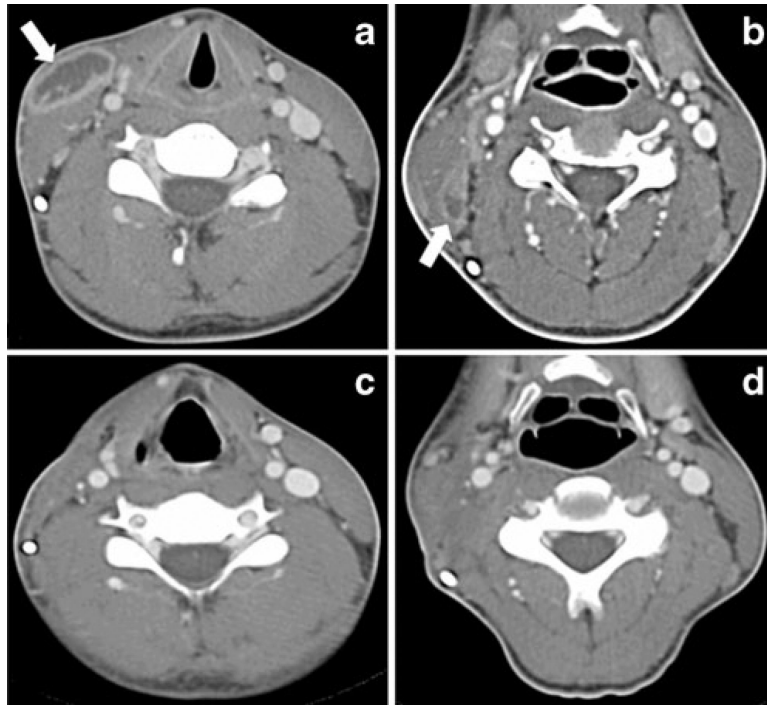


Fig. 1.

A CT scan of the neck at presentation. Irregular $6 \times 3 \times 1.5$ cm fluid density with enhancing periphery. b CT scan of the neck during second admission, prior to neck dissection. Interval resolution of the abscess overlying the right sternocleidomastoid with interval development of a cluster of necrotic nodes (level II B) deep to the right sternocleidomastoid muscle. c and d CT scan of the neck 2 months after neck dissection. Evidence of previous right neck surgery with loss of the fascial fat planes. The right sternocleidomastoid muscle is diminished with right vocal cord paralysis. No pathologic lymphadenopathy or neck masses are seen

Table IReported cases of *Rothia aeria* infection

Reference	Age/Gender	Risk Factor	Presentation	Treatment	Outcome
Present case	18 years/male	X-linked CGD	Neck abscess with necrotic lymphadenitis	Penicillin G followed by amoxicillin and probenecid	Survived
[19]	88 years/female	Dental abscesses, methotrexate and prednisone for rheumatoid arthritis	Septic shoulder	Penicillin G, 14 day course	Survived
[20]	66 years/male	Etanercept for rheumatoid arthritis, diabetes	Acute bronchitis	Amoxicillin and cefpodoxime, 3 week course followed by amoxicillin-clavulanate and moxifloxacin, 1 week course	Survived
[21]	53 years/female	Azathioprine and steroids for neurosarcoidosis	Cavitary pneumonia	Benzylpenicillin, 3 month course followed by amoxicillin, 5 month course	Survived
[22]	Neonate/female	Mother underwent extraction of decayed tooth 4 days prior to delivery without antibiotic prophylaxis	Sepsis	Ampicillin and cefotaxime, 11 day course	Survived