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LETTER TO EDITOR

Enterobacter cloacae, a Rare Cause of Cervical Lymphadenitis in X-Linked Chronic Granulomatous Disease

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To the Editor:
Chronic granulomatous disease (CGD) is a rare, life-threatening inborn error of immunity, characterized by severe recurrent catalase positive bacterial and fungal infections [1]. Though the underlying genetics of CGD are heterogeneous, all cases are caused by defects in the phagocyte nicotinamide adenine dinucleotide phosphate (NADPH) oxidase complex, which facilitates the creation of superoxide species. Loss of any one of the six protein components of the NADPH complex can cause CGD, but between 65 and 70% of cases in Europe and North America result from mutations in the X-linked *CYBB* gene that encodes the gp91phox subunit (X-CGD) [1]. The vast majority of severe infections in patients with CGD are caused by *Staphlococcus*, *Serratia*, *Klebsiella*, *Aspergillus*, and *Burkholderia* species; however, uncommon pathogens, including *Granulibacter bethesdensis* and *Enterobacteria cloacae*, have been identified as the cause of severe infections in patients with CGD [1]. In order to keep patients with CGD safe in a landscape of shifting antibiotic resistances, it is critically important to document novel pathogens that emerge and design our interventions appropriately.

Recently, a 6-year-old boy with a *CYBB* nonsense mutation (c.1272 G > A, p. Trp424Ter) and a history of *S. aureus* osteomyelitis, hepatic abscesses, and inflammatory bowel disease was admitted to our immunology service because of acute onset of a tender, rapidly growing right-sided anterior cervical lymphadenitis without associated fever. The patient's mother stated the abscess was first appreciated just 1 day prior to admission and developed despite full compliance with a standard anti-microbial prophylaxis regiment (daily itraconazole and trimethoprim-sulfamethoxazole). Upon admission, the patient's exam was notable for a $4.2 \times 2.4 \times 2.1$ cm fluctuant right cervical lymphadenitis that spanned from the middle of the neck to the posterior auricular space. The swollen mass was mobile, fluctuant, warm, and tender to palpation. There were also several other tender and mobile swollen lymph nodes in the anterior cervical chain. CRP was elevated to 2.1 mg/L, and sedimentation rate was elevated to 71 mm/h. Ultrasound showed no organized or drainable collection, and the patient was treated empirically with ampicillin/sulbactam 1032 mg twice daily for 10 days. A week into his antibiotic course, the patient presented once again, with increased neck swelling and a fever to 38.9 °C. CRP was elevated to 4.9 mg/L, the sedimentation rate was elevated to 89 mm/h, and WBCs were elevated to 17.8 with an absolute neutrophil count of 14,160. An ultrasound showed a $0.7 \times 0.6 \times 0.6$ cm right neck abscess with notable fluid collection. He was re-admitted and started on meropenem and vancomycin. The lymph node was surgically excised, drained, and cultured. A gram stain showed rare white blood cells and no organisms. Culture grew *E. cloacae* resistant to ampicillin/sulbactam and trimethoprim-sulfamethoxazole, but sensitive to levofloxacin, cefepime, ertapenem, meropenem gentamicin, and aztreonam. The patient was discharged home on ciprofloxacin 340 mg twice daily for 28 days and made a full recovery.

Here, we report a case of a pediatric patient with X-CGD who was admitted for anterior cervical lymphadenitis, which grew *E. cloacae*. *E. cloacae* is a catalase positive, gram negative, facultative anaerobic rod that has emerged as an increasingly threatening infectious agent due to its singular capacity to acquire genes that provide resistance to multiple classes of

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antibiotics including last resort carbapenems [2]. Although *E. cloacae* can cause severe nosocomial bacteremia, it remains an exceptionally uncommon pathogen even among immune-compromised individuals [3]. Our report and others describing *E. cloacae* lymphadenitis, pyomyositis, and enterocolitis suggest exquisite susceptibility among CGD patient population [3–5] and suggest *E. cloacae* should be considered in any patient with a NADPH defect and new infectious symptoms despite adherence to antibacterial prophylaxis. The means by which *E. cloacae* spread to our patient's cervical chain is unclear, but hematogenous seeding, possibly from an inflamed colon is one possibility. Additional appearances of *E. cloacae* infections in the CGD patient population may require shifts in prophylaxis and/or treatment to counter *E. cloacae*'s known capacity for multiple antibiotic resistances.

Author Contribution CKP drafted the primary manuscript. RD and JE edited manuscript and provided patient care. NR assisted in drafting the primary manuscript and led clinical decision-making.

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Declarations

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