Chryseobacterium gleum Causing Healthcare-Associated Pneumonia in an Adult Male With Diffuse Large B Cell Lymphoma

FNU Amisha 1, Tyler Fugere 2, Jose Caceres 3, Juan Carlos Rico Crescencio 4, Nathan Falls 1

1. Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, USA 2. Internal Medicine, University of Arkansas for Medical Sciences, Little rock, USA 3. Pulmonary and Critical Care Medicine, University of Arkansas for Medical Sciences, Little Rock, USA 4. Infectious Disease, University of Arkansas for Medical Sciences, Little Rock, USA

Corresponding author: FNU Amisha, amishagupta2012@gmail.com

Abstract
Chryseobacterium species are recognized as an emerging opportunistic bacterial pathogen in nosocomial settings especially in debilitated or immunosuppressed patients and neonates. The ubiquitous distribution in nature, ability to form biofilms with inherent resistance to broad-spectrum antimicrobials, and lack of clinical studies pose a further diagnostic and therapeutic challenge. This case report describes an elderly male with relapsed diffuse large B-cell lymphoma (DLBCL) status post-chemotherapy and radiation who acquired healthcare-associated pneumonia with sputum isolates showing Chryseobacterium gleum and Stenotrophomonas maltophilia. It also includes a review of literature compiling all the previously reported cases with antibiotic susceptibilities, clinical picture, and treatment outcomes.

Introduction
Chryseobacterium gleum was initially known as Flavobacterium gleum, isolated for the first time from high vaginal swabs in 1984 by Homes et al. and was made a separate genus in 1994 [1,2]. C. gleum has been associated with various healthcare-associated infections (HAIs) including septicaemia, pneumonia, urinary tract infections, wound infections, peritonitis, and meningitis [3-7]. The Sentry Antimicrobial Surveillance program sponsored by JMI Laboratories was first established in 1997 and is the longest-running surveillance program that monitors the changes in resistance patterns of pathogens worldwide through centralized testing. In the 1997-2001 Sentry dataset, Chryseobacterium was recognized for the first time as a medically relevant bacterial species, constituting 0.27% of non-fermentative Gram-negative bacilli found in samples from 16 countries. The highest prevalence was among the elderly. Among the 50 isolates, the most common pathogenic member of this genus was C. meningosepticum (24 isolates - 48%) while C. gleum (two isolates - 4%) was the most infrequent [8]. In the 2013-2017 Sentry dataset, C. gleum constituted only 13 of 151,572 isolates worldwide. Out of 13, 11 were isolated from the United States and 10 of them were HAIs. HAIs are a major cause of morbidity and mortality in the United States, affecting 2 million patients annually, causing 90,000 deaths and loss of 28-45 billion US dollars [9]. Hence, it is important for clinicians to recognize this bacterium especially in immunocompromised patients with hematological malignancies as the infection is largely preventable with infection-control practices.

Case Presentation
This is a case of a 71-year-old hypertensive and diabetic male with coronary artery disease status post percutaneous coronary intervention, idiopathic interstitial lung disease (ILD), and stage IVB diffuse large B-cell lymphoma (DLBCL) treated with chemotherapy and radiation which led to worsening of his ILD and the requirement of supplemental oxygen and daily low-dose steroid at home. Three months later, he developed a recurrence of his lymphoma and was started on salvage chemotherapy but his lung function continued to decline. Following three cycles of chemotherapy, he presented to the outpatient oncology clinic with a runny nose and nasal congestion, tested positive for rhinovirus, was breathing appropriately, continued to decline. Following three cycles of chemotherapy, he presented to the outpatient oncology clinic with a runny nose and nasal congestion, tested positive for rhinovirus, was breathing appropriately, continued to decline. On arrival, he was tachypnoeic, tachycardic, febrile, and hypoxic. The examination was significant for rhonchi in bilateral lower lung fields and observed the use of accessory muscles of inspiration. Initial laboratory investigations and chest radiographs are described in Table 1 and Figure 1, respectively. He was admitted to the medical floor and was placed on 4 liters of oxygen via nasal cannula and broad-spectrum antibiotics - azithromycin and cefepime for community-acquired pneumonia. Computed tomographic imaging of the chest is described in Figure 2.
FIGURE 1: A chest radiograph antero-posterior view - poorly inflated lungs with bibasilar fibro-atelectatic changes and bilateral pleural thickening.
### Hemogram

| Investigation               | Value                  | Reference range                      |
|-----------------------------|------------------------|--------------------------------------|
| Hemoglobin (g/dl)           | 10.3                   | 13-17                                |
| WBC K/µL (N/L/M/E/B %)      | 6.99 (69.1/18.7/9.4/0.9/0.3) | 3.6-9.5 (35-65/23-50/4.6-12/0.5-6.5/0.1-1.1) |
| Platelets (K/µL)            | 180                    | 150-450                              |
| MCV (fl)                    | 90.4                   | 80-100                               |
| MCH (pg)                    | 27.5                   | 26-33                                |
| MCHC (g/dL)                 | 30.5                   | 32-36                                |

### Renal chemistry

| Investigation               | Value                  | Reference range                      |
|-----------------------------|------------------------|--------------------------------------|
| Na/K/Ci/CO₂ (mmol/L)        | 136/3.6/102/25         | 135-145/3.5-5.1/98-107/22-32         |
| BUN/Cr (mg/dL)              | 7/0.4                  | 6-20/0.6-1.3                         |

### Liver function test

| Investigation               | Value | Reference range |
|-----------------------------|-------|-----------------|
| AST/ALT (IU/L)              | 23/24 | 15-41/4-45      |
| GGT (IU/L)                  | 20    | 7-50            |
| LD (IU/L)                   | 191   | 100-248         |
| Alk Phos (IU/L)             | 59    | 32-91           |
| Bilirubin, total (mg/dL)    | 0.9   | 0.2-1.2         |

### Miscellaneous

| Investigation               | Value            | Reference range |
|-----------------------------|------------------|-----------------|
| RPP                         | Rhinovirus positive (as was 10 days ago in-office visit) |                  |
| BNP (pg/ml)                 | 41               | ≤100            |
| D-dimer                     | 936              | <250 ng/mL      |
| Procalcitonin (ng/ml)       | 0.05             | 0.00-0.10       |

**TABLE 1: Initial laboratory investigations on admission.**

N/L/M/E/B: neutrophils/lymphocytes/monocytes/eosinophils/basophils; MCV: mean corpuscular volume; MCHC: mean corpuscular hemoglobin concentration; MCH: mean corpuscular hemoglobin; Na/K/Ci/CO₂: sodium/potassium/chloride/bicarbonate; BUN/Cr: blood urea nitrogen/creatinine; AST/ALT: aspartate aminotransferase/alanine aminotransferase; LD: lactate dehydrogenase; Alk Phos: alkaline phosphatase; RPP: respiratory pathogen panel; BNP: brain natriuretic peptide.
On the third day of admission, the patient was desaturated to the low 80s while on a non-rebreather mask, requiring him to be placed on a high-flow nasal cannula (HFNC), and he was transferred to the intensive care unit (ICU). Extensive infectious workup was negative: cultures - blood, urine, and fungal; beta-D-glucan, *Aspergillus galactomannan*; cryptococcal, legionella, Histoplasma and Blastomyces antigens; HHV-6, and CMV. His acute decompensation was thought to be from viral pneumonitis leading to ILD flare and he was started on high-dose steroids with notable improvement in his oxygen saturation. Steroids were gradually tapered, and he was transferred out from the ICU on day 16.

After five days of being on the floor, his respiratory status declined again. A chest radiograph is described in Figure 3. He was readmitted to ICU, placed on bi-level positive airway pressure (BiPAP), restarted on high-dose steroids and broad-spectrum antimicrobials - cefepime and vancomycin for hospital-acquired pneumonia. Repeat infectious workup was done and respiratory cultures returned positive for *Stenotrophomonas maltophilia* and *C. gleum*. He was started on tigecycline and trimethoprim-sulfamethoxazole (SXT) which was changed to levofloxacin after three days because of hyponatremia and once the susceptibility patterns were available (Table 2). His respiratory status continued to worsen, he declined intubation and opted for comfort care measures. He passed away eventually after the removal of BiPAP.

FIGURE 2: CT chest with contrast-diffuse mosaic attenuation with ground-glass and reticulonodular opacifications on a background of previously visualized fibrotic and bronchiectatic changes with lower lobe predominance and pleural thickening.
FIGURE 3: A chest radiograph antero-posterior view - worsening bilateral infiltrates indication acute infectious process.

| Antibiotic                  | Minimum inhibitory concentration (µg/ml) | Interpretation |
|-----------------------------|------------------------------------------|----------------|
| Tigecycline                 | 2                                        | R              |
| Amikacin                    | >32                                      | S              |
| Cefepime                    | 8                                        | S              |
| Ceftazidime                 | <1                                       | S              |
| Ceftriaxone                 | 8                                        | S              |
| Gentamicin                  | >8                                       | R              |
| Levofloxacin                | 0.5                                      | S              |
| Meropenem                   | <1                                       | S              |
| Piperacillin + tazobactam   | <4                                       | S              |
| Tobramycin                  | >8                                       | R              |
| Trimethoprim + sulfamethoxazole | <2/38                                  | S              |

TABLE 2: Summarizing the susceptibility patterns of Chryseobacterium gleum in our study.

Discussion
Chryseobacterium species are aerobic, catalase-positive, oxidase-positive, non-motile, non-fermentative Gram-negative bacilli (NFGNB) primarily found in soil and water. Environmental studies have shown that they can thrive in chlorinated water and wet surfaces and are not a part of normal flora. Risk factors that are associated with infection include prolonged hospital stay especially in ICUs, indwelling devices, and exposure to broad-spectrum antibiotics. A study from Taiwan has shown that they can form biofilms on
medical devices (respirators, intubation tubes, syringes, etc.) or surgically implanted devices (intravenous catheters or prosthetic valves) which contributes to their pathogenic potential [10]. Our patient presumably acquired the infection while in the ICU as his initial respiratory cultures were negative and he responded to steroids, but during the second admission to the ICU, he was unresponsive to steroids and had rapid respiratory deterioration. There were no cultures obtained from the medical devices, but the patient was on contact and droplet precautions during the entire hospital stay which prevented the nosocomial spread of bacteria to other patients in the ICU.

Chryseobacterium spp has been reported to be resistant to several antibiotics such as aminoglycosides, chloramphenicol, colistin, tetracycline, clindamycin, erythromycin, teicoplanin, and beta-lactams. Bellasis et al. found that these bacteria are resistant to beta-lactams as they can chromosomally encode class A beta-lactamases (CGA-1) [11]. In our case, the bacteria were susceptible to most groups of antibiotics including cephalosporins as opposed to the other two reported cases from United States [12,13]. Historically, the choice of antibiotics is not well established because of the insufficient data on minimum inhibitory concentration and no Clinical and Laboratory Standards Institute (CLSI) or EUCAST (European Committee on Antimicrobial Susceptibility Testing) guidelines.

In SENTRY studies and most of the reported cases, TMP-SMX and quinolones (Levofloxacin, Gatifloxacin, Garenoxacin) were used to treat the infection. We initially treated our patient with tigecycline and SXT and then Levofloxacin for three days before he opted for comfort care. We did not have a good clinical response because, in most other studies, patients were treated with Levofloxacin for at least 7-10 days. Other causes could be worsening of the underlying ILD due to bacterial proliferation leading to further inflammation and lung damage or poor immune response due to underlying hematologic malignancy. Other studies with documented Chryseobacterium infection have been summarized in Table 3.
TABLE 3: Summarizing and comparing different studies done on Chryseobacterium gleum.

| Study | Type of study | Date | Region | Sex age | Disease/site of source | Comorbidities | Susceptibilities | Treatment | Duration | Response |
|-------|---------------|------|--------|---------|------------------------|--------------|------------------|-----------|----------|----------|
| Nemli et al. [9] | Case report | 2015 | Croatia | Female/35 | Pneumonia/blood and tracheal aspirate | Hepatic lesion, Malignation | R: CST, DAP, IPM, MEM, VAN, S: CAZ, CIP, FEP, TGC, TZIP | TZIP | 12 days | Positive |
| Jain et al. [4] | Case report | 2017 | India | Male/62 | Septicemia and pneumonia, Blood and tracheal aspirate | CNO C-AG-MVA with septoral bleed | R: AMK, CAZ, CIP, CLI, CR, CST, CTX, DOX, ERY, FEP, GEN, IPM, MEM, TOB | LUX | 10 days | Negative |
| Rejpalovs et al. [5] | Case report | 2016 | India | Male/58 | Metabolic encephalopathy, Urine | Diabetic CKD, CVA | R: GEN, AMK, MEM, ATM, CST, S: IPM, MIN, LUX, CIP, SXT | CIP | 6 days | Lost to follow-up |
| Gang et al. [6] | Case report | 2013 | India | Male/48 | Pyelonephritis, Urethra and prostatic abscess | Bilateral renal and ureteric calcification | R: AMK, CTX, CAZ, FEP, IPM, MEM, GEN, TOB, AMK, CIP, ERY | SXT | 7 days | Positive |
| Lo and Chang [7] | Case report | 2014 | Taiwan | NA | The most common cause of urinary tract infection (38.7%, 5/14) followed by sepsis (26.9%, 4/14) | NA | R: AMK, AMG, CAZ, CIP, FEP, ROX, GEN, IPM, TAM, TZP, S: CIP, MIN, SXT, TGC | NA | NA | NA |
| Anson et al. [8] | Case report | 2020 | United States | Female/76 | CLABS infection | CHD stage I CHF, cardiovascular disease | R: SAM, ATM, CAZ, CRO, MEM, MEM, TZIP, S: LVX, SXT | LUX | 14 days | Positive |
| Tsavdides et al. [9] | Case report | 2019 | United States | Male/61 | Pneumonia, bone | Suppurative lung abscess on admission | R: AMK, ATM, CAZ, CR, FEP, IPM, MEM, TOB, S: SXT, TMAP | SXT | 7 days | Positive |
| Abdollahian et al. [10] | Case report | 2016 | Saudi Arabia | Newborn | Pneumonia, endotracheal aspiration | Neutropenic sepsis | R: AMK, CAZ, CIP, FEP, GEN, IPM, MEM, TOB, S: SXT, TMAP | SXT | 16 days | Positive |
| Ansara et al. [11] | Case report | 2017 | West Africa | Male/68 | UTI, Urine | After proctoscopy | R: MEM, ATM, CTX, TIC, T: S: IPM, CAZ, FEP, CIP | CIP | NA | Positive |
| Ural et al. [12] | Case series-3 patients | 2014 | Hungary | Newborn | Pneumonia, stomach content | NA | R: AMK, DOR, GEN, IPM, MEM, TOB, TZIP, S: CAZ, CIP, FEP, LVX | CIP | NA | Positive |
| Ramya et al. [13] | Case report | 2015 | India | Male/62 | Retinal calcification, Hydronephrosis, Urine | CNO diabetes hyperonclossis | S: TZIP, CST, CAZ, NIT, TOB, S: GEN, AMK | TZIP | 7 days | Positive |
| Ravet et al. [14] | Case series | 2017 | India | Pediatric | NA | Chronic granulomatous disease | R: NA, S: MIN, SXT | TZIP | NA | Positive |
| Mora et al. [15] | Case series | 2016 | Turkey | Pediatric | NA | Most common cystic fibrosis | R: AMK, GEN, IPM, MEM, S: CAZ, CIP, FEP, LVX, SXT | TZIP | NA | Positive |
| Singhal et al. [16] | Case report | 2017 | India | Male/64 | Sepsis/blood | Diabetes, hyperonclossis | SXT, TZIP, CST, CAZ, FEP, ROX, S: AMK, CIP, LVX, TZIP, S: TIP, SXT | LUX | 7 days | Positive |

Conclusions

Chryseobacterium gleum is an emerging opportunistic/nosocomial pathogen in critically ill patients in ICUs, on mechanical ventilation, and receiving broad-spectrum antibiotics. We emphasize that isolation of this rare organism from clinical specimens should prompt an in vitro susceptibility pattern testing to optimize the treatment as soon as possible for better clinical outcomes. Due to limited susceptibility, the chances of C. gleum becoming a major infectious threat are high, especially in immunocompromised patients with hematological malignancies. The choice of effective drug therapy for empiric treatment may be difficult due to the scarcity of succinct evidence-based data, but based on the review of literature, levofloxacin or TMP-SMX are feasible empiric options followed by piperacillin-tazobactam. Infection control practices including hand hygiene, cleaning supplies with alcohol-based hand sanitizer, aseptic procedures, and airborne...
Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Holmes B, Owen RJ, Steigerwalt AG, Brenner DJ: Flavobacterium gleum, a new species found in human clinical specimens. Int J Syst Bacteriol. 1984, 34:21-25.
2. Vandamme P, Bernardet JF, Segers P, Kersters K, Holmes B: New perspectives in the classification of the flavobacteria: description of Chryseobacterium gen. nov., Bergeyella gen-nov, and Empedobacter nom-rev. Int J Syst Bacteriol. 1994, 44:827-31.
3. Nemli SA, Demirdal T, Ural S: A case of healthcare associated pneumonia caused by Chryseobacterium indologenes in an immunocompetent patient. Case Rep Infect Dis. 2015, 2015:485923. 10.1155/2015/485923
4. Jain V, Hussain NA, Siddiqui T, Sahu C, Ghar M, Prasad RN: Simultaneous isolation of Chryseobacterium gleum from bloodstream and respiratory tract: first case report from India. JMM Case Rep. 2017, 4:e005122. 10.1099/jmm.0.005122
5. Rajendran P, Muthusamy S, Balaji VK, Rakesh GJ, Easow JM: Urinary tract infection due to Chryseobacterium gleum, an uncommon pathogen. Indian J Pathol Microbiol. 2016, 59:551-3.
6. Garg S, Appannanavar SB, Mohan B, Taneja N: Pyonephrosis due to Chryseobacterium gleum: a first case report. Indian J Med Microbiol. 2015, 33:311–3. 10.4103/0255-0857.154894
7. Béric DV, Zlopaia O, Bedenic B, Pilevo V: Chryseobacterium gleum infection in patient with extreme malnutrition and hepatic lesion: case report. Signa Viva. 2015, 10:50-52.
8. Stone PW: Economic burden of healthcare-associated infections: an American perspective. Expert Rev Pharmacoecon Outcomes Res. 2009, 9:417-22. 10.1586/erp.09.53
9. Kirby JT, Sader HS, Walsh TR, Jones RN: Antimicrobial susceptibility and epidemiology of a worldwide collection of Chryseobacterium spp: report from the SENTRY Antimicrobial Surveillance Program (1997-2001). J Clin Microbiol. 2004, 42:445-8. 10.1128/JCM.42.1.445-448.2004
10. Lo HH, Chang SM: Identification, characterization, and biofilm formation of clinical Chryseobacterium gleum isolates. Diagn Microbiol Infect Dis. 2014, 79:298-302.
11. Bellais S, Naas T, Nordmann P: Molecular and biochemical characterization of Ambler class A extended-spectrum beta-lactamase CGA-I from Chryseobacterium gleum. Antimicrob Agents Chemother. 2002, 46:966-70. 10.1128/AAC.46.4.966-970.2002
12. Aaxon D, Chauzer B, Norton J, Bansal S: Multiple drug-resistant CLABSI from an extremely rare bacterium, Chryseobacterium gleum. Case Rep Infect Dis. 2020, 2020:2097813. 10.1155/2020/2097813
13. Tsouvalas CP, Mousa G, Lee AH, Philip JA, Levine D: Chryseobacterium gleum isolation from respiratory culture following community-acquired pneumonia. Am J Case Rep. 2020, 21:e921172. 10.12659/AJCRR.921172
14. Abdalhamid B, Elhadi N, Alsammam K, Aljindan R: Chryseobacterium gleum pneumonia in an infant with neoplastic syndrome. IDCases. 2016, 5:54-6. 10.1016/j.idcr.2016.06.004
15. Arouna O, Deluca F, Camara M, et al.: Chryseobacterium gleum in a man with prostatectomy in Senegal: a case report and review of the literature. J Med Case Rep. 2017, 11:118. 10.1186/s13256-017-1269-9
16. Virok DP, Ábrók M, Szél B, Tajti Z, Mader K, Urbán E, Tálosi G: Chryseobacterium gleum infection in an infant with extreme malnutrition and hepatic lesion: case report. Signa Viva. 2015, 10:50-52.
17. Ramya TG, Sabitha B, Pravin D, Geetha R: Chryseobacterium gleum urinary tract infection. Genes Rev. 2015, 1:1-5. 10.18488/journal.105.2015.1.1/1.5
18. Rawat A, Vignesh P, Sharma A, et al.: Infection profile in chronic granulomatous disease: a 23-year experience from a Tertiary Care Center in North India. J Clin Immunol. 2017, 37:319–28. 10.1007/s10875-017-0382-x
19. Mirza HC, Tuncer Ö, Ölmelz S, et al.: Clinical strains of Chryseobacterium and Elizabethkingia spp. isolated from pediatric patients in a University Hospital: performance of MALDI-TOF MS-based identification, antimicrobial susceptibilities, and baseline patient characteristics. Microb Drug Resist. 2018, 24:816-21. 10.1089/mdr.2017.0206
20. Singhgu L, Gupta V, Mehta V, Singla N, Janmeja AK, Chander J: Septis due to Chryseobacterium gleum in a diabetic patient with chronic obstructive pulmonary disease: a case report and mini review. Jpn J Infect Dis. 2017, 70:687-8. 10.7883/yoken.JJID.2016.567