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CHRONIC LYMPHOCYTIC LYMPHOMA COMPLICATED BY MYCOBACTERIUM AVIUM AND SCEDOSPORIUM APIOSPERMUM

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ABSTRACT

Introduction: Chronic lymphocytic leukaemia (CLL), the most common adult leukaemia in Western countries, poses unique management challenges, particularly when complicated by opportunistic infections. This report presents a rare case of CLL with concurrent *Mycobacterium avium* and *Scedosporium apiospermum* infections—pathogens increasingly recognized for causing severe disease in immunocompromised individuals. Their coexistence highlights the need for heightened awareness of diverse infectious complications in CLL patients.

Case description: We present a case of a 78-year-old male with CLL receiving chemotherapy, who developed burning pain in the tongue and oral mucosa, accompanied by a non- productive cough. He was initially diagnosed with pneumonia, but further investigation revealed co-infection involving *M. avium* and *S. apiospermum*.

Discussion: The coexistence of *M. avium* and *S. apiospermum* underscores the complexity of infectious complications in CLL. The patient's chemotherapy was halted due to active pneumonitis observed on imaging in order to improve his leukocyte count. Antifungal therapy was not initiated due to a lack of evidence of invasive fungal infection. Antimycobacterial therapy for *M. avium* complex was initiated.

Conclusion: This case highlights the necessity of a multidisciplinary approach and continued research to optimize management strategies and improve outcomes in CLL patients with dual infections.

KEYWORDS

Opportunistic infection, chronic lymphocytic leukaemia/small lymphocytic lymphoma, anti-fungal treatment, pulmonary mycobacterium avium complex disease

LEARNING POINTS

- A high index of suspicion is needed for rare infections, such as *Mycobacterium avium* and *Scedosporium apiospermum*, when typical symptoms are absent or mild in immunocompromised patients with chronic lymphocytic leukaemia.
- An individualized, evidence-based approach is needed in choosing the treatment for opportunistic organisms while withholding cancer therapy.

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INTRODUCTION/BACKGROUND

Chronic lymphocytic leukaemia (CLL) is a malignancy characterized by the clonal expansion of mature B lymphocytes, making it the most prevalent leukaemia in adults in Western countries[1]. It is known for its multifaceted challenges, and when coupled with opportunistic infections, patient management becomes more complex. This case report examines an instance of CLL complicated by a co-infection involving *M. avium* and *S. apiospermum*. *M. avium*, a member of the non- tuberculous mycobacteria, is known to cause disseminated infections in immunocompromised individuals[2]. On the other hand, *S. apiospermum*, a filamentous fungus, has been increasingly identified as a causative agent of invasive fungal infections in those who are immunocompromised[3]. This coexistence highlights the importance of recognizing and addressing diverse infectious complications in CLL patients.

CASE DESCRIPTION

A 78-year-old Caucasian male with a past medical history of CLL diagnosed 7 months ago, on chemotherapy with rituximab and venetoclax, stage three chronic kidney disease with a history of Raynaud's disease, and herpes zoster, presented with chief complaints of burning pain to his tongue and oral mucosa and a non-productive cough for the past 3 days. He was previously diagnosed with pneumonia and had been on antibiotics recently. He denied any chest pain or discomfort, fever, shortness of breath, loss of weight or appetite, or night sweats. The patient had no other co-morbidities. He stated that he was a nonsmoker and consumed alcohol occasionally. The patient, now retired, gave a history of occupational exposure as a carpenter for many years. There was no significant family history. He was vaccinated for coronavirus disease 2019.

His vital signs at presentation were a heart rate of 60 beats per minute, respiratory rate of 15 per minute, blood pressure of 105/56 mmHg, oxygen saturation of 97% on room air, and a body temperature of 36.7°C. The patient was alert and oriented. The cardiac examination was normal. On pulmonary examination, normal vesicular breath sounds were heard in all lung fields. The abdomen was soft and flat on examination, with no organomegaly. White patches were seen on the tongue and oral mucosa. Blood investigations showed leukopenia with a white blood cell count of 2400 cells/mm^3 and mild thrombocytopenia of 136 ×10^3/µl *(Table 1)*. Other routine investigations were within the reference range *(Table 1)*.

A chest X-ray showed mild right infra hilar pneumonitis and calcified remnants of an old granulomatous process *(Fig. 1)*. Computed tomography (CT) scan of the chest showed tree-in-bud nodular opacities in the right lung *(Fig. 2)*, suggesting active pneumonitis.

Due to these CT findings, the chemotherapy was held. The patient was started on amoxicillin, but he developed rashes and itching. Therefore, treatment was switched to levofloxacin. As symptoms did not improve over a few weeks, the patient underwent a bronchoscopy. Bronchoscopy revealed no significant endobronchial or inflammatory issue in both lungs and a bronchoalveolar lavage was performed. The lavage was sent for culture, acid-fast bacilli (AFB) smear, and cell cytology. The bronchial culture grew *S. apiospermum* and the AFB culture grew *M. avium* complex (MAC). The chemotherapy regimen was halted due to the active pneumonitis. The patient was started on a MAC regimen for the non- cavitary nodular bronchiectatic form which includes azithromycin 500 mg orally thrice weekly, rifampin 600 mg thrice weekly, and ethambutol 25 mg/kg thrice weekly for at least 12 months after cultures are negative[4]. This regimen has demonstrated effectiveness in achieving sputum culture negativity. During the administration of antimycobacterial therapy, close monitoring of liver function, renal parameters, and other potential adverse effects is crucial. The patient was not treated for *Scedosporium* as there are no signs of active infection.

Test	Value
Alkaline phosphatase (IU/l)	76
Alanine aminotransferase (IU/l)	16
Aspartate aminotransferase (IU/l)	19
Total bilirubin (µmol/l)	0.6
Blood urea nitrogen (mg/dl)	27
Creatinine (mg/dl)	1.34
Calcium (mmol/l)	9.2
Sodium (mmol/l)	138
Potassium (mmol/l)	4.2
Chloride (mmol/l)	103
CD4 count (cells/mm^3)	171
Haemoglobin (g/dl)	12.1
Haematocrit (%)	37
Mean corpuscular volume (fl)	92
Platelet count (cells/mm^3)	136,000
Total WBC count (cells/µl)	2,400
Neutrophils (%)	41
Lymphocytes (%)	31
Monocytes (%)	24
Eosinophils (%)	2
Carbon dioxide (mmol/l)	23

Table 1. Routine blood investigations.

DISCUSSION

The American Cancer Society estimates that there will be approximately 23,690 new cases of CLL in 2025 in the United States, with about 4,460 expected deaths, confirming its status as the most prevalent leukaemia in the Western world[1]. Furthermore, the global incidence of CLL has witnessed a notable increase, with a reported 107% rise in associated mortality rates, highlighting a concerning trend in the management of this disease[1].

CLL primarily affects the aging male population, with the median age at diagnosis being 65 years[5]. This lymphoproliferative disorder is characterized by the chronic accumulation of neoplastic B cells, leading to progressive symptoms manifesting as fatigue, unexplained weight loss, and a heightened susceptibility to infections because the disease itself and treatment regimens compromise the immune system[5]. While chemotherapy has significantly improved prognoses for patients with CLL, it is crucial to acknowledge that all therapeutic modalities induce myelosuppression. This side effect can greatly compromise the body's innate defence mechanisms, making patients highly susceptible to infections, particularly opportunistic pathogens that complicate recovery and management. The patient was receiving rituximab, a monoclonal antibody that effectively targets CD20 on B cells, employing various mechanisms to neutralize malignant B cells, including complement-mediated cytotoxicity and antibody-dependent phagocytosis[6]. However, this treatment is also associated with risks such as hypogammaglobulinemia and neutropenia, which contribute to the increased likelihood of opportunistic infections. In contrast, venetoclax, while having lesser-known immunosuppressive properties, has also been linked to neutropenia, which can exacerbate the immunosuppressive risk already imposed by rituximab[7]. This combination of treatments illustrates the delicate balance required in chemotherapy due to patients' susceptibility to infections. The heightened risk of opportunistic infections in patients undergoing chemotherapy is compounded by potential delays in diagnosis. Mycobacterial infections, such as those caused by *M. avium*, present particular challenges because they are often difficult to identify through standard culture methods. Co-infections with multiple species, while rare, can complicate the diagnostic process, necessitating timely recognition and management of infections. *Scedosporium* species are recognized as environmental colonizers of the respiratory tract[3]. Detection of *S. apiospermum* in bronchoalveolar lavage fluid from an immunocompromised patient, especially in the context of concurrent MAC, raises a critical question: does this represent colonization or invasive infection requiring treatment? The distinction is essential, as *S. apiospermum* is an emerging, opportunistic mold that can be either a colonizer or a life-threatening pathogen in immunocompromised hosts[3,8,9].

S. apiospermum is frequently isolated from respiratory samples in immunocompromised patients, particularly those with underlying lung disease, solid organ or hematopoietic stem cell transplantation, or profound immunosuppression (e.g., neutropenia, corticosteroid use)[8-12]. The clinical spectrum ranges from asymptomatic colonization to invasive pulmonary or disseminated disease, with the latter associated with high morbidity and mortality, mortality rates in transplant recipients and those with hematologic malignancy can exceed 50%[9-11].

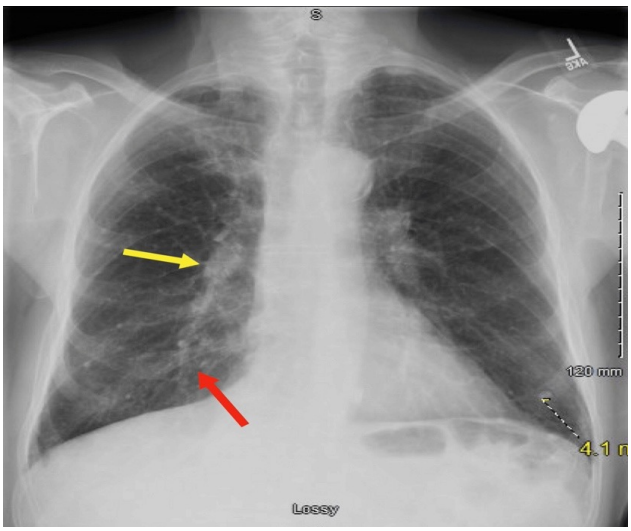


Figure 1. X-ray chest apical view. Mild right infra hilar pneumonitis (yellow arrow) and calcified remnants of old granulomatous process (red arrow).

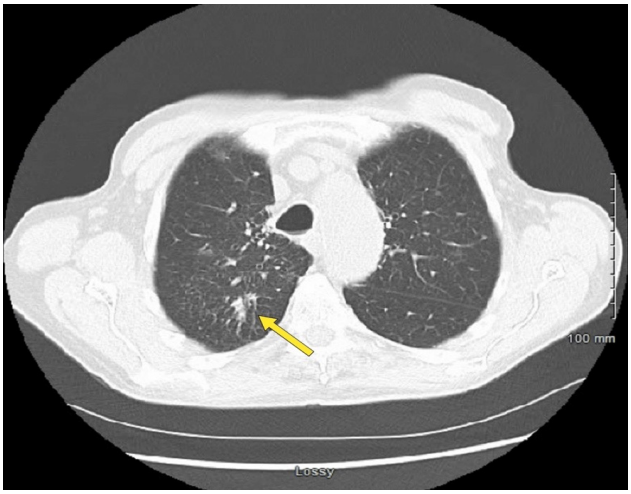


Figure 2. Coronal computed tomography image of the chest. Tree-in-bud nodular opacity (yellow arrow) in the right lung.

The need for treatment of the fungal infection is determined by evidence of invasive disease rather than colonization. Key factors that support a diagnosis of infection and thus the need for antifungal therapy include:

Clinical symptoms: New or worsening fever, cough, dyspnoea, haemoptysis, or pleuritic chest pain in the absence of another clear aetiology[3,4].

Radiological findings: New or progressive pulmonary infiltrates, nodules, cavitary lesions, or consolidation on chest imaging, particularly if these findings are unexplained by other pathogens or processes[3,12,13].

Histopathologic evidence: Demonstration of hyphal invasion in tissue (e.g., lung biopsy) is the gold standard for diagnosis

but is often not feasible in severely immunocompromised patients[3,13].

Microbiological context: Repeated isolation of *S. apiospermum* from sterile sites or in conjunction with compatible clinical and radiological findings increases the likelihood of true infection [3,9,13].

In the absence of the above features, the finding of this organism might be merely a colonizer[3,9,13]. However, the risk of progression from colonization to invasive disease is unpredictable, particularly in those with ongoing or profound immunosuppression, and warrants close clinical and radiological monitoring[10-12]. Our patient had no signs of invasive fungal disease based on the above guidelines and hence the treatment was not initiated, in contrast to Jimeno et. al where antifungal treatment was given since the patient had evidence of invasive fungal infection[14].

Physicians must carefully weigh the risks against the benefits of starting treatment, particularly in immunocompromised individuals, where treatment regimens need to be tailored to individual patient needs. Effective management of such infections involves a nuanced understanding of their presentation and the potential for rapid deterioration in the patient's condition if not promptly addressed.

CONCLUSION

This case report highlights the challenges of managing CLL patients with opportunistic infections. It underscores the importance of individualized treatment strategies, close monitoring for adverse effects, and a multidisciplinary approach to optimize patient outcomes in the complexity of managing dual infections in an immunocompromised patient. Continued research and clinical experience will further enhance our understanding and treatment options for such rare co-infections.

REFERENCES

1. Ou Y, Long Y, Ji L, Zhan Y, Qiao T, Wang X, Chen H, et al. Trends in Disease Burden of Chronic Lymphocytic Leukemia at the Global, Regional, and National Levels From 1990 to 2019, and Projections Until 2030: A Population-Based Epidemiologic Study. *Front Oncol* 2022;**12**:840616. doi: 10.3389/fonc.2022.840616
2. Akram SM, Attia FN. Mycobacterium avium Complex. [Updated 2023 Feb 25]. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK431110/
3. Reinhold I, Quiblier C, Blaser F, Bögeholz J, Imkamp F, Schuurmans MM, et al. Detection of Scedosporium spp.: Colonizer or pathogen? A retrospective analysis of clinical significance and management in a large tertiary center. *Med Mycol* 2024;**62**:myae002. doi: 10.1093/mmy/myae002
4. Kwon YS, Koh WJ, Daley CL. Treatment of Mycobacterium avium Complex Pulmonary Disease. *Tuberc Respir Dis (Seoul)* 2019;**82**:15-26. doi: 10.4046/trd.2018.0060
5. Rozman C, Montserrat E. Chronic lymphocytic leukemia. *N Engl J Med* 1995;**333**:1052-1057. doi: 10.1056/NEJM199510193331606
6. Cartron G, Dacheux L, Salles G, Solal-Celigny P, Bardos P, Colombat P, et al. Therapeutic activity of humanized anti-CD20 monoclonal antibody and polymorphism in IgG Fc receptor FcgammaRIIIa gene. *Blood* 2002;**99**:754-758. doi: 10.1182/blood.v99.3.754
7. Seymour JF, Kipps TJ, Eichhorst BF, D'Rozario J, Owen CJ, Assouline S, et al. Enduring undetectable MRD and updated outcomes in relapsed/refractory CLL after fixed-duration venetoclax-rituximab. *Blood* 2022;**140**:839-850. doi: 10.1182/blood.2021015014
8. Cortez KJ, Roilides E, Quiroz-Telles F, Meletiadis J, Antachopoulos C, Knudsen T, et al. Infections caused by Scedosporium spp. *Clin Microbiol Rev* 2008;**21**:157-197. doi: 10.1128/CMR.00039-07
9. Vazirani J, Westall GP, Snell GI, Morrissey CO. Scedosporium apiospermum and Lomentospora prolificans in lung transplant patients - A single center experience over 24 years. *Transpl Infect Dis* 202;**23**:e13546. doi: 10.1111/tid.1354613546
10. Seidel D, Meißner A, Lackner M, Piepenbrock E, Salmanton-García J, Stecher M, et al. Prognostic factors in 264 adults with invasive Scedosporium spp. and Lomentospora prolificans infection reported in the literature and FungiScope®. *Crit Rev Microbiol* 2019;**45**:1-21. doi: 10.1080/1040841X.2018.1514366
11. Husain S, Muñoz P, Forrest G, Alexander BD, Somani J, Brennan K, et al. Infections due to Scedosporium apiospermum and Scedosporium prolificans in transplant recipients: clinical characteristics and impact of antifungal agent therapy on outcome. *Clin Infect Dis* 2005;**40**:89-99. doi: 10.1086/426445
12. Cobo F, Lara-Oya A, Rodríguez-Granger J, Sampedro A, Aliaga-Martínez L, Navarro-Marí JM. Infections caused by Scedosporium/Lomentospora species: Clinical and microbiological findings in 21 cases. *Med Mycol* 2018;**56**:917-925. doi: 10.1093/mmy/myx147
13. Miller JM, Binnicker MJ, Campbell S, Carroll KC, Chapin KC, Gonzalez MD, et al. Guide to Utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases: 2024 Update by the Infectious Diseases Society of America (IDSA) and the American Society for Microbiology (ASM). *Clin Infect Dis*:104. doi: 10.1093/cid/ciae104
14. Jimeno VM, Muñoz EC. Diagnosis of atypical mycobacterial and fungal coinfection. *Int J Mycobacteriol* 2020;9:435-437. doi: 10.4103/ijmy.ijmy_98_20