CASE REPORT

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Candida Meningitis Accompanied by Upper Gastrointestinal Tract Candidiasis in an Immunocompromised Host

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ABSTRACT

Candida albicans, a normal component of the human skin, mouth, and respiratory tract flora, can cause opportunistic infections in immunocompromised individuals. It is a rare cause of meningitis. This study presents a case of *Candida* meningitis in a patient with psoriasis and ankylosing spondylitis treated with adalimumab. The patient presented with extensive oropharyngeal candidiasis lesions extending to the larynx and esophagus and was diagnosed with *Candida* meningitis. He was treated with intravenous fluconazole and liposomal amphotericin B combination therapy for 28 days. This case highlights the importance of early diagnosis and treatment of fungal meningitis in immunocompromised hosts.

Keywords: immunocompromised host, *Candida* spp., meningitis

INTRODUCTION

Central nervous system (CNS) infections can develop due to bacteria, viruses, and fungi (1). The most common cause is bacteria. Although fungal meningitis is rare, there has been an increase in the number of cases in recent years (2, 3). In the vast majority of CNS candidiasis, the primary site of infection is the lungs or skin, followed by direct or hematogenous spread to the CNS (4, 5). The most common opportunistic fungi in humans are *Candida* spp. (3). High-dose and long-term use of antibiotics, long-term immunosuppression conditions such as hematological malignancies, and solid organ or bone marrow transplants predispose to candidiasis (3, 6). It is estimated that 6% of patients with disseminated candidiasis will develop neuroinfection due to the biofilm formation of *Candida* spp., which protects yeast cells from microglial activity (3). This article presents a case of *Candida* meningitis accompanied by oral candidiasis in a patient diagnosed with ankylosing spondylitis (AS) and psoriasis who was on adalimumab therapy.

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CASE

A 37-year-old female patient was admitted to the neurology department with a diagnosis of pseudotumor cerebri due to complaints of a constricting headache starting from behind both ears and spreading to the forehead, blurred vision, double vision, nausea, and vomiting that had developed over the past 15 days. Physical examination was normal except for lesions compatible with oropharyngeal candidiasis extending to the larynx level (Figure 1). She was fully conscious, oriented and cooperative with no signs of meningeal irritation. The patient underwent endoscopy, and white plaques suggesting *Candida* esophagitis were observed. An oropharyngeal swab sample was taken. The patient was on adalimumab therapy for psoriasis and AS. A lumbar puncture was performed. Cerebrospinal fluid (CSF) tests showed low glucose and high protein levels (Table 1). Thus, the patient was transferred to the Infectious Diseases Department with the diagnosis of meningitis and or encephalitis. Intravenous (IV) treatment with 2 g ceftriaxone q12h, 1 g vancomycin q12h and 750 mg acyclovir q8h was started. Oral care with bicarbonate was done. Oral nystatin therapy was also started. Her HIV serology was negative.

The patient remained afebrile, and the headache persisted on the third day of treatment. The patient's brain magnetic resonance imaging (MRI) was normal. Because of bilateral papilledema observed in the fundoscopic examination performed for double vision, the patient was consulted by neurology, and diazomide treatment was initiated. *Candida albicans* grew in blood and CSF cultures; therefore, the patient's treatment was changed to fluconazole 200 mg q12h and liposomal amphotericin B 250 mg q24h on the fifth day. On the second day of the antifungal treatment, the headache and nausea subsided, and by the fourth day, the double vision improved. By the end of the first week, oral lesions had completely healed, and there was no deterioration in the clinical condition. Control CSF analysis was recommended to the patient but could not be performed because the patient did not accept it. The treatment was continued for 28 days, and the patient was discharged in good health at the end of antifungal treatment. No recurrence was observed in the follow-up after discharge. Informed consent was obtained from the patient.

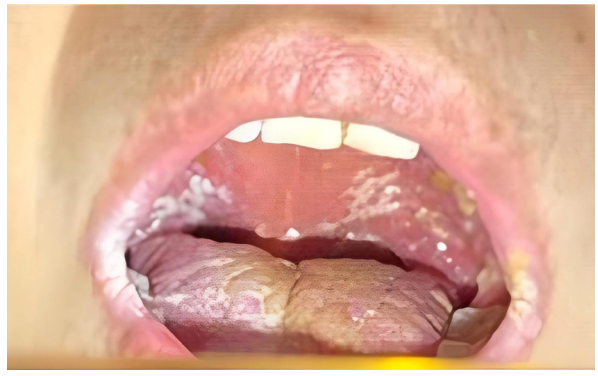

Figure 1. Findings of oral candidiasis in the patient.

DISCUSSION

Patients with rheumatic diseases are exposed to various risk factors that significantly increase the incidence of fungal infections. The use of broad-spectrum antibiotics can alter mucosal flora, leading to the proliferation of *Candida* spp., corticosteroids can affect the activity of polymorphonuclear cells, macrophages, and T cells, surgical procedures and the use of immunosuppressive drugs - especially biological agents - facilitate the spread of opportunistic pathogens (7, 8). Our patient was diagnosed with AS, and she was on adalimumab. Adalimumab is a recombinant monoclonal antibody and a tumor necrosis factor-alpha (TNF-α) inhibitor used in the treatment of various autoimmune conditions such as rheumatoid arthritis, AS, psoriasis, psoriatic arthritis, Crohn's disease, and ulcerative colitis. TNF-α is a proinflammatory cytokine that plays a crucial role in the pathogenesis of many inflammatory diseases by stimulating the release of inflammatory cytokines such as interleukin 1 beta (IL-1β), IL-6, and IL-8 (9, 10). Approximately 80% of invasive fungal infection cases related to anti-TNF use are associated with infliximab, 16% with etanercept, and only 4% with adalimumab. These fungal infections primarily affect the lungs and include histoplasmosis (30%), candidiasis (23%), and aspergillosis (23%) (9).

Various *Candida* spp., including *C. albicans*, *Candida tropicalis* and *Candida parapsilosis*, can cause infec-

Table 1. Laboratory values and physical examination findings at the time of patient admission.

Physical Examination		Findings
Body temperature (°C)		36.4
Pulse, /dk		72
Blood pressure, mmHg		120/80
Neurological examination		Conscious, oriented, cooperative. There was no nuchal stiffness and other signs of meningeal irritation.
Oropharynx		Diffuse candidiasis lesions on the oral mucosa
Respiratory system		Normal
Abdomen		Normal
Urogenital system		Normal
Extremities		Normal
Skin		No lesions suggestive of fungal infection
Laboratory parameters (Reference range)		
WBC (4-10), 10^3/uL		10.76
Hemoglobin (12-16), g/dL		13
Lymphocytes (20%-52%)		13.1
Platelets (160-370), 10^3/uL		325
TSH (0.27-4.2), mIU/L		1.24
Sedimentation (1-15), mm/sa		43
Urea (16.6-48.5), mg/dL		33.3
Creatinine (0.5-0.9), mg/dL		0.77
Sodium (133-145), mmol/L		133
Potassium (3.5-5.1), mmol/L		4.5
Chloride (97-111), mmol/L		98
CRP (0-5), mg/L		16.6
Albumin (3.5-5.2), g/dL		4.2
AST (5-40), U/L		21
Culture of orapharyngeal swab		*Candida* spp.
Blood culture		*C. albicans*
Mycobacterial tests	Microscopy for acid-fast staining bacteria	Negative
	PCR for M. tuberculosis	Negative
	Mycobacterial culture	Negative
CFS analysis		
CSF protein, mg/dL		119
CSF LDH, U/L		39
CSF glucose, mg/dL		11.1

continue to Table 2

CSF chloride, mmol/L		115
CSF microscopy Gram stain	Leukocytes, /mm^3	200
	Negative	
CSF culture		*C. albicans*
Syndromic meningitis PCR panel		Negative

WBC: White blood cell , **TSH:** Thyroid stimulation hormone, **AST:** Aspartate aminotransferase, **CRP:** C-reactive protein, **CSF:** Cerebrospinal fluid, **PCR:** Polymerase chain reaction.

tions. The positivity rate of fungal cultures in CSF for *Candida* infection is approximately 80% (11). Typically, CSF analysis shows pleocytosis, low glucose, and high protein levels. The initial symptoms of *Candida* meningitis resemble those of bacterial meningitis, such as fever, headache, neck stiffness, and altered consciousness (11, 12). However, unlike bacterial meningitis, which typically presents acutely, *Candida* meningitis can have a more insidious onset and may progress in weeks, making diagnosis challenging. This clinical course can mimic tuberculous meningitis (13). Our patient did not exhibit confusion or neck stiffness on physical examination but had long-standing, severe headaches, blurred vision, and double vision.

Managing CNS infections caused by *Candida* is challenging, with a mortality rate of 10% to 30%, even with adequate treatment (11, 14). Liposomal amphotericin B, either alone or combined with flucytosine, is recommended for treatment. If a foreign body, such as a surgically implanted device, is present in the CNS, it should be removed due to biofilm formation. Amphotericin B has broad-spectrum antifungal activity and achieves high concentrations in the CNS. Fluconazole, which penetrates the CSF well and is well-tolerated with infrequent side effects, is another antifungal agent used in treatment (14). Although fluconazole or amphotericin B is mentioned in the treatment of *Candida* meningitis, dual antifungal use is also available in the current literature, and the current literature is mentioned in references and case reports. Since meningitis may be aggressive in our patient due to the growth of *C. albicans* in both CSF and blood cultures, fluconazole and amphotericin B were administered in combination (15, 16).

CONCLUSION

Patients receiving anti-TNF-α therapy must be closely monitored for serious and opportunistic infections. The clinical presentation of *Candida* meningitis may mimic tuberculous meningitis; therefore, it should be included in the initial differential diagnosis in these patients.

Ethical Approval: N.A.

Informed Consent: Informed consent was obtained from the patient..

Peer-review: Externally peer-reviewed

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