North Clin Istanb 2023;10(2):277–280
doi: 10.14744/nci.2023.04372

Case Report PT&R

Cryptococcal endocarditis of native valve in a patient with systemic lupus erythematosus

Seyedeh Kimia Yavari,[1] Danielle Lapoint,[1] Amanda Levy,[2] Leili Pourafkari[1]

[1]Catholic Health System, University at Buffalo, Buffalo, New York, USA

[2]New York Institute of Technology College of Osteopathic Medicine, New York City, New York, USA

ABSTRACT

Cryptococcal endocarditis is an exceedingly rare entity associated with high mortality and morbidity. Hereby, we present a 37-year-old patient with underlying systemic lupus erythematosus and end-stage renal disease who was diagnosed with *cryptococcal endocarditis* involving native mitral valve. Her blood culture grew *Cryptococcus neoformans*. Echocardiography confirmed presence of vegetations and patient underwent mitral valve replacement and received appropriate anti-fungal treatment. Her course was further complicated by sternal wound dehiscence and infection of hemodialysis site as well as atrial flutter. Unfortunately, patient passed 2 weeks after discharge from hospital. *C. neoformans* is typically known to cause serious central nervous system. However, this pathogen can rarely cause serious infective endocarditis case particularly in immune compromised patients or those with prosthetic valves. Fungal endocarditis is usually treated with a combination of surgery and anti-fungal medications.

Keywords: Cryptococcal endocarditis; cryptococcus neoformans; endocarditis.

Cite this article as: *Yavari SK, Lapoint D, Levy A, Pourafkari L. Cryptococcal endocarditis of native valve in a patient with systemic lupus erythematosus. North Clin Istanb 2023;10(2):277–280.*

Fungal endocarditis accounts for 2% of infective endocarditis cases and is associated with high mortality. Most common fungi associated with endocarditis are candida and aspergillus [1]. *Cryptococcus neoformans* is a recognized cause of meningitis in patients with acquired immunodeficiency syndrome [2]. However, it is an unusual etiology for infective endocarditis. *Cryptococcal endocarditis* is an exceedingly rare form of endocarditis with only a few reported cases in the literature [3, 4]. This infection typically occurs in patients with immunocompromised state and/or valvular heart disease particularly with prosthetic valves [5]. Treatment typically includes antifungal medications and surgical debridement. However, due to rarity of the condition, data on treatment efficacy and outcomes are sparse [3].

Hereby, we will present a patient with underlying systemic lupus erythematosus (SLE) and end-stage renal disease who was diagnosed with *cryptococcal endocarditis* involving native mitral valve.

CASE REPORT

A 37-year-old female with a medical history of SLE nephritis, obesity, and end-stage renal disease on hemodialysis presented to the emergency department with complaints of feeling weak for 2 weeks. She additionally reported black runny stools and a week of missed hemodialysis. At the time of presentation, she was afebrile, blood pressure was 144/92 mmHg and heart rate was 102 beats/min. On the physical examination, she was drowsy. Heart sounds were regular in rate and rhythm

Received: June 11, 2022 *Accepted:* February 02, 2023 *Online:* April 27, 2023

Correspondence: Leili POURAFKARI, MD. Catholic Health System, Sisters of Charity Hospital, 2157 Main Street, Buffalo, NY 14214, USA.
Tel: +90 716 345-4976 e-mail: leili.p@gmail.com

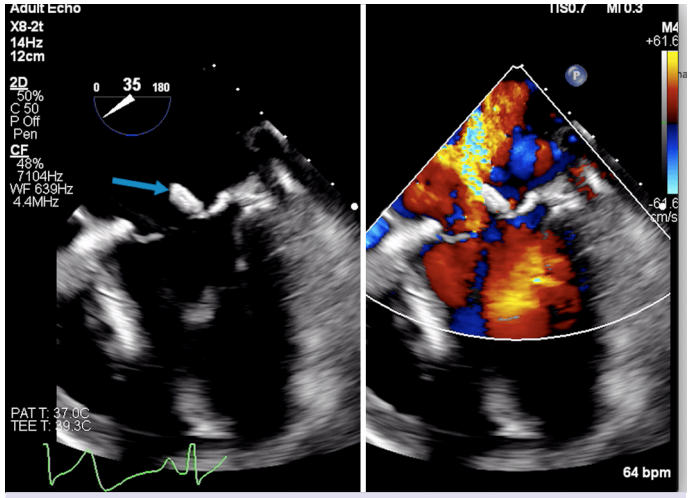

Figure 1. Transesophageal echocardiogram in mid-esophageal level at 35° showing a mobile vegetation on the anterior mitral valve leaflet (blue arrow) and significant mitral regurgitation.

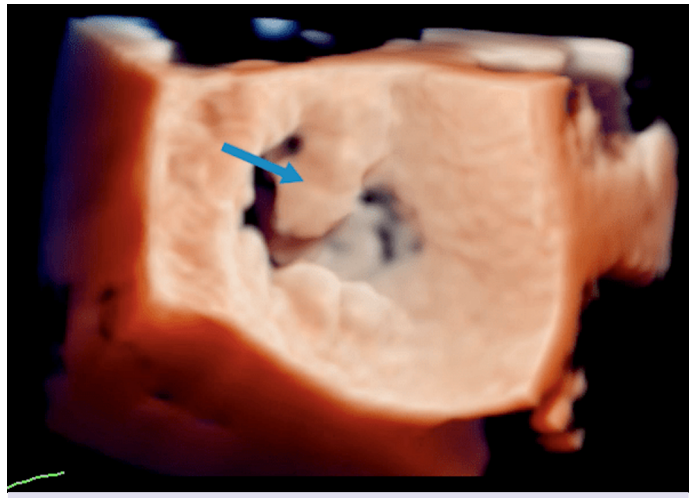

Figure 2. Three-dimensional transesophageal echocardiography of mitral valve using True View method showing the large vegetation on the anterior leaflet of mitral valve (blue arrow).

without any murmur. Her lungs had crackles at the bases bilaterally. Both the left femoral central venous catheter – which was placed in the emergency department – and the right femoral hemodialysis catheter sites were dry and clean. Blood work revealed white-blood-cell of 12.5/μL, hemoglobin 4.7 g/dL, platelet 32×10^9/L, BUN 258 mg/dL, Cr 28.22 mg/dL, and potassium 8.6 mEq/L. Electrocardiogram showed sinus rhythm with peaked T waves. She was admitted to the intensive care unit with a diagnosis of uremic encephalopathy and hyperkalemia secondary to missed dialysis and acute on chronic anemia. She underwent emergent dialysis and evaluation of blood loss. Review of her records showed that she had colonoscopy 10 months earlier which was unremarkable and upper endoscopy which showed gastric ulcer.

During her hospital stay, thrombocytopenia worsened. The patient's course was complicated by bleeding from her right upper molar and required platelet and tranexamic acid transfusion.

On day 5, the 1st-day blood culture was reported to be positive for *C. neoformans*. Chest X-ray showed no sign of significant acute or recent cardiopulmonary lesions while chest computed tomography scan showed trace right pleural effusions and atelectasis posterior right lung base with single large lymph node in the mid-right paratracheal region.

Transthoracic echo results were consistent with the evidence of mitral valve endocarditis as well as vegetation on the atrial side of the anterior the mitral valve leaflet. Transesophageal echocardiogram showed left ventricular ejection fraction of 55–60% and confirmed presence of large echodensity on the anterior leaflet (16 mm * 4 mm) with moderate-to-severe mitral regurgitation (Fig. 1, 2). The patient was started on intravenous flucytosine and amphotericin B. Her dialysis catheter also removed and temporary catheter was placed. Lumbar puncture was negative for bacteria, fungal, and acid-fast bacillus. She underwent mitral valve replacement. Intraoperatively, very large vegetations were noted on anterior and posterior leaflets which were all debrided and a 29 mm Edwards Magna bioprosthetic valve was implanted. Decision to use a bioprosthetic valve rather than a mechanical valve was due to patient's extensive comorbidities, end-stage renal disease, and history of platelet dysfunction and bleeding. She also received AV graft in left groin. She was discharged after a prolonged stay of 50 days. She presented back after 6 days with the left groin pain and discharge and concern for infection. She underwent excisional debridement of the left groin wound site. She also had sternal wound dehiscence due to infection and underwent debridement of the wound. Repeat blood cultures remained negative. Patient improved and continuing fluconazole and Bactrim after each dialysis session for 1 year was recommended. Patient was discharged from her second admission following a 21-day course of admission. Unfortunately, patient passed at home 2 weeks after discharge after missing dialysis sessions. No autopsy was performed.

DISCUSSION

C. neoformans belongs to the fungal phylum Basidiomycota and is different from other fungal pathogens with characteristics such as a thick polysaccharide capsule, formation of melanin, and urease activity [6]. These features, specifically the polysaccharide capsule, function as virulence determinants and allowing it to infect any tissue or organ of the body [6]. Majority of cases are rapidly cleared by competent immune system. Hence, most cases of *C. neoformans* are found in immunocompromised hosts and are one of the most important HIV-related opportunistic infections, primarily in developing countries [7].

C. neoformans is typically known to cause serious central nervous system that infections, most commonly causing meningitis with lung and skin infections [4]. In one study, conditions associated with Cryptococcal infection in non-HIV individuals included immunosuppressive drug treatment (41%), SLE (16%), malignancies (16%), and diabetes mellitus (14%) [8].

The previous studies have identified cryptococcal cardiac involvement to present with pericarditis, myocarditis, and endocarditis [9]. These initial findings are usually seen in immunocompromised hosts and those with prosthetic valves [10]. Cryptococcus is a rare fungal pathogen to cause endocarditis [9]. Majority of cryptococcal infections are associated with meningitis. Hence, lumbar puncture needs to be considered in event of cryptococcal infection even in the absence of symptoms [11]. Lumbar puncture was unremarkable in our patient.

Cryptococcal endocarditis is extremely rare and hence is not extensively studied in the literature. A study published in 2020 identified 12 published cases and another case report was described in 2021 [4, 5]. Unlike most of the previously reported cases of *cryptococcus endocarditis*, our case occurs in a patient without a history of underlying valvular pathology or a prosthetic valve. However, she had SLE and end-stage renal disease with a permanent hemodialysis catheter in place. The catheter line along with the prolonged immunosuppressed state may be how our patient contracted cryptococcus. Clinical presentation of infective endocarditis due to fungal pathogens is similar to those with bacterial infections. High index of suspicion needs to be maintained as symptoms may be insidious in immunocompromised patients [9].

Given the rarity of *Cryptococcal endocarditis*, there is lack of standard recommendations [3, 4]. As of now, case reports have provided evidence that Amphotericin-B is a promising treatment in addition or in rare cases in-lieu of surgical intervention [9]. It is important to note that Amphotericin B has dose-related nephrotoxicity, so patients with need to be monitored in this regard [12]. Despite the effectiveness of polyenes, there is evidence for antifungal resistance from *C. neoformans*. Amphotericin B resistance may be due to reduced drug penetration due to cell walls that thicken and become larger as older cells become resistant to reactive oxygen species [13]. Given the possible resistance of cryptococcus to polyenes and the lack of standardized treatment for *Cryptococcal endocarditis*, other antifungals could be used in treatment. For example, Li et al. [4] used initial amphotericin B and fluconazole with long-term flucytosine and fluconazole. Despite the benefits of using antifungals, specifically polyenes, mortality rates for medical treatment in cases of infective endocarditis are exceedingly high.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship Contributions: Concept – SKY, DL, AL, LP; Design – SKY, DL, AL, LP; Supervision – LP, SKY; Fundings – SKY, DL, AL, LP; Materials – SKY, DL, LP; Data collection and/or processing – SKY, DL, AL, LP; Analysis and/or interpretation – SKY, DL, AL, LP; Literature review – SKY, DL, AL, LP; Writing – SKY, DL, AL, LP; Critical review – SKY, DL, AL, LP.

REFERENCES

1. Yuan SM. Fungal endocarditis. Braz J Cardiovasc Surg 2016;31:252–5.
2. Schmalzle SA, Buchwald UK, Gilliam BL, Riedel DJ. *Cryptococcus neoformans* infection in malignancy. Mycoses 2016;59:542–52. [CrossRef]
3. Nakajima T, Oba Y, Takashima J, Ueno K, Kikuchi A, Yamada T, et al. Cryptococcus endocarditis: a case report and review of the literature. J Infect Chemother 2019;25:901–5. [CrossRef]
4. Li Y, He S, Lu Z, Ding C, Wang Q, Li Q, et al. *Cryptococcal endocarditis* of native valves without immunodeficiency or drug abuse: a case report. J Int Med Res 2020;48:0300060520970763. [CrossRef]
5. Elkhatib W, Kwon JY, Phillips MB. Overwhelming cryptococcosis complicated by *cryptococcal endocarditis*. BMJ Case Rep 2022;15:e247310.
6. Kwon-Chung KJ, Fraser JA, Doering TL, Wang Z, Janbon G, Idnurm A, et al. *Cryptococcus neoformans* and Cryptococcus gattii, the etiologic agents of cryptococcosis. Cold Spring Harb Perspect Med 2014;4:a019760. [CrossRef]

7. Park BJ, Wannemuehler KA, Marston BJ, Govender N, Pappas PG, Chiller TM. Estimation of the current global burden of cryptococcal meningitis among persons living with HIV/AIDS. Aids 2009;23:525–30. [CrossRef]
8. Kiertiburanakul S, Wirojtananugoon S, Pracharktam R, Sungkanuparph S. Cryptococcosis in human immunodeficiency virus-negative patients. Int J Infect Dis 2006;10:72–8. [CrossRef]
9. Roy M, Ahmad S, Roy AK. *Cryptococcus neoformans* infective endocarditis of native valves in an immunocompetent host. IDCases 2018;12:66–70. [CrossRef]
10. Duvall CP, Carbone PP. *Cryptococcus neoformans* pericarditis associated with Hodgkin's disease. Ann Intern Med 1966;64:850–6. [CrossRef]
11. Perfect JR, Dismukes WE, Dromer F, Goldman DL, Graybill JR, Hamill RJ, et al. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the Infectious Diseases Society of America. Clin Infect Dis 2010;50:291–322. [CrossRef]
12. Subramanian S, Mathai D. Clinical manifestations and management of cryptococcal infection. J Postgrad Med 2005;51:21.
13. Zafar H, Altamirano S, Ballou ER, Nielsen K. A titanic drug resistance threat in *Cryptococcus neoformans*. Curr Opin Microbiol 2019;52:158–64.