

## Attention to cryptococcal meningitis in patients with primary nephrotic syndrome

Dongrui Liang<sup>1</sup>, Shengnan Ma<sup>2</sup>, Xiaodong Li<sup>3</sup>

An important opportunistic pathogen called *Cryptococcus neoformans* typically affects those who have compromised immune systems.<sup>1</sup> AIDS-associated cryptococcal infections now account for 80 – 90% of all patients with cryptococcosis. Among HIV-negative patients with cryptococcal infection, studies indicated that 41 – 61% of these patients received immunosuppressive drugs, most had systemic lupus erythematosus and cancer, and only a few patients had primary nephrotic syndrome (PNS).<sup>2</sup> In PNS patients, steroid or immunosuppressive medication results in immunologic dysfunction, which enhances the risk of infection.

Cryptococcal meningitis (CM) is an unusual and frequently fatal complication in patients with PNS.<sup>3</sup> Because the clinical features of CM are normally atypical and the diagnosis is usually neglected, the infection develops and neurological injury arises. Furthermore, limited information is available about the clinical characteristics of PNS with CM to date. Usual clinical features include nausea, vomiting, headache, meningeal irritation indications, and fever, the latter of which was the early and common sign of CM.<sup>4</sup> The CM diagnosis were based on the extracting *Cryptococcus neoformans* from the cerebrospinal fluid (CSF) or a positive India ink staining. The opportunistic fungus pathogen *Cryptococcus neoformans* or *Cryptococcus gattii*, with *C. neoformans* predominating worldwide, causes CM, an infection of the meninges. CM is typically an immune-compromised condition with high morbidity and death rates, especially in those patients with HIV. Without anti-fungal therapy, the mortality rate in CM patients was reported to exceed 100%, and even after taking widely available anti-fungal medications, it can still be relatively high (20–60%).<sup>5</sup> Moreover, the widespread use of corticosteroids and other immunosuppressive medications, particularly broad-spectrum antibiotics, by

medical practitioners has steadily raised concerns about the occurrence of CM in HIV-negative patients.

Although immunosuppressive medications and corticosteroids are the primary treatment for PNS, these agents enhance immune system impairment. As a result, among those patients with PNS, infection is one of the most frequent complications, even CM and invasive fungal infections. There have been some case reports of CM in PNS patients from various countries, with China having the majority of these reports due to the country's high NS patient population.<sup>5</sup> The induction, consolidation, and maintenance phases of CM treatment are designated in the updated Infectious Diseases Society of America recommendations published in 2010. For non-HIV and non-transplant patients, amphotericin B liposome plus 5-fluorocytosine is the optimum therapy option during the induction period.<sup>4</sup> But during the treatment, these medications need to be cared for their side effects.

In conclusion, as the number of immunocompromised patients has increased, a concomitant rise in patient morbidity and mortality from fungus infections has been noticed. Due to their immunosuppression, PNS patients are more prone to developing infections than other ones. Moreover, clinicians should consider performing a lumbar puncture if necessary when treating patients with PNS who experience unexplained fever and headache. The treatment, however, remains difficult even when the diagnosis is specific, and to have the best outcomes, typical therapeutic regimens must be personalized. Prompt recognition and early treatment of cryptococcal infections are essential to improve patient outcomes and reduce the associated risks.

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### References

1. Iyer KR, Revie NM, Fu C, Robbins N, Cowen LE. Treatment strategies for cryptococcal infection: challenges, advances and future outlook. *Nat Rev Microbiol.* 2021; 19:454-66. doi:

<sup>1,2</sup>Department of Ophthalmology, Baoding No. 1 Central Hospital, Baoding,  
<sup>3</sup>Department of Nephrology, Baoding No. 1 Central Hospital, Baoding, China.

**Correspondence:** Xiaodong Li. Email: lxd\_765@sina.com

**ORCID ID.** 0000-0002-9231-4853

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- 10.1038/s41579-021-00511-0.
2. Ma H, Wang X, Yan H, Liu Q, Yang D, Bian T. Dual intracranial infection with *Nocardia farcinica* and *Cryptococcus neoformans* diagnosed by next-generation sequencing in a patient with nephrotic syndrome: A case report. *Medicine (Baltimore)*. 2022; 101:e30325. doi: 10.1097/MD.00000000000030325.
  3. Su B, Zhang Q, Lv J. Cryptococcal meningitis in adult patients with primary nephrotic syndrome. *Clin Nephrol*. 2018; 90:390-5. doi: 10.5414/CN109384.
  4. Hu D, Zhang Q, Jiang W, Arastehfar A, Ilkit M, Fang W, et al. Cryptococcal Meningitis: A Rare Complication in HIV-Negative Patients with Nephrotic Syndrome in A Chinese Teaching Hospital. *Mycopathologia*. 2020; 185:959-69. doi: 10.1007/s11046-020-00482-5.
  5. Ngan NTT, Flower B, Day JN. Treatment of Cryptococcal Meningitis: How Have We Got Here and Where are We Going? *Drugs*. 2022; 82:1237-49. doi: 10.1007/s40265-022-01757-5.
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