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# Detection of toxoplasma tachyzoites in the cerebrospinal fluid of a COVID-19 positive SLE patient: a case study

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**Abstract**

The recurrence of latent toxoplasmosis is a frequent cause of toxoplasmic encephalopathy in individuals with immunosuppressive conditions or medication. If left untreated or diagnosed is delayed, it often resulting in fatality. The pathogen of Toxoplasma gondii has been identified in cerebrospinal fluid cytology and a limited number of documented cases of cerebral toxoplasmosis, typically observed in those with acquired immunodeficiency syndrome (AIDS). We report the identification of Toxoplasma gondii tachyzoites in the cerebrospinal fluid of a patient diagnosed with systemic lupus erythematosus (SLE) and concurrent SARS-CoV-2 positive infection. The presented case suggests that cerebral toxoplasmosis should be promptly considered when patients with systemic lupus erythematosus exhibit neurological manifestations.

**Keywords** Toxoplasmosis, SLE, AIDS, Toxoplasmic encephalopathy

## Introduction

As a prevalent parasitic organism found worldwide, Toxoplasma gondii infects approximately one-third of the global population. It is an intracellular parasite that specializes in causing toxoplasmosis, primarily affecting organs such as the brain, lungs, and eyes [1, 2]. In healthy adults, initial exposure may lead to mild flu-like symptoms within the first few weeks [3]. Subsequent asymptomatic phases are known as latent infections, during which the parasite can persist indefinitely in specific tissues [4]. In individuals with compromised immune systems, the reactivation of latent neurological lesions can result in severe conditions such as encephalitis. Neurotoxoplasmosis, also known as cerebral toxoplasmosis or toxoplasmic encephalitis (TE), emerges as a prominent manifestation, particularly among those afflicted with human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome. This infection stands as a primary cause of cerebral complications in such cases [5]. Past clinical reports have revealed a concerning trend where many systemic lupus erythematosus patients, who eventually develop TE, are initially misdiagnosed with neuropsychiatric systemic lupus erythematosus (NPSLE). This misdiagnosis often leads to adverse outcomes [2]. Our case underscores the critical importance of considering TE in the diagnostic process for SLE patients

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presenting with neurological symptoms, when headache, focal deficits, confusion, and impaired consciousness are present. Clinical trials should incorporate cerebrospinal fluid cytology examinations and detecting Toxoplasma tachyzoites into differential diagnosis as early as possible to quickly and accurately identify this rare, devastating but treatable disease.

## Case presentation

The patient is a 21-year-old female with a 2-year history of SLE. In the past 2 years, she has been on oral methylprednisolone, 9 tablets once daily; mycophenolate mofetil, 750 mg twice daily; tacrolimus, 1 mg once daily for suppressive immunotherapy. One month ago, she began experiencing urinary incontinence and headaches. Upon evaluation at the local hospital, lupus cerebritis was considered, the local hospital gave methylprednisolone + cyclophosphamide treatment, while intrathecal injection of methotrexate + dexamethasone treatment, with some improvement in the symptoms. She developed a high fever five days ago, with a maximum temperature reaching up to 38.5 °C. One day ago, the patient had sudden unresponsiveness, loss of consciousness, limb convulsions, recurrent fever, urinary incontinence, accompanied by involuntary shaking of the left hand for 3–4 s, foaming at the mouth. The patient woke up on her own 7 h later and could not recall any of the symptoms after waking up. Head MRI revealed: Multiple abnormal signals and destruction of blood-brain barrier occurred in bilateral cerebral peduncles, basal ganglia, thalamus, pons, right insular lobe, bilateral frontal lobes, and cerebellar hemispheres, suggesting a high possibility of acute necrotic encephalopathy.

This patient was admitted to the hospital on January 20, 2024, and presented with symptoms of "urinary incontinence persisting for over a month and unresponsiveness for more than a day." Follow-up medical history, the patient had a 2-year history of hepatitis B, ETV treatment for 2 years. Upon admission, she tested positive for COVID-19, and the HIV antibody test was negative, indicating a concurrent infection with the coronavirus. The preliminary diagnosis includes acute necrotizing encephalopathy, possibly due to COVID-19, while lupus cerebritis and lymphoma have not been excluded. The blood test results indicate the following: an elevated white blood cell count with leukocytes at 19.20*10^9/L, absolute neutrophil count at 14.32*10^9/L, absolute monocyte count at 1.39*10^9/L, absolute eosinophil count at 0.01*10^9/L, lymphocyte percentage at 9.5%, eosinophil percentage at 0.1%, hemoglobin level at 98 g/L, hematocrit at 0.322 L/L, mean corpuscular volume at 75.6 fL, mean corpuscular hemoglobin content at 23.0 pg, mean corpuscular hemoglobin concentration at 304 g/L, and a platelet count of 398*10^9/L. Biochemical analysis of Cerebrospinal fluid (CSF): Glucose (GLU) 3.7 mmol/L (Reference range: 2.2–3.9 mmol/L), Chloride (CL) 116 mmol/L (Reference range: 120–132 mmol/L), Protein (PRO) 909 mg/L (Reference range: 150–450 mg/L); CSF immunoglobulin levels: IgG 177 mg/L (Reference range: 0–34 mg/L), IgA 12.9 mg/L (Reference range: 0–5.0 mg/L), IgM 7.4 mg/L (Reference range: 0-1.3 mg/L). CSF routine analysis: 1 ml, colorless and transparent, total nucleated cell count 12*10^6/L, Pandy test (++). Flow cytometry results of CSF: a predominance of T lymphocytes, with a CD4 + cell count of 76 cells/μL, and no evident abnormal cells observed. Cerebrospinal fluid smear was negative for bacteria; cryptococcus was not detected by cerebrospinal fluid ink staining; mycobacterium tuberculosis (TB-DNA) nucleic acid test (cerebrospinal fluid) tested negative; blood culture, CSF bacterial culture, and fungal culture yielded no growth. After admission, she was given propofol tenofovir antiviral therapy for hepatitis B virus DNA quantitative measurement of 8.032 E2IU/mL; 2019 novel coronavirus-ORF1ab gene positivity (+), CT value > 30, she was given cenotrexate/ritonavir tablets antiviral therapy; instillation of methylprednisolone shock and tacrolimus to treat SLE, and dexamethasone intrathecal injection at the same time, and the patient's the condition was better than before. On January 25, the patient complained of blurred vision, conscious, no limb convulsions, no headache, no fever; on January 28, the patient developed fever with a maximum temperature of 39℃, lethargy, unconsciousness and respiratory distress and was given tracheal intubation, ventilator-assisted respiration, and other treatments; the patient's condition deteriorated progressively, on February 3, with worsening of the impaired consciousness, and aggravation of peripheral infections, and central infections; cranial brain MRI: Bilateral cerebral peduncles, basal ganglia region, thalamus, pons, right insula, bilateral frontal lobes, cerebellar hemispheres with multiple lamellar slightly hypodense shadows, slightly enlarged in scope compared to the previous one, with blurred borders, and slightly compressed narrowing of the left lateral ventricle; on February 7th, Toxoplasma tachyzoites were detected in the CSF cytology (Fig. 1), while the NGS sequencing results of CSF metagenomic suggested acute Toxoplasma gondii infection, quantitative luminescent immunoassay for Toxoplasma gondii antibody, serum Toxoplasma gondii IgM antibody positive at 110.93 IU/ml (normal < 6.0 IU/ml) and positive IgG antibodies at 297.23 IU/ml (normal < 0.8 IU/ml). CSF testing showed weakly Toxoplasma gondii IgM positive antibodies at 8.29 IU/ml and positive IgG antibodies at 136.97 IU/ml. Clinical administration of compound sulfamethoxazole injection for anti-toxoplasma treatment for 7 days after, the patient was in a profound coma, with bilateral dilated pupils, absent pupillary light reflex, loss of oculocephalic reflex, corneal

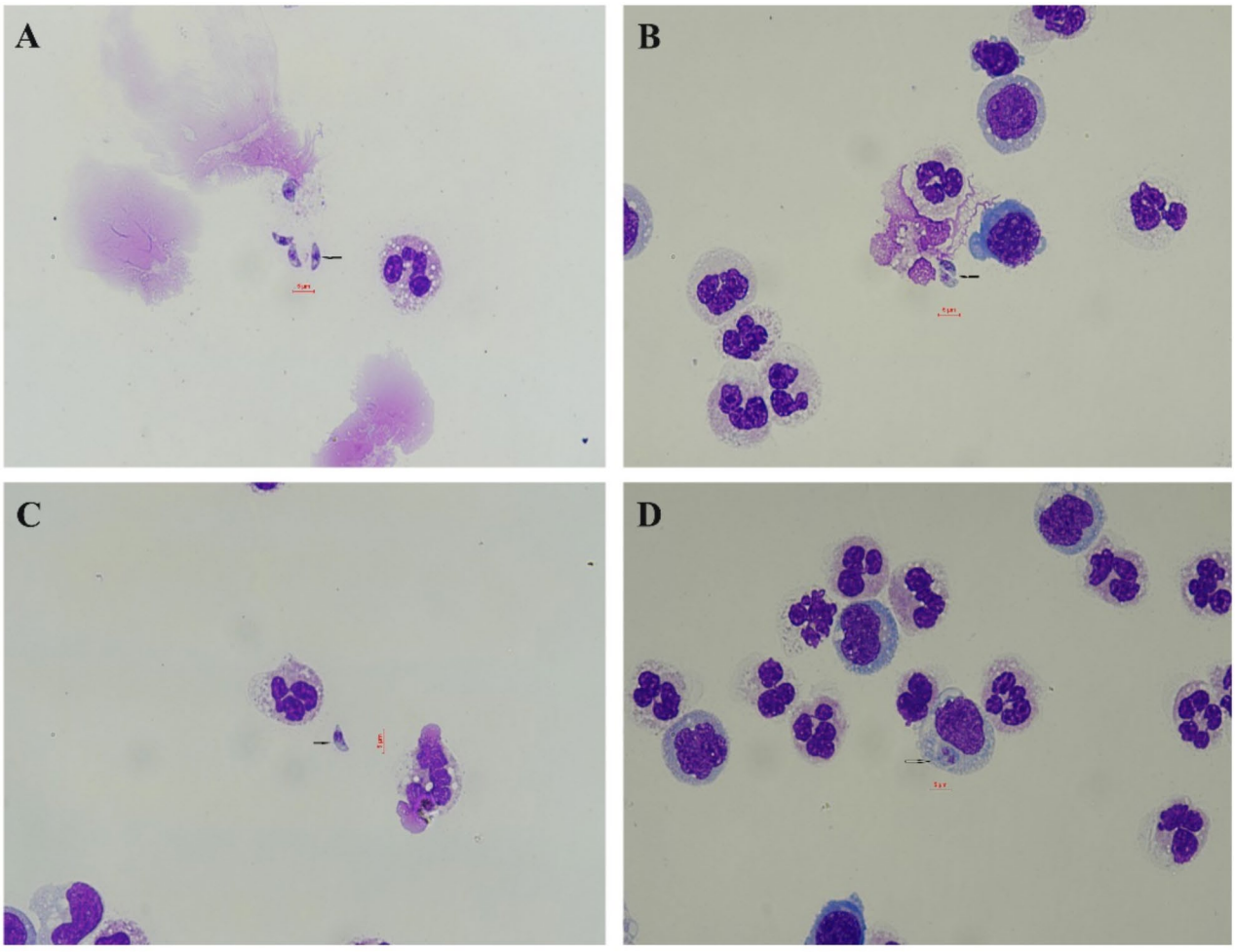


**Fig. 1** (**A**). Extracellular tachyzoites; (**B**). Four tachyzoites within neutrophils; (**C**). Extracellular tachyzoites; (**D**). Tachyzoites within macrophages (10 × 100 oil immersion lens)

reflex, cough reflex, and cessation of spontaneous respiration. EEG findings indicate severe brain injury. On February 19th, at the request of the family, the patient was automatically discharged.

CSF cytology examination under the microscope (Wright's stain).

## Discussions

Central nervous system (CNS) infection with toxoplasma gondii can lead to severe diseases and mortality in immunocompromised individuals. Its clinical manifestations may resemble those observed in patients with brain injury due to other etiologies. Therefore, accurate and timely diagnosis is crucial [6].

Recrudescence of latent toxoplasmosis is a common cause of toxoplasmic encephalitis in patients with immunosuppressive diseases or undergoing immunosuppressive therapy. This occurs when slowly dividing bradyzoites reactivate into rapidly replicating tachyzoites [7], particularly in individuals with fewer than 200 $CD4^+$ T lymphocytes per microliter of peripheral blood [8]. Current clinical diagnosis of toxoplasmosis typically relies on indirect evidence, combining clinical presentation, laboratory findings, and radiological data [1]. Enzyme-linked immunosorbent assay (ELISA) is commonly used to detect specific IgG and IgM antibodies. IgG titers peak 1–2 months after infection and remain elevated for life [8], while the toxoplasma IgG avidity test serves as an additional tool to differentiate between past and recent infections [9–16]. However, low avidity does not definitively indicate recent infection, and IgM antibodies may remain detectable for up to one year post-infection [6]. A negative IgM result can only exclude the possibility of recent infection. Consequently, experts recommend initiating treatment for symptomatic patients with positive toxoplasmosis serology and $CD4^+$ T lymphocyte counts < 100 cells/μL [6]. Metagenomic next-generation sequencing (NGS) may be a useful diagnostic

tool for toxoplasmic encephalitis [17]. PCR detection of Toxoplasma gondii DNA in cerebrospinal fluid (CSF) is specific but lacks sensitivity [18]. Neuroimaging modalities such as brain CT or MRI hold diagnostic value for toxoplasmic encephalopathy, often revealing hypodense, contrast-enhancing focal brain lesions with mass effects.

Additionally, direct identification of Toxoplasma gondii tachyzoites in secretions, excretions, body fluids, or tissues is rarely reported [19, 20]. Detection of tachyzoites in CSF from adult patients is exceptionally uncommon, with only six documented cases, for example, Dement et al. detected Toxoplasma gondii in cerebrospinal fluid from HIV patients [21], Eggers et al. also found cerebral toxoplasmosis from patients with acquired immunodeficiency syndrome [22], Jyothi et al. saw many Toxoplasma tachyzoites on cytologic examination of cerebrospinal fluid samples from 3-day-old neonates [23], Dunphy et al. reported a case of a 52-year-old HIV-infected patient diagnosed with fulminant diffuse cerebral toxoplasmosis by cerebrospinal fluid examination [24], Palm et al. find Toxoplasma tachyzoites in the cerebrospinal fluid cytology of a 50-year-old female patient with HIV [20]. Although some researchers question the utility of direct CSF examination for Toxoplasma gondii [25], one study identified tachyzoites in 2 of 6,090 CSF specimens (0.03%) over 12 years [26]. Experts propose that CSF cytology may aid in identifying Toxoplasma gondii. In China, a consensus on CSF cytomorphological examination and diagnostic techniques has been established to support clinical diagnosis [27]. Through standardizing the routine morphological examination, tangible components and their classifications in the effusion can be identified, especially aiding in the recognition of rare and abnormal morphological cells, thus assisting in the diagnosis of clinical diseases.

In this case, the patient had a 2-year history of systemic lupus erythematosus (SLE) with long-term immunosuppressive therapy and a $CD4^+$ cell count of 76 cells/μL. While some studies report no significant correlation between latent toxoplasmosis and COVID-19 severity [28], the patient resided in an area where consumption of raw or undercooked meat is common, raising the possibility of latent infection. Thus, we emphasize that toxoplasmic encephalopathy should be considered in the differential diagnosis for SLE patients presenting with severe neurological symptoms, even in those with negative HIV antibody tests. Early clinical suspicion is paramount.

## Conclusions

Toxoplasmosis, a common parasitic infection, can cause severe neurological complications in immunocompromised individuals. Early diagnosis is crucial for effective treatment. Serological testing, PCR, and brain imaging are useful diagnostic tools, but direct observation of parasites in CSF provides a definitive diagnosis. In immunosuppressed patients with neurological symptoms, cerebral toxoplasmosis should be considered early to reduce morbidity and mortality.

### Abbreviations

| | |
|---|---|
| COVID-19 | Corona Virus Disease 2019 |
| SLE | systemic lupus erythematosus |
| AIDS | acquired immunodeficiency syndrome |
| HIV | Human Immunodeficiency Virus |
| TE | toxoplasmic encephalitis |
| NPSLE | neuropsychiatric systemic lupus erythematosus |
| CSF | Cerebrospinal fluid |
| GLU | Glucose |
| CL | Chloride |
| PRO | Protein |

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### Author contributions

C.L. and H.X. Wrote the main manuscript text; Z.R. designed the work; F.H. and X.Y. was responsible for data acquisition and analysis; X.L. provided financial support along with their source of funding and manuscript revised; D.Y. confirmed that data and figures accurately reflects the original.

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### Data availability

Data is provided within the manuscript or supplementary information files.

## Declarations

### Ethics approval and consent to participate

The experiment performed was approved by the Medicine Ethics Committee of The First People's Hospital of Yunnan Province under the ethical approval codes GN003/2024. Written informed consent was obtained from individual or guardian participants.

### Consent for publication

We have the written informed consent obtained from the patient. The patient has consented to the submission of the case report for submission to the journal. Additional informed consent was obtained from participant for whom identifying information is included in this article.

### Competing interests

The authors declare no competing interests.

### Clinical Trial

Not applicable.

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## Publisher's note