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Toxoplasmosis in a case with multiple serous effusions and severe aplastic anemia

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Abstract

Toxoplasmosis, a parasitic disease, can cause fatal multi-organ failure in immunocompromised patients. The lack of specificity in the symptoms and the need to confirm a diagnosis of tachyzoites in fluids or tissues through microscopic examination leads to a delay in reaching a diagnosis. A 28-year-old woman with severe aplastic anemia received stem cell transplantation seven months ago, presented with fever. Computed Tomography scan and ultrasonography showed moderate pleural, pericardial, peritoneal, and pelvic effusions. Metagenomic next-generation sequencing of blood and alveolar lavage fluid was done, 11,082 and 17,154 sequence readings of *Toxoplasma gondii* were detected, accounting for 1.34% and 17.09% of genome coverage, respectively. Then, marrow aspirate smears showed *Toxoplasma gondii* tachyzoites and pseudocyst. This case report alerts clinicians about *Toxoplasma gondii* infection in stem cell transplantation patients with multiple serous effusions and fever. Clinical trial: Not applicable.

Keywords *Toxoplasma gondii*, Stem cell transplantation, Multiple serous effusions, Severe aplastic anemia

Introduction

Toxoplasmosis is a parasitic disease that can cause fatal multi-organ failure in immunocompromised patients [1–3]. Stem cell transplantation patients routinely receive trimethoprim-sulfamethoxazole (SMZ) for prophylaxis and have a lower risk of *Toxoplasma gondii* infection, especially those with toxoplasma-seronegative recipients and donors [4]. However, once ignored, it can be fatal. Here we present a case of a patient with disseminated toxoplasmosis with moderate pleural, pericardial, peritoneal, and pelvic effusions.

Case presentation

A 28-year-old female with severe aplastic anemia underwent haploidentical stem cell transplantation seven months ago, presented with fever for four days without cough, sputum, shortness of breath. Physical examination showed anemia, coarse breathing sounds in both lungs, and no dry or wet rales heard. Continuous oral administration of cyclosporine A (begining with 3 mg/kg.d and dosage ajusted according to the concentration of cyclosporine A), acyclovir (0.8 g/day), and trimethoprim-sulfamethoxazole (1.92 g/day) is recommended for conditioning in order to prevent graft-versus-host disease, viruses, pneumocystis pneumonia, and toxoplasmosis infection. She lived in a city in Shaanxi province, China. She gave no history of recent travel and no history of pet ownership. The donor and recipient had negative IgG

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antibody of *Toxoplasma gondii* serological tests before transplantation.

A computed tomography of the head, chest, abdomen, and pelvis showed pleural, pericardial, peritoneal, and pelvic effusions (Fig. 1a and c). Laboratory investigations were showed in Table 1.

Aerobic and anaerobic blood bacterial culture, as well as fungal culture was negative. Metagenomic next-generation sequencing (mNGS, NextSeq CN500,high throughput DNA sequencing) of blood and alveolar lavage fluid was done, and 11,082 and 17,154 sequence readings of *Toxoplasma gondii* were detected and accounting for 1.34% and 17.09% of genome coverage, respectively. One day later, bone marrow aspiration was done and bone marrow smears, with wright staining showed *Toxoplasma gondii* tachyzoites (Fig. 1d, red arrow) and pseudocyst (Fig. 1e, green arrow). Diagnosis of toxoplasmosis was confirmed.

Discussion

Common presentations of toxoplasmosis include fever, encephalopathy, and pneumonia [5]. The symptoms of this patient included fever and multiple serosal cavity effusions, which could easily lead to a misdiagnosis as ordinary parapneumonic effusion and hypoproteinemia [6]. However, the speculation is that the heart, pancreas, lungs, bone marrow, liver, and kidneys were all involved, indicating disseminated toxoplasmosis. Febrile pancytopenia may be a clinical manifestation of disseminated toxoplasmosis. The other frequently involved organs

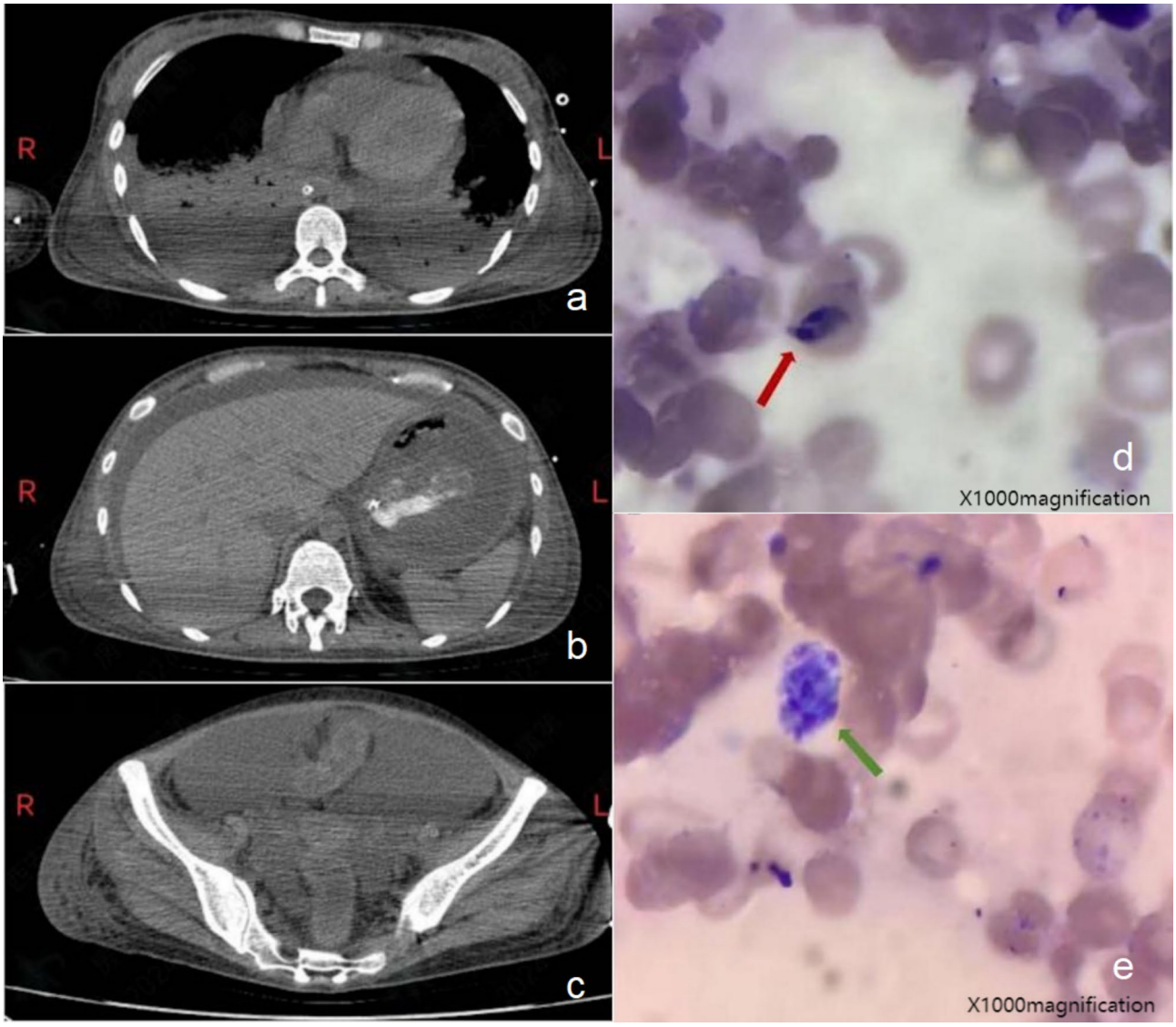

Fig. 1 Imaging and pathology findings. (**a**) Computed tomography (CT) of the thoracic cavity and moderate pleural and pericardial effusion. (**b**) CT of abdominal cavity and peritoneal effusion. (**c**) CT of pelvic cavity and pelvic effusion. (**d**) Bone marrow smear of *Toxoplasma gondii* tachyzoites (Red arrow, wright staining,×1000magnification). (**e**) Bone marrow smear of *Toxoplasma gondii* pseudocyst (Green arrow, wright staining,×1000magnification)

Table 1 Laboratory findings and their respective reference values

Test	Result	Reference Range
Hemoglobin	6.2 g/dL	14 to 18 g/dL
Absolute neutrophil count	0.64×10^9/L	2.5 to 7×10^9/L
Platelets	43×10^9/L	150 to 400×10^9/L
Albumin	21.5 g/L	40 to 55 g/L
Prothrombin time	14.7s	11–14 s
Activated partial thrombin time	47.5s	28–45.3 s
Fibrinogen	1.96 g/L	2–4 g/L
D-Dimer	9.99 mg/L	0-1 mg/L
Fibrinogen degradation products	20.7.mg/L	0-5 mg/L
Erythrocyte sedimentation rate	23 mm/h	0–20 mm/h
1-3-β-D glucan	< 10pg/ml	< 60pg/ml
Galactomannan	0.15 μg/L	< 0.5 μg/L
Procalcitonin	2.8ng/mL	< 0.05ng/mL
Pro-Brain natriuretic peptide	7723pg/mL	< 125pg/mL
Cardiac troponin I	2126.17pg/mL	24-30pg/mL
Cardiac troponin T	1.120ng/mL	0 to 0.01ng/mL
Glutamic-pyruvic transaminase	147U/L	7 to 40U/L
Aspartate transaminase	275U/L	13 to 35U/L
Alkaline phosphatase	313U/L	35-100U/L
Total bilirubin	99.5μmol/L	3.4–17.1μmol/L
Direct bilirubin	83.7μmol/L	0-3.4μmol/L
Urea nitrogen	16.08mmol/L	1.8 to 7.1mmol/L
Creatinine	190μmol/L	61.9 to 114.9μmol/L
Serum amylase	230U/L	40 to 140U/L

include eyes, heart, liver, pancreas, bone marrow, bladder, lymph nodes, kidney, spleen, and skin. The lack of specificity in the symptoms often leads to a delay in diagnosis [7]. Therefore the specific symptoms presented in this patient were not noticed as toxoplasmosis at first.

A timely and accurate diagnosis of toxoplasmosis is critical. Post-transplantation toxoplasma serology is unreliable because of profound immunosuppression. PCR-based testing has become the preferred method for diagnosis [8, 9]. Confirmation of the diagnosis is provided by the demonstration of tachyzoites in fluids or tissues by microscopic examination [10]. Although a direct examination of tachyzoites is the fastest and cheapest means of diagnosis, it frequently lacks sensitivity. Metagenomic next-generation sequencing of bronchoalveolar lavage fluid, blood, bone marrow aspirate, and cerebrospinal fluid may give clues for early diagnosis and avoid missed diagnosis [11]. For this patient, *Toxoplasma gondii* was identified in peripheral blood and alveolar lavage fluid by metagenomic next-generation sequencing. Then, marrow aspirate smears showed *Toxoplasma gondii* tachyzoites and pseudocyst.

For stem cell transplantation, patients with toxoplasmosis should be started as soon as possible with first-line medications, including pyrimethamine, sulfadiazine, and leucovorin [12]. This patient was infected based on oral trimethoprim-sulfamethoxazole prevention, and it may be related to poor drug enteric absorption. Intravenous trimethoprim-sulfamethoxazole was given once diagnosed.

While prophylactic agents are effective in reducing the risk of toxoplasmosis, certain patients may still experience reactivation of latent infection or primary infection or infection from blood transfusion because of incomplete suppression of the parasite [5]. This can occur because of drug resistance, suboptimal dosing, or altered pharmacokinetics in patients with compromised immune systems [13], such as those undergoing organ transplantation. When toxoplasmosis develops despite prophylaxis, it often presents more aggressively, leading to complications like toxoplasmic encephalitis or disseminated infection. These cases are associated with high morbidity and mortality [14], requiring prompt diagnosis and intensified treatment regimens. The occurrence of toxoplasmosis in this context underscores the importance of close clinical monitoring and possibly adjusting prophylactic strategies.

Unfortunately, the patient died of multiple organ failure *Toxoplasma gondii*.

This report has several limitations. First, pleural, pericardial, peritoneal, and pericardial effusions were not pathologically tested for. We could not confirm that damage to pancreas and liver and myocarditis was caused by *Toxoplasma gondii* infection. Second, we did not detect the concentration of trimethoprim- sulfamethoxazole and could not explain why we failed to prevent the *Toxoplasma gondii* infection for this patient.

Conclusion

This case underscores the importance of considering *Toxoplasma gondii* infection in stem cell transplantation patients presenting with multiple serous effusions and fever. While a single case cannot represent the broader population, it highlights the need for careful monitoring and a high index of suspicion in at-risk patients. Early diagnosis, potentially through metagenomic next-generation sequencing, may improve outcomes by facilitating timely and targeted treatment of toxoplasmosis.

Abbreviations

SMZ	Trimethoprim-sulfamethoxazole
CT	Computed tomography
mNGS	Metagenomic next-generation sequencing

Author contributions

Xiaoning wang, writing original draft. Hao Li and Le Ma, Data collection. Zhao Jing and Zhang Mei, investigation. Fatahichegeni Mahsa and Ansarian Mohammad Amin edited the manuscript. Pengcheng He, Design and data analysis. All authors revised and approved the final manuscript.

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Data availability
The datasets used may be made available by the corresponding author upon reasonable request.

Declarations

Ethics approval
The study was approved by the ethical review boards of the first affiliated hospital of Xi'an jiaotong university.

Consent for publication
Written informed consent for publication was obtained from the patient's husband.

Competing interests
The authors declare no competing interests.

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