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Case Report

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Pulmonary and Renal Toxoplasmosis in an Immunocompetent Adult Patient

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Abstract

Toxoplasmosis is caused by the protozoan parasite *Toxoplasma gondii* (*T. gondii*), which is one of the most widespread zoonotic pathogens known today. It is a global health hazard as they infect 30-50% of the world's human population. Acute toxoplasmosis is usually asymptomatic and self-limited in immunocompetent people, recovering without treatment and do not require specific therapy. Therefore, rare complications are associated with infection in the individuals with normal immune systems. However, we present a rare case of an immunocompetent man with acute *T. gondii* infection confirmed by serology, subsequently presented with two life-threatening organ dysfunctions: severe renal and pulmonary involvement, requiring hospitalization and anti-parasitic treatment.

Keywords: Toxoplasmosis; Immunocompetent; Renal disease; Pulmonary disease

Introduction

Toxoplasmosis is a disease caused by an obligate intracellular protozoan of worldwide spread. There are three infective stages of *Toxoplasma gondii* (*T. gondii*) infection: invasive tachyzoites, tissue cyst bradyzoites, and environmental sporozoites, which are protected inside an oocyst. Bradyzoites can persist inside human cells during protracted periods of time. Remarkably stable oocysts are transmitted to other hosts through inadvertent ingestion [1]. Domestic cats and other felids are the known definitive hosts of the agent and can eliminate viable oocysts through their feces [2]. It is a global health hazard as they infect 30-50% of the world's human population [2, 3]. *T. gondii* prevalence in humans varies across countries and regions [2-4]. A possible explanation is that *T. gondii* incidence is higher in regions with higher humidity and temperature, such as South America (prevalence in Brazil reaches 77.5%) [2, 4], in the same way that infection by the parasite is lower in some European countries and the Far East [1, 4]. This is because the oocysts are more long-lived in humid environments during the parasite's reproduction cycle [1].

Toxoplasmosis is also the most common foodborne parasitic infection that necessitates hospital treatment and ranks third among foodborne infections that require hospitalization [1]. Most immunocompetent individuals infected with *T. gondii* either remain asymptomatic [1, 3, 5], or have a subclinical course with minor symptoms that mimic other ailments such as the flu [1, 3]. We present a rare case of an immunocompetent man with acute *T. gondii* infection confirmed by serology. He subsequently developed severe renal and pulmonary involvement and required hospitalization.

Case Report

Investigations

A 38-year-old previously healthy, southern Brazilian male presented to an emergency unit with a chief complaint of darker-than-usual urine and pale stools. He was transferred to a tertiary health center due to the progressive worsening of the condition, with the onset of myalgia and hematuria. Leptospirosis was suspected.

The patient reported no comorbidities or use of any medication before the presentation of symptoms. The patient denied smoking or recreational drug use. However, he reported being an alcoholic with a daily consumption of approximately 6,300 mL of fermented and distilled beverages. He also mentioned living in a house with many street cats with an unknown vaccination history.

Physical examination on hospital admission revealed a temperature of 38.6 °C, blood pressure of 110/80 mm Hg, heart rate of 128 beats/min (tachycardia), and respiratory rate of 16 breaths/min. Systemic examination results were unremarkable except for jaundice in the sclera (1 on a scale of 4).

Laboratory tests on admission revealed elevated levels of liver enzymes (aspartate aminotransferase; 183; alanine aminotransferase: 283 (normal range (NR) < 50 U/L), mild hyperbilirubinemia (total bilirubin: 1.81; direct bilirubin: 0.79; NR: total bilirubin < 1.3 mg/dL; direct bilirubin > 0.4 mg/dL)), gamma-glutamyl transferase: 350 (NR < 86 U/L); white blood cells: 4.230/µL (NR: 4 - 11 × 10^3/mm^3); platelets: 72,000 (NR:

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150 - 400 × 10^3/mm^3); normal levels of renal function; and electrolytes (urea: 25 (NR < 50 mg/dL); creatinine: 0.86 (NR < 1.5 mg/dL); Na: 131 (NR: 135 - 145 mEq/L) and K: 3.5 (NR: 3.5 - 4.5 mEq/L).

The initial hypotheses were leptospirosis and liver involvement caused by alcohol libation. The patient was administered intravenous ceftriaxone (1 g/day). Blood cultures and serology for hepatitis B and C, human immunodeficiency virus (HIV), and leptospirosis were requested and were non-reactive. Abdominal ultrasonography and computed tomography (CT) were performed, and no acute biliary disease was found.

Between the fourth and sixth days of hospitalization, the symptoms worsened. The patient presented with persistent fever, pain mainly in the shoulders and thighs, dysuria with frothy and earthy urine, and desaturation requiring supplemental oxygen (nasal catheter, 2 L/min). On physical examination, the patient had mobile, elastic lymph nodes (0.5 cm) bilaterally in the lateral cervical chain, temperature of 39.5 °C, blood pressure of 110/70 mm Hg, pulse of 120 beats/min, respiratory rate of 20 breaths/min, and oxygen saturation of 91%.

Serological investigation of mono-like disease revealed non-reactive HIV, cytomegalovirus, and Epstein-Barr virus infection. Serological testing revealed the presence of *T. gondii*-specific immunoglobulin (Ig)M antibodies by enzyme-linked immunoassay (ELISA), with IgG being non-reactive. Chest angiotomography revealed elevation of the right hemidiaphragm with a band of atelectasis at the lung base, ruling out pulmonary thromboembolism. Blood culture results were negative. A 24-h urinalysis revealed proteinuria of 2,000 mg/L, which raised the suspicion of glomerulonephrosis.

Diagnosis

The two initial hypotheses were leptospirosis and liver involvement caused by alcohol libation. The first was due to the symptoms of dark urine, fever, and marked muscle pain in the lower limbs. The second was due to the patient's daily consumption of large quantities of alcoholic beverages. However, based on the data collected associated with the symptoms presented, toxoplasmosis became a strong diagnostic hypothesis. The patient in this case lived with many unvaccinated cats and had poor hygiene. He also presented with signs and symptoms related to the mono-like syndrome, which was confirmed by laboratory tests and improved with treatment for toxoplasmosis. In addition to toxoplasmosis, mononucleosis and other mono-like syndromes have been considered. Due to worsening of fever and desaturation, other infectious diseases were suspected. This included coronavirus disease 2019 (COVID-19) because of the pandemic and hantavirus disease because of pulmonary and renal involvement. Both were ruled out by using complementary examinations.

Treatment

Treatment was initiated with trimethoprim-sulfamethoxazole, three capsules every 6 h, with toxoplasmosis as the central hypothesis. Prednisone 80 mg/day was started to reduce the inflammatory response elicited by *T. gondii* in the lungs and kidneys.

Follow-up and outcomes

The patient showed marked improvements in clinical and laboratory findings after the first week of treatment for *T. gondii*. The clinical signs included no pain, no respiratory symptoms, preserved appetite, clear urine, no hematuria, and no foam. The patient was discharged 16 days after admission. Toxoplasmosis treatment was maintained for 42 days, and the patient was referred to a nephrologist.

Discussion

This clinical case illustrates an immunocompetent patient with acute toxoplasmosis and associated renal and pulmonary dysfunctions.

Fever, cervical lymphadenopathy, myalgia, and fatigue are the most important symptoms of acquired toxoplasmosis. Symptoms are not age-dependent, in the same way as our patient presented these findings [2, 3]. Furthermore, hepatomegaly and hepatitis with an increase of 5 - 10 times the aminotransferase levels occur frequently [2]. *T. gondii* can cause an increase in lymph nodes [2]. While this clinical finding is not mandatory, our patient had an enlarged chain of cervical lymph nodes. *T. gondii* has the potential to invade all nucleated cells in the body, although the preferred target organs are the lymph nodes, brain, heart, and lungs [2].

Adequate management of toxoplasmosis involves prompt and accurate diagnosis. Though diagnosis of toxoplasmosis by detection of the parasite using microscopy and bioassays is regarded as the gold standard, its clinical diagnosis is more likely made by serological methods [4]. The diagnosis of acute infection is made by looking for positive IgM antibodies, although they can remain that way for months or years [4]. For this reason, other forms of diagnosis have been developed, which include serial samples, measurement of IgG avidity, and detection of parasite DNA [4]. The correct diagnosis is important for medical practice, as the drugs for treatment preferentially target the tachyzoite form of the parasitosis [4].

In this case report, the first serological test revealed IgM reactive and IgG non-reactive for *T. gondii*, confirming acute toxoplasmosis. IgG for *T. gondii* was reactive only in the second week. IgM antibodies are usually detectable about 1 week after the infection and IgG antibodies appear after 2 weeks of infection and peak at 3 months [5].

Pulmonary toxoplasmosis is commonly observed in immunosuppressed patients; however, acute toxoplasmosis rarely culminates in clinical lung involvement in immunocompetent patients. In these individuals, it usually develops into an atypical pneumonia. Despite being very rare, toxoplasmosis pneumonia has been recognized since the 1940s [2].

Pulmonary toxoplasmosis can be difficult to diagnose due to a nonspecific and variable presentation and low awareness among healthcare providers due to its rarity [6].

In a review and case report by Leal et al, they identified only nine cases of *T. gondii* pneumonia with parasitic confirmation in the medical literature [2]. Most patients were young men, with a median age of 34 years, as per our case report [2]. A common epidemiological feature in this review was the consumption of raw or undercooked meat [2]. Our patient denied having consumed this type of food; however, he lived with many street cats. One of the sources of infection is attributed to the direct ingestion of food or water contaminated with cat feces containing *T. gondii* oocysts [2].

Pneumonia caused by *T. gondii* tends to manifest with fever, dyspnea, persistent non-productive cough, myalgias, arthralgias, and lymphadenopathy. These are the same symptoms that the patient in this case presented with during hospitalization. In addition to the symptoms mentioned, rash and weakness can also be associated [2, 6, 7]. As the interstitial infiltrate spreads, exudation of fibrin along with neutrophils and macrophages into the alveolar spaces can eventually develop into a pattern of diffuse alveolar damage, with pneumocyte proliferation and focal necrosis [7].

Although the isolation of the organism in bronchoalveolar lavage is the diagnostic gold standard, serological confirmation in typical clinical presentations is sufficient for the diagnosis to be made [2, 6].

CT findings usually include diffuse interstitial infiltrates and ground-glass opacities with thickening of the interlobular septa. This may mimic other pulmonary conditions such as atypical pneumonia, pneumocytosis, and methotrexate lung disease [7]. Our patient had pleural thickening at the lung bases on CT, a nonspecific finding.

No parasitic strains exhibited specific pulmonary tropism. But there are some suggestions that strains from the Amazon could be more virulent or aggressive, leading to severe disseminated disease [2].

T. gondii infection activates the mononuclear phagocytic system and plays a role in phagocytosis. The immune system of an immunocompetent host then generates an immune response, the infection is controlled [8]. The hypotheses for pulmonary involvement by *T. gondii* in immunocompetent patients are related to the means of contamination. Toxoplasmosis pneumonia occurs either by infection with high parasitic loads or by means other than the usual ones, such as inhalation. However, there are no studies that support such an association [2].

Our patient also had renal involvement, in addition to pulmonary involvement. To the best of our knowledge, this is the first case report detailing pulmonary and renal involvement in an immunocompetent patient with acquired toxoplasmosis. The first reported case of generalized toxoplasmosis with nephrotic syndrome in an immunocompetent adult was described by Oseroff. He cautioned that the report served to alert clinicians to the possibility of toxoplasmosis in the diagnosis of fever of unknown origin and adult nephrotic syndrome [9].

The mechanisms of renal injury in the association of nephrotic syndrome and toxoplasmosis are not well understood [10]. Concerning its etiology, nephrotic syndrome is recognized as idiopathic and secondary, with the former appearing as a frequent pathology in pediatrics [11]. The presentation outside of this age group requires the clinician to look for secondary causes of the etiology, including parasites [11]. *T. gondii* has a tropism for the kidneys. Although it is an intracellular parasite, glomerular damage is caused by immune complexes. These contain a toxoplasmosis antigen identified in infected mice and congenital nephrotic syndrome due to toxoplasmosis [11]. Others possible explanations for renal dysfunction and toxoplasmosis are severe systemic infection, activation of the immune system that leads to glomerulonephritis, and direct infection of the parasite in the urinary tract [12]. According to a study by Gharadaghi et al, the rise of apoptotic cells in mice infected with *T. gondii* was higher when compared to twice as many apoptotic cells in mice that did not show zoonosis. It also revealed an increase in the fibrosis-mediating cytokine (transforming growth factor (TGF)-β) and a urea level that was eight times higher than the reference value in animals infected with the parasite. Ultimately, this study found histopathological changes that included tubular degeneration, tubular dilatation, pulmonary congestion, glomerular deficiencies, and necrosis [13]. It is important to remember that other parasites have also been associated with kidney damage and urinary disorders (e.g., proteinuria, lymphocituria, and pyuria). As examples, there are schistosomiasis, malaria, filariasis, leishmaniasis, trichinosis, echinococcosis, and trypanosomiasis [13].

Specific antimicrobial therapy should be initiated as soon as toxoplasmosis is suspected. This is due to the course of the disease, which has a fatal potential and the possibility for complete recovery [2]. The standard treatment for toxoplasmosis is sulfadiazine and pyrimethamine. However, trimethoprim-sulfamethoxazole is supported as an option in the treatment of disseminated infection in immunocompetent people for a total of 4 - 6 weeks [6].

This case illustrated that toxoplasmosis should be thought of as a differential diagnosis even in immunocompetent people with mono-like symptoms and organ dysfunction in order to have an adequate diagnosis and specific treatment.

Learning points

Toxoplasmosis with organ dysfunction is rare in immunocompetent individuals; however, atypical pneumonia and renal involvement can occur. The standard treatment for toxoplasmosis is sulfadiazine and pyrimethamine, but trimethoprim-sulfamethoxazole is supported as an option for the treatment of disseminated infections in immunocompetent individuals. This disease should be considered in patients with mono-like symptoms and organ dysfunction, even if they are immunocompetent.

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None to declare.

Conflict of Interest

None to declare.

Informed Consent

Informed consent was obtained.

Author Contributions

Erika Pangracio contributed to the data analysis tools, performed the analysis, and wrote the paper. Viviane de Macedo conceived and designed the analysis, collected the data, contributed to the data analysis tools, and performed the analysis. Priscilla Koppe Alves collected the data.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author.

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