Short Communication

Severe Toxoplastic Hepatitis in an Immunocompetent Patient

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SUMMARY: Acute Toxoplasma gondii infection causes different clinical courses in 10–20% of cases. In immunocompetent patients, toxoplasmosis most often presents as asymptomatic cervical lymphadenopathy. Clinical manifestations such as pneumonia, myocarditis, hepatitis, and encephalitis are rarely reported. We present the case of an immunocompetent patient with a serious and complicated clinical course of toxoplastic hepatitis with a maculopapular rash. The diagnosis was confirmed by serology and identification of bradyzoites in liver biopsy samples.

Toxoplasmosis is caused by infection with the obligate intracellular parasite Toxoplasma gondii. Primary infection is usually subclinical, but cervical lymphadenopathy or ocular disease can occur. Infections acquired during pregnancy may cause severe damage to the fetus (1). Some patients develop severe symptoms, including high fever (39–40°C), myalgias, arthralgias, fatigue, dry cough, dyspnea, generalized lymphadenopathy, hepatosplenomegaly, and maculopapular rash (2). Clinical manifestations such as pneumonia, myocarditis, hepatitis and encephalitis are rarely reported (3).

Toxoplasmosis can be fatal in immunodeficient or immunocompromised patients. Immunocompromised hosts often experience a life-threatening involvement of one or more organs during primary infections and can suffer reactivation of pre-existing tissue cysts due to a deficient of the immune system (3). We present a case of toxoplastic hepatitis in an immunocompetent woman, highlighting the need for increased awareness of the etiology in cases of severe unknown conditions despite their presumed relative rarity.

46-yr-old woman was admitted for complaints of fever, nausea, vomiting, fatigue, loss of appetite, and myalgia since 2 days. She reported having consumed raw meat since childhood. She had used paracetamol for her high fever. Physical examination revealed a fever of 39.5°C, with a pulse of 102 beats/min, and blood pressure of 120/70 mmHg. She did not have neck stiffness, lymphadenopathy, or cardiac or respiratory abnormalities. Disseminated maculopapular rashes, hepatomegaly, and pain on the right upper abdominal quadrant with palpation were noted. Laboratory analysis showed values and concentrations as follows: hemoglobin (Hb): 13.4 g/dL, hematocrit: 41.1%, platelet count (Plt): 218 × 10^3/µL, white blood count (Wbc): 13.94 × 10^3/µL (36% granulocytes, 40% lymphocytes, and 16% eosinophiles), aspartate aminase (AST): 633 U/L (normal: 0–38 U/L), alanine transaminase (ALT): 698 U/L (normal: 0–49 U/L), alkaline phosphatase: 260 U/L (normal: 45–129 U/L), lactate dehydrogenase: 848 U/L (normal: 120–246 U/L), gamma glutamyl transpeptidase: 140 U/L (normal: 0–38 U/L), albumin: 3.0 g/dL (normal: 3.2–4.8 g/dL), total serum protein: 5.6 g/dL, IgE: 1,050 IU/mL (normal: ≤100), rheumatoid factor: 15.7 IU/mL (normal: ≤15), ferritin 210 ng/mL (normal: 13–150 ng/mL), and C-reactive protein: 124 mg/L (normal: 0–5 mg/L). Electrolyte, blood urea nitrogen, creatinine, calcium phosphate, and bilirubin levels as well as sedimentation rates were within normal limits. Abdominal ultrasonography revealed hepatomegaly (195 mm). However, there was no evidence of steatosis, biliary canal dilatation, or lymphadenopathy. Skin lesions were believed to be eruptions due to paracetamol use. Methylprednisonelone treatment (60 mg/day) was initiated. However, her high fever (39–40°C), maculopapular rashes, and itching persisted under this treatment.

Further testing revealed laboratory values as follows: Wbc: 30.98 × 10^3/µL, Hb: 13.2 g/dL, and Plt were 160 × 10^3/µL. Bilirubin levels had increased, with total bilirubin (TB) and direct bilirubine (DB) levels reaching 3.1 mg/dL and 2.6 mg/dL, respectively. Based on her high fever, leukocytosis, TB and DB levels, and pain in the right upper quadrant, the patient was preliminary diagnosed with acute cholangitis, and piperacillin tazobactam (3 × 4.5 g) treatment was started. In order to investigate the source of her fever and the hepatitis etiology, the patient was tested for hepatitis B, C, and E; human immunodeficiency virus, cytomegalovirus, Epstein-Barr virus, rubella, herpes simplex virus, and brucella. The patient was negative for anti-nuclear antibodies, anti-mitochondrial antibodies, anti-dsDNA, perinuclear anti-neutrophil cytoplasmic antibodies, anti-smooth muscle antibodies, and liver-kidney microsome antibodies. Chest X-rays, cranial magnetic resonance imaging, ophthalmic examination, and echocardiography were normal.

T. gondii serology findings revealed anti-Toxoplasma IgM and IgG antibodies (result: 2, cut off: 0.9 and result: 83.4, cut off: 8, respectively) (Capture ELISA system, Chorus). Therefore, based on these laboratory findings as well as her history of eating raw meat, the patient was diagnosed with toxoplasmosis, and clin-
damycin treatment (4 × 600 mg) was started. Two weeks later, there was a 4-fold increase in anti-Toxoplasma IgG titers (result: 464).

Liver and skin biopsies were performed to assess the persistence of increased liver enzyme values and itchy maculopapular rashes. Liver biopsy revealed mixed inflammatory cell infiltration with fewer eosinophil leukocytes in the sinusoids and portal regions. Focal necrosis, cholestasis in the perportal regions, and cloudy swellings along with widening in the sinusoids were noted. Pathological examination with hematoxylin-eosin, Giemsa, and Periodic Acid Schiff (PAS) stains revealed *T. gondii* bradyzoites and hepatitis (Fig. 1). Skin biopsy showed chronic vasculitis. The piperacillin/tazobactam treatment was discontinued on day 14. AST and ALT levels decreased to 44 U/L and 141 U/L, respectively, on the 8th day of clindamycin treatment. The patient was discharged on clindamycin treatment (4 × 600 mg) in a generally healthy condition. On follow-up, her clinical and laboratory findings had ameliorated. Treatment was discontinued on day 21.

Toxoplasmosis is mainly acquired by ingestion of food or water contaminated with oocysts shed by cats or by eating undercooked or raw meat containing tissue cysts (1). Our patient reported a history of eating raw meat. Acute *T. gondii* infection causes different clinical courses in 10–20% of cases. In immunocompetent patients, toxoplasmosis most often presents as asymptomatic cervical lymphadenopathy (3). However, pneumonia, myocarditis, and myositis may also occur. Rarely, hepatitis has been reported in immunocompetent and immunodeficient patients (4–8). Vischer et al. reported 2 cases of hepatitis due to *T. gondii* in 1967 (9).

Severe cases of toxoplasmosis have been previously reported in French Guiana, Suriname, and Brazil (10–12). Patients commonly develop a generalized infectious syndrome with visceral involvement such as mild hepatitis, jaundice, atypical pneumonia, enlarged lymph nodes, and, less frequently, myositis and chorioretinitis (8,10). Patients are often admitted with fever, rash, and a clinical picture of hepatitis.

Diagnosis of acute toxoplasmosis typically requires amplification of parasite DNA from blood and body fluids, revealing and isolating *T. gondii* bradyzoites in histopathological examination of biopsy materials (direct), or detection of antibodies against parasites in blood (indirect). Bradyzoites are rarely seen in stained tissue sections during histopathological examination. Bradyzoites are present in primary and reactive infections and indicate active infection (3). We detected bradyzoites in the liver tissue of our patient. Therefore, diagnosis was confirmed by histopathologic and serologic means.

The standard treatment for acquired toxoplasmosis in both immunocompetent and immunodeficient patients is the synergistic combination of pyrimethamine and sulphonamides. However, because of toxicity, the therapeutic efficacy of pyrimethamine-sulphonamide combinations may be limited. Alternatively, newer macrolides and clindamycin may be used (3). Due to severe clinical signs and visceral involvement in our patient (maculopapular rash and hepatitis), we initiated clindamycin treatment, although this therapy is rarely indicated in immunocompetent patients. We preferred clindamycin due to being easier to reach and because pyrimethamine and sulfadiazine combination were not

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**Fig. 1.** (Color online) *Toxoplasma gondii* bradyzoites seen in hepatocyte stained by PAS.
available in our regional market. A 21-day treatment regimen managed the disease and cured the infection.

In conclusion, in order to provide prompt treatment, the potential for toxoplasmosis should be considered for patients with hepatitis, especially those presenting with fever and rashes.

Conflict of interest None to declare.

REFERENCES