**CASE REPORT**

**DISSEMINATED TOXOPLASMOSIS PRESENTING AS SEPSIS IN TWO AIDS PATIENTS**

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**SUMMARY**

This report describes two patients who presented acute disseminated and severe toxoplasmosis as the first opportunistic disease related to acquired immunodeficiency syndrome. At admission, clinical and laboratory findings were similar to sepsis or septic shock and a fast evolutive course to death occurred in both cases. At necropsy, an inflammatory reaction and presence of a great number of *Toxoplasma gondii* cysts and tachyzoites were observed in most organs examined.

**KEYWORDS:** AIDS; Acute disseminated toxoplasmosis; Sepsis; *Toxoplasma gondii*.

**INTRODUCTION**

Acute disseminated toxoplasmosis is a rare event in immunocompetent individuals, but it can occur most frequently in immunosuppressed patients or undergoing immunosuppressive therapy for several disorders. Since the first acquired immunodeficiency syndrome (AIDS) cases described, it was observed an increased number of meningoencephalitis by *Toxoplasma gondii* in these patients due to reactivation of latent foci in the central nervous system (CNS). This disease is considered one of the most frequent AIDS defining condition around the world. Pneumonitis and myocarditis are also commonly diagnosed usually associated to disseminated disease, but any organ or system can eventually be involved. Toxoplasmosis reactivation risk in AIDS patients is related to their toxoplasma antibody prevalence and the immunodeficiency severity state, and it occurs mainly when CD4+ count is less than 100 cells/mm³.

Occasionally, a disseminated toxoplasmosis picture with clinical and evolutive course like sepsis or septic shock has been reported, most of them as necropsy features due to difficult diagnosis, perhaps because there are other more frequent infectious agents causing sepsis in these patients. The aim of this report is to present two AIDS patients with clinical, laboratory and necropsy features similar to the cases previously described.

**CASES REPORTS**

**CASE 1:** a 33-year-old white female patient was admitted at the teaching hospital emergency with a seven-day history of fever, asthenia, adynamia, weight loss, dry cough and decreased mental status. She was confused with Glasgow scale coma score of 10, positive Brudzinsk sign, but neither stiff neck, papilledema nor focal deficit were observed. Axillary temperature 37.8 °C, arterial blood pressure of 80/40 mmHg, mild tachypnea and tachycardia, but no other cardiac, respiratory and abdominal abnormalities were noticed.

Laboratory assessment: hemoglobin 13.2 mg/dL, hematocrit 37.4, white blood cells 1.3 X 10⁹/L (band cell forms 6%, neutrophils 47%, eosinophils 9%, basophils 0, lymphocytes 37% and monocytes 1%), platelets 5.3 X 10⁹/L, fibrinogen 3.53 g/dL, glycemia 77 mg/dL, serum urea 60 mg/dL, serum creatinine 2.2 mg/dL, Na 154 meq/L, K 3.1 meq/L, Ca 8.1 mg/dL, Mg 1.9 mg/dL, LDH 1,015 IU/L, AST 212 IU/L, ALT 54 IU/L. CSF analysis: 4 cells, glucose 7 mg/dL, proteins 104 mg/dL, Cl 903 meq/L, and bacteria, mycobacteria and fungi stains were negative. Cryptolatex® test was negative, HIV antibodies positive by ELISA test and confirmed by Western Blot. CD4+ count 4 cells/mm³; a chest X-ray plain showed an interstitial and alveolar infiltrate pattern similar to Acute Respiratory Distress Syndrome (ARDS) and the skull computerized tomography was normal.

She presented apnea and needed mechanic ventilation. An empiric treatment to neurotuberculosis with isoniazid, rifampicin and pyrazinamide was administered. She fastly evolved to hemodynamic instability, disseminated intravascular coagulation (DIC) with hemorrhagic diathesis (epistaxis, gingival hemorrhage, massive hemoptisis) and died one day after admission.

At necropsy, it was observed a great amount of *T. gondii* cysts and tachyzoites, stained with H&E and immunoperoxidase technique, in...
the brain, heart, tongue, pancreas, bladder, adrenal glands, lungs, esophagus, small bowel, liver, kidneys, bone marrow, lymphnodes, palatine tonsilla and thyroid gland. However, meningoen cephalitis, myocarditis, pneumonitis, esophagitis, hemorrhagic colitis, severe tubular necrosis, hemorrhagic cystitis, hypophysitis and thyroiditis by *T. gondii* were well characterized.

Besides, ARDS lung findings, with extensive bleeding areas, as well as hyaline thrombi formation in small vessels, suggestive of DIC were observed. Adrenal gland presented inflammatory reaction with large sized cells and basophilic intranuclear inclusions, characteristic of cytomegalovirus infection. Specific stains from all organs were negative for fungi, mycobacteria, bacteria and spirochetes (Fig.1).

**CASE 2:** a 24-year-old white female patient was admitted at the teaching hospital emergency with a 15-day history of fever, anorexia, asthenia, adynamia, urinary incontinence, dysuria, mental confusion, and weight loss of 12 kg in the last months.

At admission, she presented torpor, slurring speech, positive Babinski sign, stiff neck and bilateral papilledema, generalized mucocutaneous pallor and hypoperfusion signs. She was tachypneic, tachycardiac, blood pressure was of 80/40 mmHg. In addition, basal pulmonary rales, hepatomegaly, splenomegaly and severe muscle hypotrophy were noticed. Laboratory assessment: hemoglobin 5.9 mg/dL, hematocrit 18.4, white blood cells 1.89 X 10^9/L (88% neutrophils, 4% eosinophils and 8% lymphocytes), platelet count 1.08 X 10^9/L. Urinary sediment analysis: density 1.020; leukocytes 170,000; red cells 330,000, and Trichomonas spp. Serum urea 78 mg/dL, serum creatinine 0.7 mg/dL, Na 125 meq/L, K 4.0 meq/L, Ca 8.1 mg/dL, glycemia 82 mg/dL, AST 265 IU/L, ALT 240 IU/L, proteins 5.8 g/dL, albumin 2.8 g/dL, creatinine clearance 95 mL/min. CSF analysis: six cells, glucose 24 mg/dL, Cl 675 meq/L. Specific stains to mycobacteria, bacteria, spirochetes and fungi were negative. IgG serum antibodies to HIV and *T. gondii* were positive by ELISA test. Serum antibodies tests to *Treponema pallidum*, *Trypanosoma cruzi*, Epstein Barr virus and hepatitis C virus also were negative. CD4+ count six cells/mm³ and viral load 276,915 copies RNA/mL. A chest X-ray plain showed a severe interstitial and alveolar bilateral infiltrate pattern and skull computerized tomography was normal.

Empirical therapy to sepsis with ceftriaxone and vancomycin was administered. The patient evolved with pancytopenia, prothrombin activity of 28%, ARDS, and hypotension, requiring mechanical ventilation. Death occurred on day ten.
Necropsy showed: diffuse encephalitis with presence of multiple inflammatory foci lesions on basal nucleus with necrotic center and macrophages in the periphery, inflammatory infiltrate, gliosis and great number of T. gondii cysts and pseudocysts stained with H&E and immunoperoxidase technique. Besides interstitial pneumonitis with extensive mononuclear inflammatory infiltrate, localized mainly in the intralveolar septa, hyaline membrane aspect and T. gondii cysts were also noticed. The parasite was seen in the bone marrow, trachea, pancreas, adrenal gland and ovaries. In addition, scarce intranuclear cells inclusions identical to CMV were observed in lung, pancreas, adrenal gland and uterus (Fig. 2).

**DISCUSSION**

Meningoencephalitis is the most common clinical presentation of toxoplasmosis in AIDS patients and occurs in 70% of them, followed by myocarditis and pneumonitis. However, when the infection is disseminated, any organ or system can eventually be involved as occurred in the two reported cases.

At admission, their signs, symptoms and laboratory assessment were similar to those seen in sepsis or septic shock patients. During early evaluation, miliar tuberculosis, cryptococcosis, disseminated histoplasmosis and bacterial sepsis diagnoses were considered but negative laboratory results lead to empirical treatment to tuberculosis in one of them and to bacterial sepsis in the other.

Necropsy showed disseminated toxoplasmosis with inflammatory reaction in most organs involved what might explain clinical severity and early death observed in both cases. Scarce cytomegalovirus inclusion cells were observed in adrenal gland in the two cases, and in the lung, pancreas and uterus in one of them, however no inflammatory process was observed and probably it has no relation with the clinical picture. Moreover, CMV inclusions is a very common finding in necropsies of AIDS patients. Nevertheless, no other associated infectious agents were seen or cultured. Toxoplasmosis was the first defining AIDS condition related to an advanced immunodeficiency state as demonstrated by low CD4 count in both patients. Meningoencephalitis was evident at necropsy in the two cases, but neither of them presented suggestive lesions at skull computed tomography despite a report of atypical features with normal CT.

At present, no T. gondii related toxins have been identified to explain the severity of these cases, but the dissemination of microorganism might arouse the cascade of inflammatory mediators as it happens in other infectious diseases, culminating in sepsis or septic shock. Different T. gondii strains have been characterized and each one shows tropism and/or virulence to specific host such as type II strain that has been associated to patients with immunosuppressive disorders. Recent report on American AIDS patients showed more prevalence and virulence of strain I when compared to strain III and Abscense of strain II, unlike Europe. American AIDS patients showed more prevalence and virulence of strain II, unlike Europe. Nevertheless, no other associated infectious agents were seen or cultured. Toxoplasmosis was the first defining AIDS condition related to an advanced immunodeficiency state as demonstrated by low CD4 count in both patients. Meningoencephalitis was evident at necropsy in the two cases, but neither of them presented suggestive lesions at skull computed tomography despite a report of atypical features with normal CT.

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Thus, in AIDS patients with fever and sepsis-like picture without other infectious identified agents, the probability of disseminated toxoplasmosis must be considered among other clinical diagnosis. On the other hand, necropsy is essential in these cases to best understand the natural evolution and to improve the accuracy of clinical diagnosis of several opportunistic infections.

**Conflicts of interest statement**

The authors have no conflicts of interest concerning the work reported in this paper.

**RESUMO**

Toxoplasmose disseminada sepsis simile em dois pacientes com AIDS

O presente relato descreve dois pacientes que apresentaram toxoplasmose aguda, disseminada e grave como primeira manifestação oportunista da síndrome da imunodeficiência adquirida. Os achados clínicos e laboratoriais foram similares aos de sepsis ou choque séptico e, em ambos os casos houve evolução rápida para óbito. A necropsia, foi observada reação inflamatória e presença de taquizoitos e cistos de Toxoplasma gondii na maioria dos órgãos examinados.

**REFERENCES**


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