

Diffuse Cerebral Toxoplasmosis in an Immunocompetent Patient

İmmun Bağışıklığı Normal Olan Bir Hastada Diffüz Serebral Toksoplazmozis

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Summary

Cerebral involvement of toxoplasmosis is an unusual presentation in non-immunocompromised individuals, and the diagnosis may be challenging due to insignificant radiological findings. We present a case of severe toxoplasma encephalitis in an immunocompetent individual mimicking clinical picture of vertebrobasilar ischemia at onset. The highest diagnostic yield was the detection of DNA by polymerase chain reaction (PCR) examination of the brain tissue which has been also diagnostic in our patient. (*Turkish Journal of Neurology 2012; 18:43-5*)

Key Words: Toxoplasmosis, immunocompetence, encephalopathy

Özet

İmmun sisteminde bozukluk olmayan bir bireyde toksoplazmozisin beyni diffüz olarak tutması son derece enderdir. Radyolojik olarak spesifik bir görüntüsü olmaması ve ağır bir ansefalopatiyle gitmesi nedeniyle tanı da zorluklar olabilir. Başlangıçta vertebrobaziler iskemik inme klinik tablosunu andıran ciddi toksoplazma ansefaliti olan bir olgu sunulmuştur. Hastaya, PCR tekniğiyle DNA incelemesi sonucunda serebral toksoplazma tanısı konmuş ve tedavisine başlanmıştır (*Türk Nöroloji Dergisi 2012; 18:43-5*)

Anahtar Kelimeler: Toksoplazmozis, immün yeterlilik, ansefalopati

Introduction

Toxoplasmosis is a common parasitic infection in humans with a high seroprevalence in the general population.

Although, it is usually subclinical, it may be life-threatening in immunocompromised patients. The disease has a wide spectrum depending on the immune status of the patient; asymptomatic disease is the most common condition in immunocompetent individuals. The morbidity and mortality of CNS involvement in immunocompromised patients is high, (1-4) and the definitive diagnosis requires either the demonstration of the parasite histopathologically or the use of advanced

microbiologic methods including polymerase chain reaction (PCR), hybridization, and isolation (5).

We present a case of severe toxoplasma encephalitis in an immunocompetent individual diagnosed by brain biopsy, and discuss the lesion patterns on conventional and diffusion MRI.

Case Report

A 45 year old female presented with nausea, vomiting and headache to the Neurointensive Care Unit of Neurology Department, Ege University. She was admitted to the hospital with a mimicking clinical picture of vertebrobasilary

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infarction. Neurological examination revealed apathy, somnolence, right internuclear ophthalmoplegia (INO), bilateral positive Babinski's sign, and increased deep tendon reflexes with mild quadriparesis. Her clinical course rapidly progressed into coma, and her consciousness level was Glasgow coma scale 7 (E2M4V1). Body temperature and blood pressure were normal. Initially, high blood glucose levels were controlled with intravenous insulin infusion.

Magnetic resonance imaging (MRI) was performed in the first day of admission, and there was no abnormality on no abnormality on T2W, T1W and FLAIR images, but diffusion-weighted images at $b = 2000 \text{ s/mm}^2$ revealed numerous small lesions in the periventricular white matter of both hemispheres (Figure 1a). On contrast enhanced T1-weighted images, no contrast enhancement was noted, and MR angiography was normal. A second MRI examination was performed 5 days later, revealed numerous hyperintense lesions on both diffusion weighted images and T2W FLAIR images, and hypointense lesions on ADC sequence (Figure 1b). A third MRI scanning was performed 12 days later, which demonstrated hyperintense lesions on T2W, T1W, FLAIR and diffusion weighted images spreading over the basal ganglia, pons, cerebellum, medulla oblongata and middle cerebellar peduncle (Figure 2). One month later T2W, T1W, FLAIR and diffusion-weighted images showed multiple hyperintense

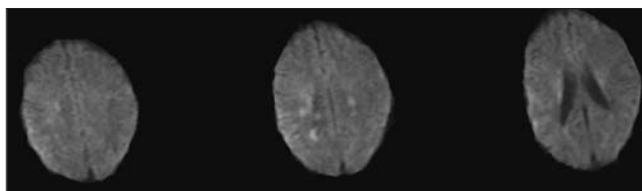


Figure 1a. First diffusion weighted images showed bilateral multiple small hyperintense lesions.

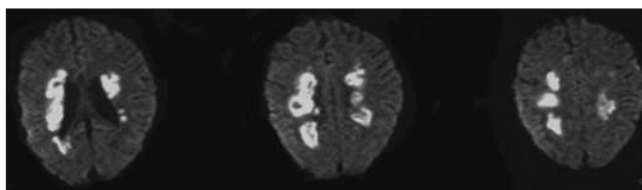


Figure 1b. Second diffusion weighted MRI showed confluent lesions involving centrum semiovale.

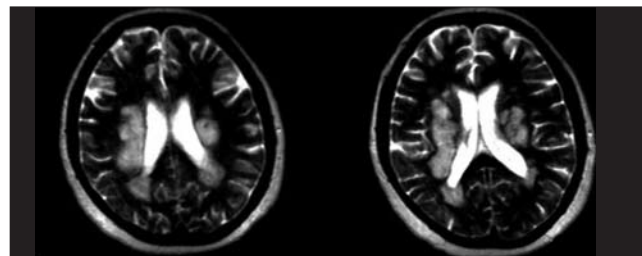


Figure 2. On the second MRI, T2 weighted images demonstrated confluent and diffuse hyperintense lesions.

lesions and T1-weighted images showed hyposignal intensity. Contrast enhancement was not noted on any MRI. Abdominal and thoracic computed tomography (CT) imaging studies revealed no lymphadenopathy. Electroencephalographic (EEG) analysis showed bioelectrical activity with diffuse slowing pattern without any localization or lateralization with theta waves of 6-7 c/s. At that time the cerebrospinal fluid (CSF) analysis, biochemical analysis, vasculitis markers, serum levels of anticardiolipin antibodies, anti-Ro, anti-LA, anti-JO-1, anti SM, anti scl-70, and rheumatoid factor were within normal limits but erythrocyte sedimentation rate was 76 mm/h. No oligoclonal bands were observed in the CSF and the IgG index was normal (0,61). Bacterial mycobacterial and mycotic cultures of the CSF, PCR analysis for Herpes Simplex Virus (HSV) and neurotropic viruses in the blood and CSF were negative. At the first week of admission, blood serology for *Toxocara canis/catis*, *Leishmania* and *Ecchinococcus granulosus* revealed high anti-*T. gondii* IgG titers measured by immunofluorescence (IF) (1:64) and enzyme linked immunosorbent assay (ELISA) (1:256) with high avidity IgG antibodies (56%); IgM titers were negative for toxoplasmosis. A second CSF analysis was performed on day 20 of admission; all parameters (biochemical analysis, direct microscopy, specific and nonspecific cultures, oligoclonal band, IgG index) were within normal limits and PCR for HSV and JC virus were negative. All laboratory parameters of immunodeficiency including flow cytometric lymphocytic panel were normal and repeated tests for HIV infection were negative.

We used intravenous pulse steroid therapy 1g/d for 10 days starting on day 7 of admission for probable progressive multifocal leukoencephalopathy or primary cerebral lymphoma. A brain biopsy specimen was obtained after one month of hospitalization since there was no improvement with pulse corticosteroid therapy and the etiology could not be revealed. Brain biopsy demonstrated toxoplasma encephalitis which was confirmed by PCR examination of the brain tissue. Examination of the biopsy material revealed tissue destruction with proliferation of histiocytes of which some had PAS (+) granules; infiltration of lymphocytes, tachyzoites and cysts and numerous CD 68 (+) cells were noted also. Trimethoprim-sulphamethoxazole (TM-SMX) was initiated with 5 mg/kg two times a day after the histopathological diagnosis of cerebral toxoplasmosis. Clindamycin 900 mg three times a day was added to the regimen a week later. Upon the availability of primethamine and sulfadiazine, TM-SMX was stopped on the second week of therapy and the treatment was continued with primethamine (after a loading dose of 200 mg, 100 mg/day) plus sulfadiazine 1.5 g every six hours and leucovorin 10 mg/day.

The patient's consciousness level improved after 6 weeks of drug therapy, and she started to have verbal outbursts with few words as well as eye contact at the time of control MRI

examination, which revealed regression of the brain lesions. The patient was discharged from the hospital after four months of hospitalization to continue using oral clindamycin 600 mg every six hours to complete a four-month course of therapy. She was discharged with mild dysarthria and gait ataxia. At discharge, MRI lesions showing constricted diffusion had diminished in number and size, and were not as bright as those seen in previous MRI examinations.

Discussion

Our case is an unusual presentation of toxoplasmosis, and the diagnosis may be challenging due to insignificant radiological findings. Cerebral toxoplasmosis may be presented with many neurological conditions such as mental status changes, seizures, focal motor deficits, cranial nerve disturbances, sensory abnormalities, cerebellar signs, movement disorders, and even symptoms of Alzheimer's disease, while meningeal signs are rare (6). Reports indicate that the clinical manifestations of acquired toxoplasmosis in the immunocompetent patient rarely include localized neurological signs, which are frequent in the immunosuppressed patient (1,2,5).

On MRI of immunocompromised patients, cerebral toxoplasmosis could be appeared either with multiple abscesses, solitary brain abscess or meningoencephalitic forms (6,7). The patient presented here was one of the rare cases with diffuse necrotizing encephalitis with lesions disseminated over the periventricular white matter, basal ganglia, thalamus, brainstem and cerebellum without an immunodeficiency syndrome. In our patient, there was no contrast enhancement on T1 weighted images with hypointensity which is a pathognomonic sign and helpful signs for the diagnosis of toxoplasmic encephalitis. Vastava et al. (3) observed that the imaging characteristics of CNS toxoplasmosis in immunocompetent individuals was characterized with radiating enhancement in cortical/subcortical regions having very few nodular or ring-enhancing lesions quite different from those in the immunocompromised patients. A previous report on 27 patients with toxoplasma encephalitis demonstrated three distinct MR imaging patterns; 37% had predominantly T2-weighted hyperintense lesions, 37% had T2-weighted isointense lesions, and 26% patients had lesions with mixed signal on T2-weighted images (7). Autopsy material from four additional patients revealed the presence of organizing abscesses in three and necrotizing encephalitis in one, while one patient with a brain biopsy had both types of lesions. The authors suggested that regarding to heterogeneity in the appearance of lesions on T2-weighted images is hard to make a definitive diagnosis based on signal characteristics alone, as it is the case presented here with no diagnosis within

one month of admission. It has been proposed that the transition from hyperintensity to isointensity may reflect a response to antibiotic therapy, and that such signal changes could be used to assess the effectiveness of medical therapy (8). Similar findings in our case with loss of hyperintensity on T2-weighted images and transition to isointensity on T1-weighted images after specific therapy parallel to clinical improvement support this opinion. Such pleomorphic clinical and radiologic findings necessitate the use of microbiological methods for the definitive diagnosis of cerebral toxoplasmosis. However, serological tests may not be useful for the diagnosis of CNS involvement as in our patient who had high serum IgG titers with no IgM antibodies and a high avidity rate. It has been noticed that the detection of antibodies and IgG avidity were not diagnostic and the detection of serum antigens by enzyme linked immunosorbent assay (ELISA) had a low sensitivity (8). The test with the highest diagnostic yield was the detection of DNA by polymerase chain reaction (PCR) which was also diagnostic in our patient. Cerebral toxoplasmosis should be considered in immunocompetent patients with neurological findings without an identified etiology particularly in areas with a high seroprevalence, and prolonged duration of treatment with drug combinations is required for an effective cure.

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