Toxoplasmic Encephalitis in Patients with Acquired Immunodeficiency Syndrome

—Four Case Reports—

Susumu NAKAZAKI, Naokatsu SAEKI, Seiro ITOH, Katsunobu OSATO, Osamu WATANABE, Norikazu HAMADA, Hiromitsu MITSUHASHI, Hideo SHIN, Ichirou KIUCHI, Chizuko KOBAYASHI*, Akihiko YANO*, and Akira YAMAURA

Departments of Neurological Surgery and *Parasitology,
Chiba University School of Medicine, Chiba

Abstract

Four patients, all males aged 40–64 years, presented with toxoplasmic encephalitis associated with human immunodeficiency virus (HIV) infection manifesting as nonspecific neurological deficits such as epilepsy or hemiparesis. Magnetic resonance imaging showed single or multiple lesions with ring enhancement, mimicking metastatic brain tumor or brain abscess. Marked eosinophilia was noted in three patients. Two patients who received anti-toxoplasma chemotherapy in the early stage had a good outcome. However, the other two patients suffered rapid neurological deterioration and needed decompressive surgery, resulting in a poor outcome. Toxoplasma diffusely infects the whole central nervous system from the early stage. The outcome for patients who needed emergency surgery was poor. Therefore, this rare but increasingly common infectious disease must be considered in the differential diagnosis of a patient with neuroimaging findings similar to those of metastatic tumor or brain abscess. Appropriate chemotherapy should be started immediately after HIV-positive reaction is identified in patients with single or multiple mass lesions with ring enhancement.

Key words: toxoplasmic encephalitis, acquired immunodeficiency syndrome, toxoplasma, metastasis, brain abscess

Introduction

Toxoplasmic encephalitis is an opportunistic infection found in at least 5% of patients with acquired immunodeficiency syndrome (AIDS) and may be as high as 40%.^{3,10,11} Although the number of AIDS patients is at present around 1400 in Japan, it is increasing.⁶ Accordingly, toxoplasmic encephalitis will become more common. However, serum human immunodeficiency virus (HIV) examination is not always done as a screening test on admission in Japan, because of medicolegal restrictions and policies. Without HIV examination results, early stage toxoplasmic encephalitis may be misdiagnosed as a metastatic brain tumor or brain abscess. The clinical symptoms occasionally deteriorate immediately after admission, so the delay in correct diagnosis at the early stage may cause a critical failure of treat-

ment and result in a poor outcome.

We describe four cases of toxoplasmic encephalitis associated with HIV infection and discuss the clinical importance of early diagnosis and treatment.

Case Reports

Case 1: A 63-year-old Japanese male presented with right hemiparesis to a nearby hospital. Magnetic resonance (MR) imaging showed ring-enhanced mass lesions associated with severe edema in the left high frontal and right temporal lobes (Fig. 1 left). The patient was admitted under a diagnosis of multiple brain tumors. On admission, the right hemiparesis was more marked in the lower extremity. Blood examinations found counts of 5300 white blood cells and 12.2% eosinophils. There were no other remarkable findings. One week after admission, the paralysis rapidly advanced. Decompres-

Fig. 1 Case 1. *left:* T₁-weighted magnetic resonance image with gadolinium showing a ring-enhanced mass lesion in the left frontal lobe. *right:* Computed tomography scan with contrast medium 2 weeks after the operation showing multiple enhanced new lesions.

Fig. 2 Case 2. Magnetic resonance image with gadolinium showing a ring-enhanced mass with severe brain edema in the right frontoparietal area.

sive craniectomy showed a mass with an unclear margin. After the operation, the disturbance of consciousness became even worse. Computed tomography (CT) with contrast medium after the operation showed multiple new lesions (Fig. 1 right). Histological examination revealed a few toxoplasma cysts within extensive coagulation necrosis. The diagnosis was toxoplasmic encephalitis. Further blood examination found a toxoplasma antibody titer of 4096 and positive reaction for HIV antibody. The patient was then transferred to an institution specified for AIDS treatment, without neurological recovery.

Case 2: A 40-year-old Peruvian male suffered an at-

Fig. 3 Case 3. Magnetic resonance images with gadolinium revealing ring-enhanced mass lesions in the right parietal and temporal lobes.

tack of epilepsy. He consulted the emergency department of our institution. The major neurological finding was motor weakness on the left. Blood tests found no abnormalities (Later, positive reaction for HIV antibody was found). On admission, MR imaging with gadolinium showed a ring-enhanced mass lesion associated with severe edema in the right frontoparietal area (Fig. 2). Further examinations were performed under the suspicion of metastatic brain tumor. His hemiparesis and disturbance of consciousness worsened, and CT showed increased mass effect. One week after admission, craniotomy revealed a mass with an unclear margin and inflammatory thickening of the meninges. The patient did not recover consciousness and died 12 days after surgery. Histological examination was compatible with toxoplasmic encephalitis.

Case 3: A 49-year-old Japanese male suffered an episode of epilepsy. He consulted a local hospital. MR imaging depicted ring-enhanced mass lesions associated with severe edema in the right parietal and temporal lobes (Fig. 3). On admission, blood tests showed counts of 5400 white blood cells and 37% eosinophils, a toxoplasma antibody titer of 4096, and positive reaction for HIV antibody. The diagnosis was toxoplasmic encephalitis associated with HIV infection. The patient was treated by chemotherapy with sulfamethoxazole-trimethoprim mixture and pyrimethamine. Five days after admission, his neurological conditions and imaging findings worsened temporarily. Two weeks later, these neurological symptoms disappeared. He was able to return to his normal daily activities. Two years after the initial episode, he is still free of neurological deficit.

Case 4: A 64-year-old Japanese male presented with pneumonia and was treated in a local clinic. He

Fig. 4 Case 4. Magnetic resonance image with gadolinium revealing a ring-enhanced mass lesion in the right basal ganglia.

suffered an episode of the motor weakness on the left, and was admitted to a local hospital. Neurological examination found slightly disturbed consciousness and left hemiplegia. MR imaging depicted a ring-enhanced mass associated with severe edema in the right basal ganglia (Fig. 4). Chest radiography showed findings compatible with pneumonia. Blood tests showed a white blood cell count of 4200, and an increased count of eosinophils to 24.2%. The HIV antibody test was positive and the toxoplasma antibody titer was 32,768. The diagnosis was carinii pneumonia associated with HIV infection and toxoplasmic encephalitis. Anti-toxoplasma chemotherapy was started. Three weeks later, his consciousness level and imaging findings improved.

However, the left hemiplegia persisted and the patient was transferred to an institution specified for AIDS treatment.

Discussion

The clinical features of our four cases are summarized in Table 1. All patients had large ring-enhanced mass lesion(s) associated with severe edema on MR images. However, such findings are not specific to toxoplasmic encephalitis, and may be misdiagnosed as metastasis or abscess. An accurate diagnosis cannot be made based on the imaging findings, if the HIV test is not performed in a patient with such nonspecific intracranial lesions. Nonspecific radiological features in toxoplasmic encephalitis were reported previously.⁴⁾

Mild to marked eosinophilia was found in three patients by differential white blood cell count, but there was no association between toxoplasma infection and eosinophilia.⁵⁾ On the other hand, peripheral eosinophilia was present in 77% of patients with AIDS.¹³⁾ Therefore, the eosinophilia probably resulted from AIDS in our patients. Diagnosis of toxoplasmic encephalitis is generally based on the toxoplasma antibody titer, but about 10% of patients with toxoplasmosis related to AIDS showed no serum anti-toxoplasma antibody response.⁸⁾ Therefore, a negative result for the anti-toxoplasma antibody titer does not always indicate that toxoplasmosis is absent. HIV examination is not done as a screening examination on admission in Japan. Eosinophilia is a nonspecific finding of AIDS or allergic reaction, but may be the key indicator of the presence of HIV infection in a patient with intracranial mass lesions.

The postoperative CT findings in Case 1 clearly showed that the toxoplasmic encephalitis was not focal but multiple. Most histological findings of

Table 1 Clinical summary of four patients

Case No.	Nationality	Age/Sex	Chief complaints	Eosinophil (%)	MR imaging findings	Treatment	Outcome
1	Japanese	63/M	rt hemiparesis	12	multiple ring-enhanced lesions at lt frontal and rt temporal lobes	craniectomy	severely disabled
2	Peruvian	40/M	convulsion, lt hemiparesis	not tested	ring-enhanced lesion at rt frontoparietal lobes	craniotomy	dead
3	Japanese	49/M	convulsion	37	multiple ring-enhanced lesions at rt parietal and temporal lobes	chemotherapy	excellent
4	Japanese	64/M	consciousness disturbance, lt hemiplegia	24	ring-enhanced lesion at rt basal ganglia	chemotherapy	moderately disabled

MR: magnetic resonance.

toxoplasmic encephalitis are mainly nonspecific coagulative necrosis without toxoplasmic cysts.⁷⁾ Therefore, a definitive diagnosis of toxoplasmic encephalitis is sometimes difficult to make based on the histological findings. Brain biopsy is a diagnostic necessity in only a few cases.⁹⁾ In addition, the mortality for brain biopsy in patients with AIDS has been estimated at as high as 10%,^{1,12)} which is extremely high compared with that of other patients. In our study, patients treated with chemotherapy in the early stage had a favorable outcome (Cases 3, 4). In contrast, the two patients who underwent surgery suffered deterioration in neurological symptoms. Consequently, we consider chemotherapy is the treatment of choice for patients with toxoplasmic encephalitis associated with HIV infection and surgical treatment is auxiliary.

Recent developments in AIDS treatment have shown that early diagnosis of toxoplasmic encephalitis has a great impact on the prognosis for patients with HIV infection.²⁾ Chemotherapy is effective in patients with toxoplasmic encephalitis, and earlier initiation of chemotherapy provides a better prognosis. Therefore, chemotherapy should be started as soon as toxoplasmic encephalitis is suspected. We suggest that the possibility of toxoplasmic encephalitis should be considered in the differential diagnosis on a routine basis, since the number of patients with HIV infections may increase in Japan in the future. Early detection and immediate chemotherapy will provide a good prognosis for the patient.

References

- 1) Artigas J, Grosse G, Niedobitek F: Neuropathology of AIDS, in Artigas J, Grosse G, Niedobitek F (eds): *The Central Nervous System in AIDS*. Berlin, Springer-Verlag, 1993, pp 120-133
- 2) Artigas J, Grosse G, Niedobitek F: Diagnostic imaging of intracranial manifestations of AIDS, in Artigas J, Grosse G, Niedobitek F (eds): *The Central Nervous System in AIDS*. Berlin, Springer-Verlag, 1993, pp 31-37
- 3) Dina TS: Primary central nervous system lymphoma versus toxoplasmosis in AIDS. *Radiology* 179: 823-828, 1991
- 4) Grant IH, Gold JWM, Rosenblum M, Niedzwiecki D, Armstrong D: Toxoplasma gondii serology in HIV-infected patients: The development of central nervous system toxoplasmosis in AIDS. *AIDS* 4: 519-523, 1990
- 5) Hakim SL, Radzan T, Nazma M: Distribution of anti-Toxoplasma gondii antibodies among Orang Asli (aborigines) in Peninsular Malaysia. *Southeast Asian J Trop Med Public Health* 25: 485-489, 1994
- 6) Kihara M, Ichikawa S, Kihara M, Yamasaki S: Descriptive epidemiology of HIV/AIDS in Japan, 1985-1994. *J Acquir Immune Defic Syndr Hum Retrovirol* 14 (Suppl 2): S3-12, 1997
- 7) Luft BJ, Remington JS: Toxoplasmic encephalitis. *J Infect Dis* 157: 1-12, 1988
- 8) Oksenhendler E, Cadranet J, Sarifati C, Katolama C, Datry A, Marche C, Wolf M, Roux P, Derouin F, Clauvel JP: Toxoplasma gondii pneumonia in patients with the acquired immunodeficiency syndrome. *Am J Med* 88: 18-21, 1990
- 9) Pons VG, Jacobs RA, Hollander H: Nonviral infections of the central nervous system in patient with acquired immunodeficiency syndrome, in Rosenblum ML, Levy RM, Bredesen DE (eds): *AIDS and the Nervous System*. New York, Raven, 1988, pp 263-283
- 10) Rosenthal D, LeBoit PE, Klumpp L, Berger TG: Human immunodeficiency virus-associated eosinophilic folliculitis. A unique dermatosis associated with advanced human immunodeficiency virus infection. *Arch Dermatol* 127: 209-216, 1991
- 11) Rossitch E Jr, Carrazana EJ, Samuels MA: Cerebral toxoplasmosis in patients with AIDS. *Am Fam Physician* 41: 867-873, 1990
- 12) Wong SY, Remington JS: Toxoplasmosis in the setting of AIDS, in Broder S, Merigan TC, Bolognesi D (eds): *Textbook of AIDS Medicine*. Baltimore, Williams & Wilkins, 1994, pp 223-258
- 13) Zimmer C, Marzheuser S, Patt S, Rolfs A, Gottschalk J, Weigel K, Gosztanyi G: Stereotactic brain biopsy in AIDS. *J Neurol* 239: 394-400, 1992

Address reprint requests to: N. Saeki, M.D., Department of Neurological Surgery, Chiba University School of Medicine, 1-8-1 Inohana, Chuo-ku, Chiba 260-8670, Japan.