Cerebral Infarction in Patients with AIDS

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PURPOSE: To establish the frequency, distribution, and pathogenesis of cerebral infarction as confirmed with MR imaging in a cohort of patients with acquired immunodeficiency syndrome (AIDS). **METHODS:** We reviewed all (71) abnormal cranial MR studies obtained at our institution in human immunodeficiency virus (HIV)-positive patients over a 2-year period and recorded the number and distribution of ischemic lesions, any associated abnormalities, and the MR angiographic findings, where available. Patients' charts were studied for relevant clinical data, biochemical and culture results, and potential etiologic factors. **RESULTS:** Twenty-two infarcts were seen in 13 of the 71 patients. Of these 22, the basal ganglia area was affected in 15, the middle cerebral artery territory in two, and the vertebrobasilar territory in five. Five patients had concomitant evidence of infection, six others used cocaine or were intravenous drug abusers. MR angiography was performed in eight patients; two of these had multiple lesions consistent with vasculitis, two had isolated lesions that corresponded with their parenchymal infarct, and four had normal findings. **CONCLUSIONS:** The frequency of infarction was 18%, higher than previously reported. The pathogenesis of infarction was multifactorial. Underlying infectious causes were identified in 39% of patients. Two patients had an idiopathic vasculitis.

Index terms: Acquired immunodeficiency syndrome (AIDS); Brain, infarction

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Of the numerous causes of acute neurologic dysfunction occurring in human immunodeficiency virus (HIV)-positive patients, cerebral infarction, although well described, is often forgotten. Indeed, two recent review articles of the neurologic complications of acquired immunodeficiency syndrome (AIDS) mentioned cerebral infarction only in passing or not at all (1, 2). Early pathologic studies ascribed infarction in AIDS patients to marantic endocarditis, disseminated intravascular coagulation, or hypoxia (3). In fact, several potential factors contribute to an increased frequency of infarction in these patients. The best recognized are the infectious complications, which include varicella-zoster virus and cytomegalovirus infection, tuberculosis, cryptococcosis, syphilis, and toxoplasmo-sis. The frequency of both intravenous drug abuse and cocaine/crack use in this patient population adds other potential causes of cerebral infarctions, including vasoconstriction, vasculitis, increased platelet aggregations, emboli of foreign material, and infective endocarditis (4, 5). In addition, there have been several reports alluding to the possibility of a primary HIV vasculitis (6). Autopsy reports place the frequency of cerebral infarction in AIDS patients between 19% and 34% (7, 8), whereas the clinical frequency is between 0.5% and 7% (9, 10).

The purpose of this study was to establish the frequency, distribution, and pathogenesis of cerebral infarction as confirmed with magnetic resonance (MR) imaging in a cohort of AIDS patients.

Materials and Methods

We retrospectively reviewed all abnormal MR studies of the brain obtained in HIV-positive patients at our institution over a period of 2 years. There were 71 such patients. Fifteen had toxoplasmosis, six had cryptococcosis, three had tuberculosis, one had herpes encephalitis, two had nonspecific meningitis, four had lymphoma, four had progressive multifocal leukoencephalopathy, 22 had HIV-re-

Fig 1. A 32-year-old man with a history of toxoplasmosis and a current acute episode of left-sided weakness.

Axial T2-weighted fast spin-echo (3000/120/1) (*A*) and coronal T1-weighted spin-echo (600/15/2) (*B*) MR images show infarction in the territory of the left posterior inferior cerebellar artery. There is no evidence of recurrent toxoplasmosis.

A   **B**
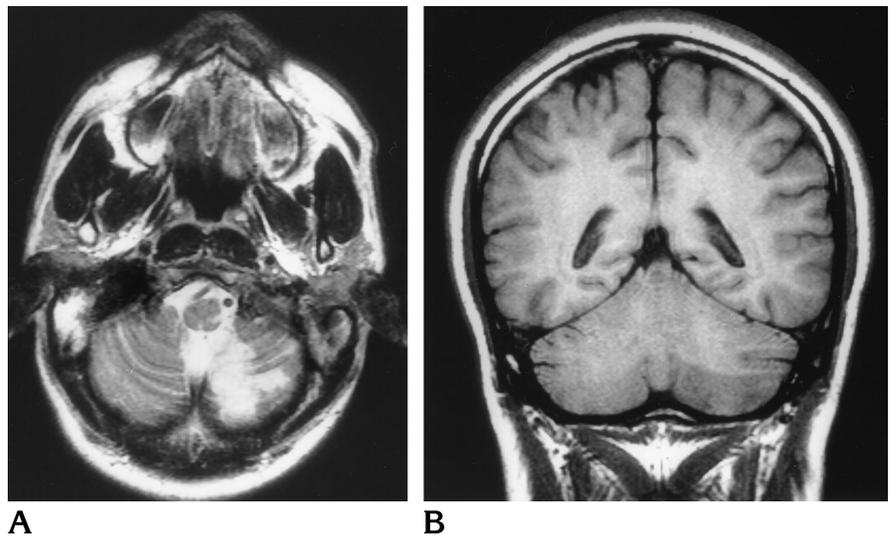
lated encephalopathy, one had subdural hemorrhage, one had parenchymal hemorrhage, six had miscellaneous lesions, and 13 had ischemic lesions (seven patients had more than one abnormal finding). Of the 13 patients with infarcts, 10 were men and three were women. The median age was 40 years (range, 28 to 56 years). The diagnosis of ischemia was made on the basis of a combination of clinical, radiologic, and, where available, angiographic (either conventional or MR) data. Twelve patients were examined in an acute setting (ie, within a few days of the initial ictus) and one patient was studied during the chronic phase of the illness. Thirty-eight MR studies were obtained in these 13 patients: four had one study, three had two studies, one had three studies, four had four studies, and one patient (with a protracted and relapsing course of central nervous system tuberculosis complicated by three cerebral infarcts) had nine studies in 10 months. Autopsy findings were available in one patient and follow-up data, obtained at a median of 60 days (range, 14 days to 10 months), were available in seven patients.

All studies were performed at 1.5 T. The routine MR examination was composed of a dual-echo T2-weighted fast spin-echo sequence (3000/30,120 [repetition time/echo times]; echo train length of 14) and a coronal T1-weighted spin-echo sequence (600/15) performed both before and after intravenous administration of a standard dose (0.1 mmol/kg) of contrast material. All studies were evaluated by two experienced radiologists and note was made of the number of lesions and their distribution and estimated size; their signal intensity on T1-, proton density–, and T2-weighted images; their enhancement pattern; and the probable radiologic diagnosis. For the areas of infarction, the vascular territory was also noted. The MR criteria for diagnosing infarction included arterial distribution, the presence of vascular or cortical enhancement, relative lack of mass effect for lesion size, and temporal evolution.

MR angiography of the circle of Willis was performed in eight patients with the use of either the three-dimensional time-of-flight technique (27/7; flip angle of 20°) or the 3-D phase-contrast technique (28/8; flip angle of 20°, velocity encoding of 50 cm/s). Maximum intensity projections were generated and evaluated for areas of narrowing or loss of signal, length of signal loss, asymmetry of peripheral branches, and relationship to any parenchymal abnormality. One patient also had conventional angiography with selective catheterization of both internal carotid arteries and the left vertebral artery.

The charts for these 13 patients were reviewed and note was made of all bacteriological, laboratory, and culture findings, as well as biopsy and, where available, autopsy results. Patients' histories were also recorded, including length of time since diagnosis of HIV-positive status, prior HIV-related illness, CD4 count, and potential etiologic factors both for HIV and cerebral infarction.

Results

We found a total of 22 ischemic lesions. One patient had four ischemic lesions, one had three, four had two, and seven had one. Fifteen ischemic lesions involved the lenticulostriate territory, which was bilateral in four patients. One patient had occlusion of the middle cerebral artery, another had infarction of the posterior middle cerebral artery territory, and five had infarction in the vertebrobasilar territory (Fig 1). The median infarct size was 2 cm (range, 7 mm to several centimeters). Six infarcts were less than 15 mm in diameter, these included three of four infarcts in a patient with vasculitis and one of three infarcts in the patient with tuberculosis. The other two infarcts occurred in a patient with cryptococcus but were distinguished from gelatinous pseudocysts or dilated Virchow-Robin spaces by their shape and signal intensity. Sim-
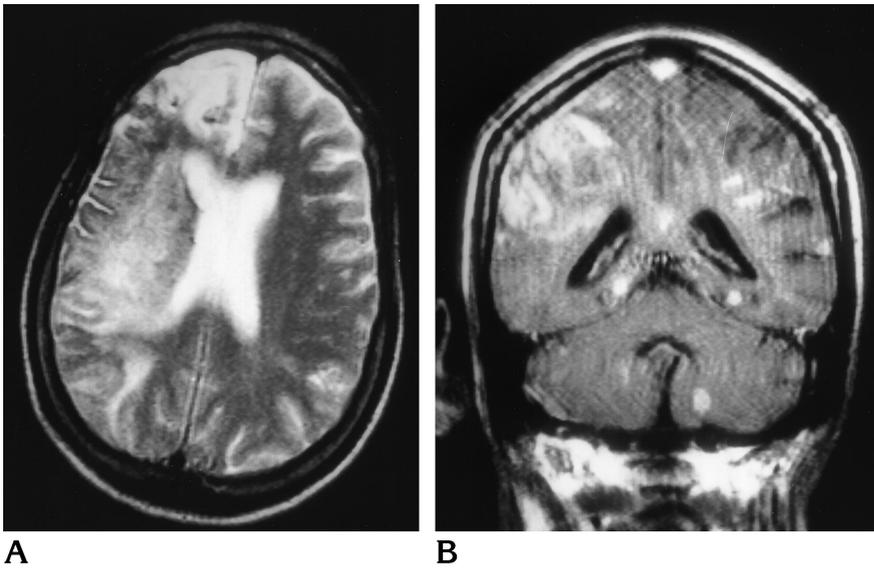
A   B

Fig 2. A 46-year-old woman found unresponsive in whom MR imaging showed both acute infarction and multiple intracerebral abscesses.

A, Axial T2-weighted fast spin-echo (3000/120/1) MR image shows abnormal signal in the right middle cerebral artery territory consistent with infarction. The area of high signal anteriorly is related to concomitant toxoplasmosis.

B, Coronal contrast-enhanced T1-weighted (600/15/2) MR image shows multiple enhancing nodules, consistent with toxoplasmosis, and abnormal high signal in the right middle cerebral artery territory caused by a combination of methemoglobin and enhancement in the infarcted region. MR angiography (not shown) confirmed main-stem right middle cerebral artery occlusion.
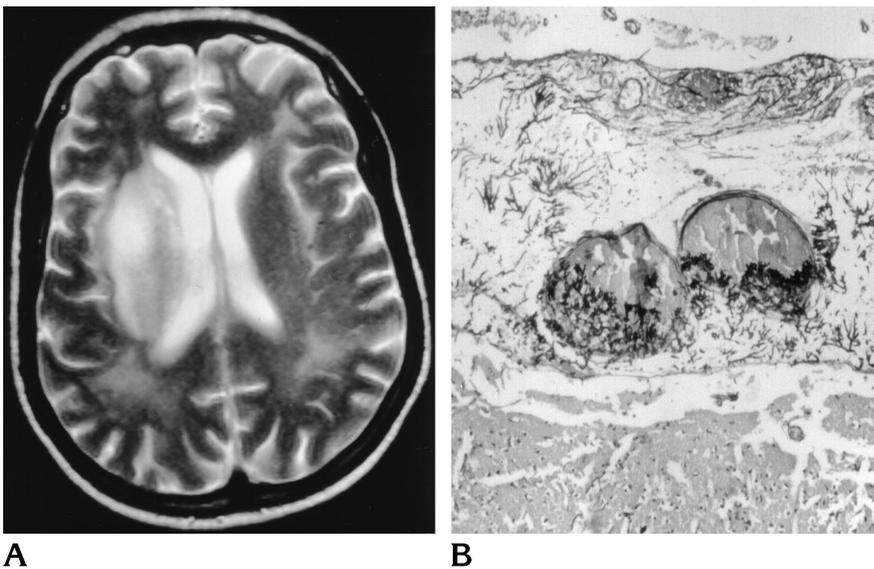

A   B

Fig 3. A 47-year-old man with a history of AIDS and pulmonary aspergillosis presenting with acute confusion. Autopsy findings showed disseminated aspergillosis with associated cerebral infarction.

A, Axial T2-weighted fast spin-echo (3000/120/1) MR image shows abnormal signal in the right periventricular region consistent with infarction. Also noted is bilateral, symmetric white matter changes consistent with HIV encephalopathy.

B, Histologic section obtained at autopsy shows hypha-packed intracranial vessels caused by disseminated aspergillosis.

ilarly, it was possible to distinguish between the enhancement patterns seen in toxoplasmosis and cerebral infarction.

Of this group with infarcts, eight were intravenous drug abusers (one also bisexual), another was bisexual, and three were heterosexual Haitian males. The median known length of time since the first AIDS-defining illness in this group was 2 years (range, 1 month to 4 years). The median recent CD4 count, available in seven patients, was 80 (range, <25 to 130).

Concurrent opportunistic intracerebral infection was present in five patients, two had multiple cerebral abscesses: there was one case of confirmed toxoplasmosis, one of cryptococco-

sis, one of tuberculosis, and one of aspergillosis (Figs 2 and 3). Eight patients had a history of intravenous drug abuse, including the patient with tuberculosis and both patients with multiple cerebral abscesses. Of these eight, five gave a history of cocaine/crack use. One other patient had a history of cocaine use without intravenous drug abuse. In two patients, a specific etiologic factor, apart from HIV infection, was not identified. Both these patients had segmental narrowing of medium-sized vessels at MR and/or conventional angiography consistent with vasculitis.

Four of the eight patients who had MR angiography had normal findings: three of these

had lesions in the basal ganglia and the fourth had involvement of the posterior inferior cerebellar territory. Two other patients had MR angiographic abnormalities that were focal and corresponded to their ischemic parenchymal lesions: a right main stem middle cerebral artery occlusion and peripheral middle cerebral artery branch occlusion. Follow-up MR imaging showed the normal evolution of infarction, with loss of edema, development of gliosis, and secondary features of volume loss.

Discussion

The frequency of cerebral infarction in our population was 18% (13 of 71), higher than that quoted in clinical or computed tomography–based series and lower than that reported in autopsy studies (7–10). The lenticulostriate vessels were most commonly affected. Fifteen of 22 lesions were restricted to the basal ganglia region and were bilateral in four patients. Five patients had concurrent infection as a potential cause of cerebral infarction, although this was only proved as causative in one patient at autopsy. Evidence of opportunistic infection was aggressively sought in all these patients; however, some microorganisms (eg, cytomegalovirus) can be very difficult to isolate. It is possible that in some of these patients an infective cause of infarction was missed.

Six other patients had a history of drug use: two, intravenous drug abuse and cocaine; one, cocaine alone; and three, intravenous drug abuse alone. This may have accounted for or contributed to their cerebral infarction. It is noteworthy, however, that in one study, the frequency of infarction in homosexuals with AIDS and that of intravenous drug abusers with AIDS was the same (7). The mechanisms for drug-related infarction are multiple and not well understood; however, cocaine-associated infarction most commonly affects the cerebral cortex and posterior circulation (4, 5). In two of the three cocaine users in our group, the infarctions were restricted to the basal ganglia, an atypical site. The third patient had a posterior inferior cerebellar infarct. We would postulate a multifactorial hypothesis, whereby altered vascular reactivity in the presence of HIV renders the patient increasingly vulnerable to vasoconstrictive drugs.

We have no explanation for the infarction

seen in two patients who had multiple vascular lesions at angiography and may have had a primary HIV vasculitis. There is increasing evidence of an HIV-related vasculitis, including a primary HIV vasculitis of the central nervous system (6, 11). Cerebral vasculitis has been described in pathologic studies of AIDS patients (12). One study found vasculitis in two of 13 patients with cerebral infarction (13). The literature includes a number of case reports of adult HIV patients with suspected cerebral vasculitis (14–16) and three reports of children with vasculitis and secondary aneurysmal formation affecting the circle of Willis (17, 18). In other reports, three children and six adults with AIDS and infarction of unknown cause have been described, again invoking a primary HIV vasculitis (9, 19).

MR angiography was contributory in defining isolated lesions corresponding to the area of infarction in two of our patients and in showing multiple lesions in the two patients with vasculitis. Case reports of the MR angiographic appearance of vasculitis have been published (20, 21). However, MR angiography cannot depict the smaller vessels (in particular, the leptomeningeal vessels are not seen), so a false-negative rate is inherent to the present technique.

In summary, the frequency of cerebral infarction as evidenced by MR imaging in our AIDS patients was 18%. The lenticulostriate vessels were most vulnerable. Only five of 13 patients had evidence of concurrent infection. Two patients had evidence of a primary HIV vasculitis. Six other patients had infarcts that may have been due to drugs, HIV-related stroke, or possibly a combination of these factors.

References

1. Simpson DM, Tagliati M. Neurologic manifestations of HIV infection. *Ann Intern Med* 1994;121:769–785
2. Berger JR, Levy RM. The neurologic complications of human immunodeficiency virus infection. *Med Clin North Am* 1993;77:1–23
3. Anders KH, Guerra WF, Tomiyasu U, Verity MA, Vinters HV. The neuropathology of AIDS: UCLA experience and review. *Am J Pathol* 1986;124:537–558
4. Caplan LR, Hier DB, Banks G. Stroke and drug abuse. *Stroke* 1982;13:869–872
5. Levine SR, Welch KMA. Cocaine and stroke. *Stroke* 1987;22:25–30
6. Calabrese LH. Vasculitis and infection with the human immunodeficiency virus. *Rheum Dis Clin North Am* 1991;17:131–147
7. Mizusawa H, Hirano A, Llena JF, Shintaku M. Cerebrovascular

lesions in acquired immune deficiency syndrome (AIDS). *Acta Neuropathol* 1988;76:451–457

8. Levy RM, Bredesen DE. Central nervous system dysfunction in acquired immunodeficiency syndrome. In: Rosenblum ML, Levy RM, Bredesen DE, eds. *AIDS and the Nervous System*. New York, NY: Raven Press; 1988:29–63

9. Engstrom JW, Lowenstein DH, Bredesen DE. Cerebral infarctions and transient neurologic deficits associated with acquired immunodeficiency syndrome. *Am J Med* 1989;86:528–532

10. Levy RM, Bredesen DE, Rosenblum ML. Neurological manifestations of acquired immunodeficiency syndrome (AIDS) at UCSF and review of the literature. *J Neurosurg* 1985;62:475–495

11. Guiloff RJ, Fuller GN. Other neurological diseases in HIV-1 infection: clinical aspects. *Baillieres Clin Neurol* 1992;1:175–209

12. Cho ES, Sharer LR, Reress NS, Little B. Intimal proliferation of leptomeningeal arteries and brain infarcts in subjects with AIDS. *J Neuropathol Exp Neurol* 1987;46:385

13. Berger JR, Harris JO, Gregorios J, Norenberg M. Cerebrovascular disease in AIDS: a case-control study. *AIDS* 1990;4:239–244

14. Scaravilli F, Daniel SE, Harcourt-Webster N, Guiloff R. Chronic basal meningitis and vasculitis in acquired immunodeficiency syndrome. *Arch Pathol Lab Med* 1989;113:192–195

15. Atalaia A, Ferro J, Antunes F. Stroke in an HIV-infected patient. *J Neurol* 1992;239:356–357

16. Yankner BA, Skolnik PF, Shoukimas GM, Gabuzda DH, Sobel RA, Ho DD. Cerebral granulomatous angiitis associated with isolation of human T-lymphotropic virus type III from the central nervous system. *Ann Neurol* 1986;20:362–364

17. Philippet P, Blanche S, Sebag G, Rodesch G, Griscelli C, Tardieu M. Stroke and cerebral infarcts in children infected with human immunodeficiency virus. *Arch Pediatr Adolesc Med* 1994;148: 965–970

18. Park YD, Belman AL, Kim TS, et al. Stroke in pediatric acquired immunodeficiency syndrome. *Ann Neurol* 1990;28:303–311

19. Moriarty DM, Haller JO, Loh JP, Fikrig S. Cerebral infarction in pediatric acquired immunodeficiency syndrome. *Pediatr Radiol* 1994;24:611–612

20. Sarazin L, Dong H, Bourgoin PM, et al. Herpes zoster vasculitis: demonstration by MR angiography. *J Comput Assist Tomogr* 1995;19:624–627

21. Gradon JD, Wityk R. Diagnosis of probable cocaine-induced cerebral vasculitis by magnetic resonance angiography. *South Med J* 1995;88:1264–1266