Haemorrhage in cerebral toxoplasmosis
A report on a patient with the acquired immunodeficiency syndrome

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Summary
A patient with the acquired immunodeficiency syndrome (AIDS) presented to hospital with a haemorrhagic cerebral lesion. The lesion was biopsied and electron microscopy confirmed a diagnosis of toxoplasmosis. Although known in congenital cases, haemorrhagic infarction is unknown in adults suffering from cerebral toxoplasmosis. Severe vasculitis with subsequent thrombosis and extensive fibrinoid necrosis of the vessel wall or direct parasitism of endothelial cells with subsequent destruction and seepage of blood appear to be the possible mechanisms in a situation where the T-cell immune mechanism and tissue cell response are compromised. Other intracerebral haemorrhagic lesions in AIDS were reviewed.

The spectrum of clinical presentations in the acquired immunodeficiency syndrome (AIDS) remains vast and as yet fathomless. An ever-increasing list of publications on AIDS is a reflection of this diversity, which is caused by the inexorable involvement of most tissues in the body. The extent of a lesion may vary according to the defect in the overall T-cell-mediated immune mechanism and the residual local tissue response against the invading organism.

A case of toxoplasmosis with haemorrhage in a cerebral lesion, which showed Toxoplasma gondii on electron micrography, is reported. To our knowledge, cerebral haemorrhage in adults with toxoplasmosis has not previously been reported. This case is described in order to highlight the possible mechanisms of infection.

Case report
A 31-year-old non-promiscuous woman was admitted to our medical service on 11 November 1986 with features of the AIDS-related complex (ARC), characterised since 1985 by persistent fever, weight loss, generalised lymphadenopathy, peri-anal condylomas, disorientation, and the development of oral thrush and herpetic lesions in both nostrils. After 2 weeks she developed conjunctivitis with photophobia and blurring of vision and 4 days later complained of bitemporal headaches. She had been treated with clotrimazole and nystatin. The past medical history was significant for ophororectomy, anaemia, generalised seizure disorder and bronchial asthma treated with phenytoin and anhydrous theophylline.

On examination, the patient was somewhat anaemic and dehydrated but vital signs were normal. She was obtunded but arousable and had normal orientation to time, place and person. She had mild conjunctivitis, fungal lesions on optic funduscopy, slight left central facial weakness and mild left hemiparesis. She had residual oral candidiasis and healed pustules on the skin. Lumbar puncture revealed clear, colourless cerebrospinal fluid (CSF) under normal pressure, which contained 27 red blood cells (RBCs) (mostly crenated), 22 white blood cells (WBCs) (2 polymorphs and 20 lymphocytes), proteins 46 mg/dl and glucose 54 mg/dl.

Laboratory tests for acid-fast bacilli (AFB), cryptococcal antigen and VDRL, India ink preparation, countercurrent immuno-electrophoresis (CIE) and Toxoplasma titres in the CSF were normal. Serum Toxoplasma titre was 1:128 (immunofluorescence assay), cytomegalovirus 1:4 and hepatitis AB titres were negative. A complete blood count revealed: haemoglobin 8.7 g/dl; haematocrit 28%; red blood cells 3 110 x 10⁶/λ; white blood cells 72 x 10⁶/λ; mean corpuscular volume 90 μm³; mean corpuscular haemoglobin 28; mean corpuscular haemoglobin concentration 31%; prothrombin time 11.8/11.9; partial thromboplastin time 30.5/31.6. The platelet count ranged between 317 000/mm³ and 341 000/mm³. The serum glutamic oxalo-acetic transaminase value was 158 IU/l, creatine kinase 203 IU/l, lactase dehydrogenase 426 lU/l and y-glutamyltransferase 262 IU/l. Fasting blood sugar was 65 g/dl and 80 g/dl on two occasions.

Ultrasoundography of the liver, gall bladder, spleen and kidneys was normal. A rectosigmoid biopsy specimen showed mild, chronic inflammation. Bacteriological examination of the sputum revealed mixed growth of Staphylococcus aureus, α-streptococcus and Nisseria species. Computed tomography (CT) of head was normal and without contrast medium revealed a solitary deep-seated lesion close to the internal capsule on the right. This hypodense lesion was enhanced by the administration of intravenous contrast medium (Fig. 1). The patient was treated with acyclovir for 10 days on a presumptive diagnosis of viral encephalitis. In fact, there was a mild subjective improvement and repeat CT revealed decreased enhancement without any change in the size of the lesion (Fig. 2).

A repeat spinal tap on 4 December 1986, yielded clear and colourless CSF under normal pressure. It contained no RBCs, 3 WBCs and was negative for cryptococcal antigen, India ink preparation, CIE, VDRL, AFB smear and Toxoplasma titres.

Twenty-four days after admission to hospital there was a sudden deterioration in the patient's condition. She became apathic and developed right facial weakness and right hemiparesis, which was worse in the arm than the leg. A repeat CT showed a discrete round haemorrhagic lesion in the left posterior frontal cortical area (Fig. 3).

This lesion was approached by a left frontotemporal craniotomy under ultrasonographic guidance and a biopsy yielded two irregular pieces of whiteish-tan soft tissue with
Fig. 1. CT of the head showing deep-seated contrast-enhancing lesion in right hemisphere close to internal capsule.

Fig. 2. CT of the head showing decreased enhancement but no change in the size of the lesion following acyclovir treatment.

Fig. 3. CT of the head without contrast showing a haemorrhagic lesion in the left posterior frontal region.

Fig. 4. Electron micrograph shows Toxoplasma gondii containing nucleus, toxomeres and vacuoles in cortical grey matter (x 64000).

Focal areas of haemorrhage measuring 0.9 x 0.6 x 0.2 cm. Light microscopy showed neuronophagia, glial nodules and perivascular lymphocytic cuffing. Immune-peroxidase stain for Toxoplasma was negative. Electron microscopy showed Toxoplasma gondii in the cortical grey matter (Fig. 4).

The patient was treated with antitoxoplasmosis medication, including pyrimethamine, trimethoprim and folinic acid.
Discussion

According to the Centers for Disease Control, Atlanta, Georgia, AIDS is defined as a reliably diagnosed disease that is at least moderately indicative of an underlying cause of cellular immunodeficiency in a person who has no known underlying cause of immunodeficiency nor any other cause of reduced resistance reported to be associated with that disease. The victims of this disease have characteristically opportunistic infections, which are rarely seen in immunocompetent persons, and also malignant tumors such as Kaposi's sarcoma and non-Hodgkin's lymphoma. Involvement of the central nervous system, with obvious clinical manifestations, accounts for 10% of all AIDS patients according to the most recent US national survey of the neuro-epidemiology of AIDS in 16,574 adult patients. Cerebral toxoplasmosis alone accounts for about a quarter of this 10%. A typical cerebral toxoplasmosis lesion comprises a micro-nodule showing areas of necrosis with varying degrees of inflammatory response around it. Our case fulfilled all the criteria for AIDS. The precise nature of intracerebral hemorrhage remained elusive until examination of the biopsy specimen proved it to be toxoplasmosis beyond any doubt.

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REFERENCES