

Acute Fulminant Toxoplasma Meningoencephalitis in a Homosexual Man

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Summary. A homosexual man with a history of sexually transmitted infections including recent giardiasis and high cytomegalovirus (CMV) titer was admitted with generalized weakness, headache, and depression. He rapidly became comatose and developed signs of increased intracranial pressure. CT scan revealed a right cerebral lesion. Pathologic examination disclosed an acute necrotizing granulomatous toxoplasmosis involving the cerebrum. This case represents an example of an opportunistic infection in a male homosexual associated with fulminant clinical course, probably on the basis of immune deficiency.

Key words: Cerebral toxoplasmosis – Homosexual

Introduction

Toxoplasma gondii invades all cells except non-nucleated erythrocytes. Toxoplasma encephalitis may be congenital or acquired. The acquired typical form is more common in adults and is characterized by random foci of necrosis with numerous intracerebral organisms. An atypical form is less common and resembles congenital toxoplasmosis [1].

Acquired toxoplasmosis is an opportunistic infection in patients who are immunocompromised for a variety of reasons including malignant neoplasm [27], organ transplantation [24, 27], and collagen vascular diseases [27, 28]. Recently, two reports by Hauser et al. [14] and Vilaseca et al. [31] on the occurrence of acquired fatal cerebral toxoplasmosis in male homosexuals have been published. We are presenting a clinical, radiologic, and neuropathologic study of a case

of acute fulminant cerebral toxoplasmosis in a homosexual man.

Case Report

A 35-year-old white man from New York City was admitted to hospital on August 8, 1982, complaining of generalized weakness and depression. Seventeen days prior to admission, he was seen by a physician because of anorexia, fatigue, and 4.6 kg weight loss (2–3-month period). He had three brief ($1/2$ -day) episodes of diarrhea over the past 2 months; the last episode was associated with a fever of 38.9°C for 24 h. Physical examination was normal except for enlarged axillary, submental, and inguinal lymph nodes. Laboratory investigations revealed eosinophilia, sedimentation rate of 43 mm/min, CMV titer of 1:1,024, negative hepatitis B surface antigen, and febrile agglutinins. Stool examination revealed *Giardia lamblia*. Chest X-ray showed a right hilar calcific lesion. A PPD skin test was negative. He was treated with Metronidazole. Four days prior to admission, he developed nausea, vomiting, increasing diarrhea, headaches, and generalized weakness. Metronidazole was discontinued, but the symptoms persisted.

On admission he was depressed and had suicidal ideations. His past history was significant for gonorrhoea, syphilis and frequent homosexual activities. On examination his temperature was 36.5°C, blood pressure 138/80 mm Hg, pulse rate 78/min. General physical examination was unchanged. Neurologically, he was oriented but drowsy. He moved all extremities equally, but quantitative assessment was impossible because of lack of cooperation. He refused to have his fundi examined. Laboratory data: Hct 42%, corrected sedimentation rate 37, WBC 5,400/ μ l (neutrophils 69%, bands 5%, lymphocytes 11%, atypical lymphocytes 1%, monocytes 9%, eosinophils 1%). Serum titer for CMV in a single specimen by enzyme-linked immunosorbent assay (ELISA) screen was 2+ (low titer). (Retrospectively, toxoplasma titer in the same serum by indirect fluorescent-antibody test was 1:128 with less than 1:10 IgM and CMV titer was 1:256 with less than 1:10 IgM.)

He became agitated and confused that evening and was given a total of 4 mg Haloperidol over an 8-h period. At 7:45 a.m. the next morning he was found comatose. His pupils were equal and reactive to light. He had bilateral papilloedema, left greater than right. The examination was otherwise nonfocal. Decadron and Mannitol were administered i.v. At 9:00 a.m. his respiration remained spontaneous but became irregular. The pupils were fixed and dilated (6 mm), and oculovestibular reflexes were absent. At 9:30 a.m. he was intubated, hyperventilated, and had an emergency CT scan, which revealed a large isodense lesion in the right hemisphere (Fig. 1). There is no

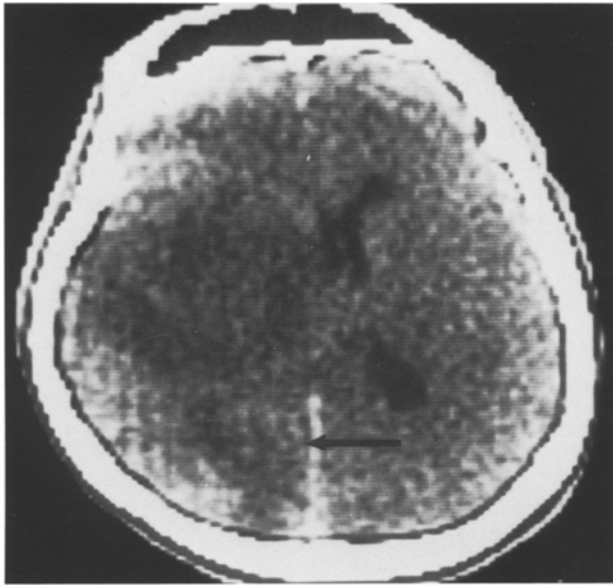


Fig. 1. Isodense lesion surrounded by edema in right basal ganglia compressing the lateral ventricle and shifting the midline. There is another lesion in right occipital lobe (arrow)

enhancement in post-contrast study. His neurologic condition deteriorated. He died 28 h after admission.

Postmortem Examination

Gross. Autopsy was limited to the brain. The brain weighed 1,620 g. The dura and dural sinuses were unremarkable, while the leptomeninges were slightly thickened and opaque at the vault over the right cerebral hemisphere. Both hemispheres were edematous and swollen. The surface of the right temporo-parietal region near the operculum was softened. There was evidence of herniation of the right cingulate gyrus, unci, and cerebellar tonsils. The superficial veins were congested. Coronal sections of the cerebral hemispheres revealed an edematous cortical and white matter, particularly on the right side. The anterior portion of the right lateral ventricle was reduced in size because of the edematous frontal white matter and bulging right basal ganglia. There were multiple circular hemorrhagic yellow-tan necrotic lesions (up to 3 cm in diameter) involving cerebral cortex and adjacent white matter of frontal, parietal, and occipital lobes. The largest lesion (approximately 5 cm) involved the entire right lenticular nucleus and extended to the internal capsule and lateral portion of the anterior thalamus; had a central brown induration surrounded by narrow irregular space containing necrotic material.

The ependymal surface had a focal cloudy and yellowish-tan appearance in both lateral ventricles greatest near the third ventricle. The midbrain and pons showed edema and secondary hemorrhages near the midline. The cerebellum and medulla were mildly edematous.

Microscopic. Tissue fixed in 10% buffered formaldehyde were processed for histology and stained with HE, Cresyl violet, trichrome, and reticulin stains. Large numbers of toxoplasma cysts but few tachyzoites were present throughout the older lesion in the right basal ganglia. Fewer cysts but relatively more tachyzoites were found in other younger lesions located mostly at the bottom of the sulci with extension to both gray and white matter. There was a microscopic lesion with numerous cysts in the right hippocampus between the fascia dentata and entorhinal cortex. The toxoplasma organisms were closely packed in cysts with argyrophilic walls inside neurons,

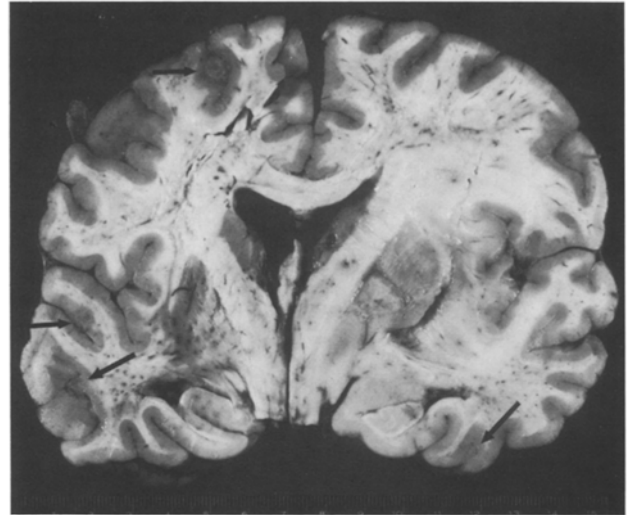


Fig. 2. Coronal section of the brain showing lesion in the right basal ganglia and multiple irregular lesions in the cortex (arrows)

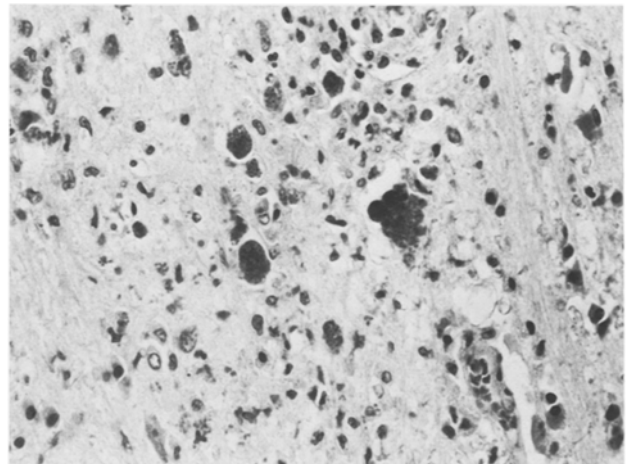


Fig. 3. Basal ganglia lesion reveals widespread necrosis with hemorrhagic infiltration and cysts of *Toxoplasma gondii*. HE, × 235

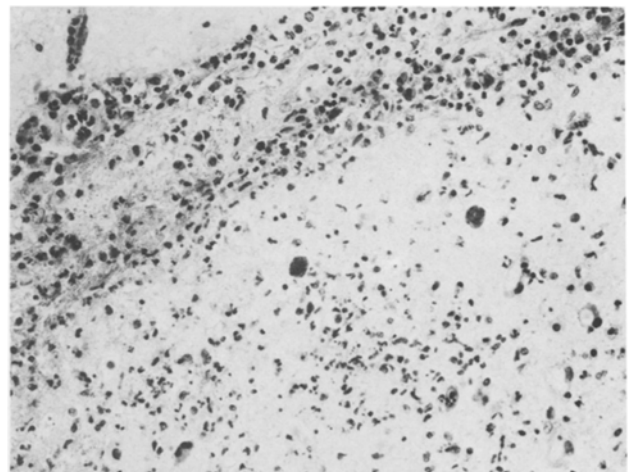


Fig. 4. Cerebral meninges demonstrating infiltration with inflammatory cells (HE, × 185) and toxoplasma cysts

macrophages, and glial perikarya or loosely in neuropile. The older lesions at the center were extensively necrotic with inflammatory infiltrate and capillary thrombosis. The central zone was surrounded by larger vessels with pronounced edema and transmural mononuclear cell infiltration. There was also parenchymal necrosis with retention of large vessels and collagen. The organisms were most frequently found in this necrotic zone. The outermost zone exhibited extensive capillary proliferation, gliosis, and edema. The lesions had atypical morphologic features, as described by previous authors [1, 8, 16]. Judging by glial reaction and histological pattern, none of these lesions were older than 2–3 weeks. The periventricular area revealed focal rarefaction of subependymal tissue with macrophagic activity and reactive astrocytes. The overlying ependymal lining was focally duplicated. Diffuse anoxic neuronal changes were noted in the remaining sections. Sections from the midbrain and pons revealed secondary hemorrhages near the midline, surrounded by eosinophilic neurons.

Discussion

Several diseases have been reported recently to occur with higher frequency among male homosexuals. These include Kaposi's sarcoma [3, 9–11, 29, 31], Burkitt's-like lymphoma [33], squamous carcinoma of the oral cavity [19], cloacogenic carcinoma of the rectum [2, 4], autoimmune thrombocytopenic purpura [22], cytomegalovirus [5, 7, 26]. *Pneumocystis carinii* [7, 10, 12], *Cryptococcus neoformans* [6], *Candida albicans* [6, 12], *Herpes simplex* [7, 15], *Mycobacterium tuberculosis* [6], meningococcal urethritis/proctitis, enteric protozoas [32] – bacteria-parasites (e.g., campylobacter enteritis, giardiasis, typhoid, amebiasis, enterobias, and strongyloidiasis), hepatitis A and B viruses [15] and the more common sexually transmitted diseases, such as gonorrhea, syphilis, and condyloma acuminatum [7, 15]. A recent paper by Vilaseca et al. [31] reported CMV inclusions in adrenal, liver, and lungs of a Spanish homosexual with Kaposi's sarcoma and fatal *Toxoplasma gondii* brain abscess. However, necropsy was limited to the thorax and abdomen. Histological examination was done in a brain biopsy material (3 cm mass). Another brief report by Hauser et al. [14] documented two homosexual males with high toxoplasma titers and cerebral involvement.

The relatively high incidence of these diseases in male homosexuals may be related to an immunocompromised status associated with the use of drugs [11, 13], recurrent infections, or idiosyncrasy. Repeated CMV infection, acquired from contaminated semen, urine, or saliva [5, 17, 18] has been proposed as the primary causative agent. Recurrent CMV infection may cause reversal of the ratio of inducer/helper T-cells subset to suppressor/cytotoxic T-cell subsets [6, 12, 21, 29]. No remarkable change has been noted in humoral immunity [6, 12, 21, 29]. In our case, the marked decrease in CMV titer and low toxoplasma titers, in spite of a fulminant infection, could be due to malnutrition, chronic diarrhea, and infections rather than

impairment of B-cell functions. The coexistence of DNA viral infection (e.g., CMV infection) and toxoplasmosis is not uncommon and usually has a more serious outcome [27, 30]. In a VD clinic, CMV titers were found in 94% of homosexual patients when compared to 54% of heterosexual patients [5]. In addition, it is known that CMV impairs macrophagic phagocytosis which plays a role in toxoplasma eradication. CMV also causes transient immunosuppression in apparently normal hosts [25]. This all supports the contention that toxoplasmosis is secondary to CMV infection. Alternatively, toxoplasma may be the result, rather than the cause, of immunosuppression. The association of enteric infestation acquired from orofecal infection may serve as a secondary contributor to the immunocompromised state.

The acquired opportunistic infection primarily affects the brain from toxoplasma parasitemia or rupture of latent cysts. The liberated, actively motile tachyzoites penetrate and destroy the nerve tissue [23] with granuloma formation. The rapid demise of these patients is secondary to tissue destruction and cerebral herniation. Because pathologically, cysts are usually associated with immunity, and proliferating tachyzoites with lack of immunity. This case might be interpreted as a condition with immunosuppression of relatively sudden onset, permitting organisms escaping cysts to multiply.

Cerebral toxoplasmosis or other opportunistic infections should be suspected in homosexuals who have high CMV titers presenting with vague neurologic symptoms. CT scan and serologic (Sabin-Feldman dye, indirect fluorescence antibody and direct agglutination) tests should be obtained early. Biopsy or aspiration of the lesions can be performed for histological or cytologic studies [20]. Biopsies of other tissues, such as lymph nodes may facilitate the diagnosis if the infection is generalized. Prompt, aggressive therapy may help to improve the morbidity and mortality.

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References

1. Best T, Finlayson M (1979) Two forms of encephalitis in opportunistic toxoplasmosis. *Arch Pathol Lab Med* 103:693–696
2. Cooper HS, Patchefsky AS, Marko G (1979) Cloacogenic carcinoma of the anorectum in homosexual men: an observation of four cases. *Dis Colon Rectum* 22:557–558
3. Curran JW and the members of the Task Force (1982) Report of the Centers for Disease Control and Task Force on Kaposi's sarcoma and opportunistic infections. Epidemiologic aspects of the current outbreak of Kaposi's sarcoma and opportunistic infections. *New Engl J Med* 306:248–252

4. Daling JR, Weiss NS, Klopfenstein LL, Cochran LE, Chow WH, Daifuku R (1982) Correlates of homosexual behavior and the incidence of anal cancer. *JAMA* 247:1988–1990
5. Drew WL, Mintz L, Miner RC, Sands M, Ketterer B (1981) Prevalence of cytomegalovirus infection in homosexual men. *J Infect Dis* 143:188–192
6. Fauci AS (1982) The syndrome of Kaposi's sarcoma and opportunistic infections: an epidemiologically restricted disorder of immunoregulation. *Ann Int Med* 96:777–779
7. Follansbee SE, Busch DF, Wofsy CB, Coleman DL, Gullet J, Aurigemma GP, Ross T, Hadley WK, Drew WL (1982) An outbreak of pneumocystis carinii pneumonia in homosexual men. *Ann Int Med* 96:705–713
8. Frenkel JK (1949) Pathogenesis, diagnosis and treatment of human toxoplasmosis. *JAMA* 140:369–378
9. Friedman-Kien A, Laubenstein LJ, Rubinstein P, Buimovici-Klein E, Marmor M, Stahl R, Spigland I, Kim KS, Zolla-Pazner S (1982) Disseminated Kaposi's sarcoma in homosexual men. *Ann Int Med* 96:693–700
10. Friedman-Kien A (1981) Centers for Disease Control, report of the US Department of Health and Human Services on Kaposi's sarcoma and pneumocystis pneumonia among homosexual men – New York City and California. *Morbidity Mortality Weekly Rep* 30:305–308
11. Gold KD, Thomas L, Garrett TJ (1982) Aggressive Kaposi's sarcoma in a heterosexual drug addict. *New Engl J Med* 307:498
12. Gottlieb MS, Schroff R, Schanker HM, Weisman JD, Fan PT, Wolf RA, Saxon A (1981) Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a new acquired cellular immunodeficiency. *New Engl J Med* 305:1425–1431
13. Hanrahan JP, Wormser GP, Maguire GP, DeLorenzo LJ, Gavis G (1982) Opportunistic infections in prisoners. *New Engl J Med* 307:498
14. Hauser WE, Luft BJ, Conley FK, Remington JS (1982) Central nervous system toxoplasmosis in homosexual and heterosexual adults. *New Engl J Med* 307:498–499
15. Judson FN, Penley KA, Robinson ME, Smith JK (1980) Comparative prevalence rates of sexually transmitted diseases in heterosexual and homosexual men. *Am J Epidemiol* 112:836–843
16. Kass EH, Andrus SB, Adams RD, Turner FC, Feldman HA (1952) Toxoplasmosis in the human adult. *Arch Int Med* 89:759–782
17. Lang DJ, Kummer JF (1972) Demonstration of cytomegalovirus in semen. *New Engl J Med* 287:756–758
18. Lang, DJ, Kummer JF (1975) Cytomegalovirus in semen: observations in selected populations. *J Infect Dis* 132:472–473
19. Lozada F, Silverman S, Conant M (1982) New outbreak of oral tumors, malignancies and infectious disease strikes young male homosexuals. *Calif Dent J* 10:39–42
20. McLeod R, Berry PF, Marshall WH, Jr, Hunt SA, Rynning FW, Remington JS (1979) Toxoplasmosis presenting as brain abscesses. Diagnosis by computerized tomography and cytology of aspirated purulent material. *Am J Med* 67:711–714
21. Mildvan D, Mathur U, Enlow RW, Romain PL, Winchester RJ, Colp C, Singman H, Adelsberg BR, Spigland I (1982) Opportunistic infections and immune deficiency in homosexual men. *Ann Int Med* 96:700–704
22. Morris L, Distenfeld A, Amorosi E, Karpatkin S (1982) Autoimmune thrombocytopenic purpura in homosexual men. *Ann Int Med* 96:714–717
23. Powell HC, Gibbs CJ, Jr, Lorenzo AM, Lampert PW, Gajdusek DC (1978) Toxoplasmosis of the central nervous system in the adult. Electron microscopic observations. *Acta Neuropathol (Berl)* 41:211–216
24. Reynolds ES, Walls KW, Pfeiffer RI (1966) Generalized toxoplasmosis following renal transplantation. *Arch Int Med* 118:401–405
25. Rinaldo CR, Carney WP, Richter BS, Black PH, Hirsch MS (1980) Mechanisms of immunosuppression in cytomegaloviral mononucleosis. *J Infect Dis* 141:488–495
26. Rozenbaum W, Coulaud JP, Saimot AG, Klatzmann D, Mayaud C, Carette MF (1982) Multiple opportunistic infection in a male homosexual in France. *Lancet* 1:572–573
27. Ruskin J, Remington JS (1976) Toxoplasmosis in the compromised host. *Ann Int Med* 84:193–199
28. Sharp GC, Irvin WS, Tan EM, Gould RG, Holman HR (1972) Mixed connective tissue disease. An apparently distinct rheumatic disease syndrome associated with a specific antibody to an extractable nuclear antigen (ENA). *Am J Med* 52:148–159
29. Stahl RE, Friedman-Kien A, Dubin R, Marmor M, Zolla-Pazner S (1982) Immunologic abnormalities in homosexual men. Relationship to Kaposi's sarcoma. *Am J Med* 73:171–178
30. Vietzke WM, Gelderman AH, Grimley PM, Valsamis MP (1968) Toxoplasmosis complicating malignancy. *Cancer* 21:816–827
31. Vilaseca J, Arnau JM, Bacardi R, Mieras C, Serrano A, Navarro C (1982) Kaposi's sarcoma and *Toxoplasma gondii* brain abscess in a Spanish homosexual. *Lancet* 1:572
32. William DC, Shookhoff HB, Felman YM, DeRamos SW (1978) High rates of enteric protozoal infections in selected homosexual men attending a venereal disease clinic. *Sex Transm Dis* 5:155–157
33. Ziegler JL, Drew WL, Miner RC, Mintz L, Rosenbaum E, Gershow J, Lennette ET, Greenspan J, Shillitoe E, Beckstead J, Casavant C, Yamamoto K (1982) Outbreak of Burkitt's-like lymphoma in homosexual men. *Lancet* 2:631–633

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