1P284

50% of pts who died + came to autopsy had signif CNS sx (not excluding biochem derangements)

crypto — thickened meninges, hypercellular ① lo power
multinuc giant cell, yeast are clear ② hi
typically crypto has poor-absent inflammatory response

③ extension from meninges to perivascular spaces

④ cryptococcomas in parenchyma

temporal lobe area of parenchymal destruction along lateral ventricle

4/29 had crypto

MAI – only bacteria encountered elsewhere
3 cases, seemed to be a 2nd opportunist
found in areas of parenchymal dest 2° to CMV
not found in meninges
Listeria rare in AIDS

viral – CMV most common
5 cases c̄ obvious inclusions

all cases c̄ obvious CMV inclusions had MGN
and in cases ō CMV inclusions there was
evidence of CMV elsewhere

① intracytoplasmic and intranuc inclusions cells eye
② isolated nuc + MGN
③ a MGN ō organisms

Microglial nodules non-spec rickettsia, herpes, protozoa, CMV and others. Response of brain MΦ to a focus.

papovavirus

PML 3 cases

starts at junc of gray and white matter
small areas demyelination coalesce and extend to white

PML + probable hops / spheroids filaments

EM papovavirus virions 4+

toxo - incidental finding cyst c̄ trophs inside

1° CNS lymphoma - thick vessel walls
atypical lymphoid infilt
not suspected clinically most m i.t. called "Burkitt's"
B - small cleaved

1° CNS lymphomatoid granulomatosis
mainly mature lymphs, plasma cells
histiocytes, fibrinoid necrosis in vessel walls

non bact thrombotic endocarditis c̄ emboli to brain
fibrin thrombus
classically in debilitated pts c̄ tumors
now pts c̄ indwelling catheters (L) mid cerebral a

mainly infectious
tumors - lymphomas KS rarely if ever
postulated lymphatics

Michael S. Gottlieb, M.D.
Medicine Grand Rounds

NEUROLOGICAL COMPLICATIONS OF AIDS

A 29 year old homosexual white male was evaluated at UCLA in June, 1983, for concerns about sexual exposure to two individuals who subsequently developed AIDS. He was found to have generalized adenopathy, cutaneous anergy and lymphopenia (200/mm3). T cells with the helper phenotype were 34/mm3 (nl 331-1286) and T cells with the suppressor phenotype 94/mm3 (nl 200-1002).

In February, 1984 he developed fevers to 103, night sweats, dyspnea, and non-productive cough associated with pulmonary infiltrates. Flexible bronchoscopy was performed at a Hollywood hospital, and high dose intravenous Bactrim therapy was initiated for presumed Pneumocystis. The patient developed paranoia, signed out AMA, and presented to the UCLA emergency room. The neurologic examination was normal. On day 2 at UCLA he developed a paranoid psychosis for which haloperidol and perphenazine were administered. He had a history of psychiatric disorder in his teens for which chlorpromazine had been prescribed. A CT scan with contrast revelaed slight widening of the third and lateral ventricles. Lumbar puncture was revealed 5 cells/mm3, 53 total cells (40% lymphs), protein 57 mg/dl and glucose 51 mg/dl. Cultures and india ink prep were negative; CSF cryptococcal antigen was not requested. He was treated with Bactrim for a total of 14 days with clearing of pulmonary symptoms and infiltrates, however the stains from the bronchoscopy were inconclusive. He was discharged on Bactrim prophylaxis, and antipsychotic medication was easily tapered over one month in the clinic.

He was readmitted April 24, 1984, complaining of a two week history of diffuse headache increasing in severity. He was fully oriented, appropriate, and had a normal neurologic examination. A CT scan was normal. Lumbar puncture was performed. Cells were 18/mm3 (93% lymphs). CSF glucose was 41 mg/dl and protein 99 mg/dl. Cryptococcal antigen was positive at 1:2 (CSF) and 1:16 (serum). He was treated with amphotericin B and 5 fluorocytosine with gradual resolution of headache. He developed a 1 cm ulcer of the hard palate from which Herpes simplex was cultured. Repeat lumbar puncture on May 15, 1984 had 22 cells/mm3 (62% lymphs), glucose 46 mg/dl and protein 106 mg/dl. CSF cryptococcal antigen was negative. He was discharged to receive outpatient amphotericin to a total dose of 1000 mg, and a total 6 weeks of 5FC as per recommendations of the ID service.

References

Snider, WD, Simpson, DM, Nielsen, S, Gold, JWM, Metroka, CE, Posner, JB. Neurological Complications of AIDS: Analysis of 50 Patients. Ann Neurol 14:403-418, 1983.

Horowitz, S, Bentson, JR, Benson, DF, Davos, I, Pressman, B, Gottlieb, MS. CNS Toxoplasmosis in Acquired Immunodeficiency Syndrome. Arch Neurol. 40:649-652.

1. CORNELL SERIES
2. UCLA SERIES 1
3. UCLA SERIES 2
4. PRESENTING SX OF CNS INV.
5. DIFF DX OF MENTAL STATUS CHANGES

6. CRYPTO MENINGES
7. CRYPTOCOCCOMA in brain parenchyma, temporal lobe along lat vent,
8. CRYPTO HIGH POWER

9. SUBACUTE ENCEPHALITIS
10. LARGE VENTRICLES
11. WIDENED SULCI

12. CMV SUBEMENDYMAL
13. MGN WITH CMV
14. MGN

15. TOXO CT 1
16. TOXO CT 2
17. TOXO CYST

18. PML CT
19. PML BRAIN
20 PML EM papovavirus virions
21. MAI
22. PONS LYMPHOMA thick vessel, atypical
23. EVALUATION OF PT
24. ALGORITH FOR BRAIN LESIONS

Case presentation

Major points in relation to the case are the following:

(1) Opportunistic infections are most common cause of CNS disease in AIDS.

(2) They most commonly occur in late stage patient, debilitated by other infections or KS, however they may be the presenting manifestation

(2) Crypto meningitis is the most common treatable CNS infection in setting of AIDS

(3) Persistent headache most common presentation of crypto meningitis; may be slight meningismus and photophobia

(4) The spinal fluid examination in crypto meningitis especially in @ is notable for minimal pleocytosis, however crypto ag is usually positive, and the organism frequently cultured.; this test was not requested on this patient's first spinal fluid examination.

A wide spectrum of CNS lesions has been described in AIDS making mandatory a complete laboratory examination of all spinal fluid specimens.

Complete studies include: SLIDE

LIST THE NEUROLOGICAL COMPLICATIONS

Snider and associates at NYH and Memorial noted neuro complications in 50 of 160 AIDS patients evaluated 1/80-1/83. 80% homosexual males.

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INFECTIONS
NEOPLASMS
VASCULAR PHENOMENA

LIST OF ANDERS AUTOPSY SERIES

Largest group (18) in Cornell had a distinct clinical and pathological syndrome which they designated "subacute encephalitis." An encephalopathy notable for subtle cognitive changes, withdrawal, psychomotor retardation. Early behavioral change was often erroneously attributed to general debilitation or depression. Detrioration over weeks-months with marked dementia.

CT showed large ventricles with prominent cortical sulci indicating cerebral atrophy. Spinal fluids mild pleo, elevated protein and/or lowered glucose.

SLIDE Major autopsy findingsin CNS were nodular collections of microglial cells diffusely, moreso in grey matter, on occasion in association with a typical CMV cell. Etio not established, glial nodules are non-specific, however CMV is suspect. MGN's: 20 cases (aggregates of MG cells and astrocytes) widely distributed throughout the brain. Lesions are non-spec, however most pts with them had CMV inclusions present elsewhere at autopsy.CMV: intranuc and intracyto CMV inc bods classic owls eye

Both dissem and focal lesions seen. All cases had widespread microglial nodules (SLIDE) sometimes with associated CMV inclusions. Severity of mental status change correlated with the # of inclusions.

Neurobehavioral abns may be presentation of CNS infections in AIDS; subtle cognitive defects or depression are often the first manifestations of organic CNS disease.

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Cornell series had 5 cases of intracerebral toxo; dx at post in 2, bx in 1, and inferred in 2 on basis of serology and response to pyri/sulfa. Present usually with focal findings. 1 at UCLA with seizures. Lesions may be single, but often are multiple, usually in grey matter with a predisp for basal ganglia. Frequestly show contrast enhancement. CSF may be normal. Most patients have measurable antibodies by SF dye of IFA, however titers usually not in range suggestng active infection. SLIDE

Toxo: Toxo can cause a meningoencephalitis, multiple progressive mass lesions in the brain and brainstem, and chorioretinitis in ID patients.Very common in Haitian patients dying of AIDS, but also occurs in the homosexual patients as we reported in the second reference. This slide from Dr. A. shows an unruptured cyst containing trophs in cortex probably representing ltent infection. Pt not clinically symptomatic.

PML- headaches, focal weakness, hemiparesis, dementia
CT low-density lesions which do not contrast enhance or produce a mass effect
CSF nl (2); PML: more severe necrosis and demyelination than classic PML.. Typical homo, eos, inranuc inc on LM and apparent sine qua non of dx papovavirus particles on EM

MAI- may be cultured or observed in brains of pts with disseminated MAI. Not clinically apparent in cases at Cornell (2) or at UCLA (1) SLIDEMAI: In 2 cases present in areas of demy associated wuth CMV.
CNS MAI only occasional in pts dying of dissem MAI, and lesions were silent.

Of interest no cases of proved H. simplex or zoster of CNS, however several cases in NY and here of suspected arteritis with infarction as a complication of H. zoster infection.

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LYMPHOMA-PRIMARY CNS

1 case here and 2/3 at Cornell clinically silent discovered at post. Normal CSF and neg toxo serologies.

SLIDE Primary intracranial lymphoma: not clinically suspected or found elsewhere at autopsy. Tumor cells mainly confined to a thickened blood vessel ealls but foci extended into parench and meninges.

A number of categories of abnormal immune states are associated with an increased risk of lymphoma; these include congenital ID, autoimmune disease, renal transplant recipients, treated HD patients, and AIDS.

CNS lymphomas account for less than 1% of lymphomas in general, but for 50% of lymphomas in renal transplant patients. Second lymphomas in HD patients with HD usually occur in the gi tract.

The CPC in the NEJM of August 11, 1983, V 309:359 concerns a patient with AIDS and multiple cranial nerve palsies due to a malignant lymphoma of the immunoblastic type of the cerebellum and brainstem.

Immunoblastic lymphomas are most common type in renal tx and pts with autoimmune disease. @ pts with primary lymphoma of the CNS have been described as immunoblastic, poorly differentiated lymphocytic, and "diffuse histiocytic" in contrast to the Burkitt's like lymphomas reported in @ pts at other sites.

STUDIES USEFUL IN W/U INCLUDED

SEVERAL PATTERNS

LOS ANGELES: UCLA SCHOOL OF MEDICINE
DEPARTMENT OF MEDICINE