EANS/UEMS European examination in neurosurgery

Variants of questions with answers (compilation - Vyacheslav S. Botev, Department of Neurosurgery, M.Gorky Donetsk National Medical University)

HIV/AIDS

Human immunodeficiency virus infection

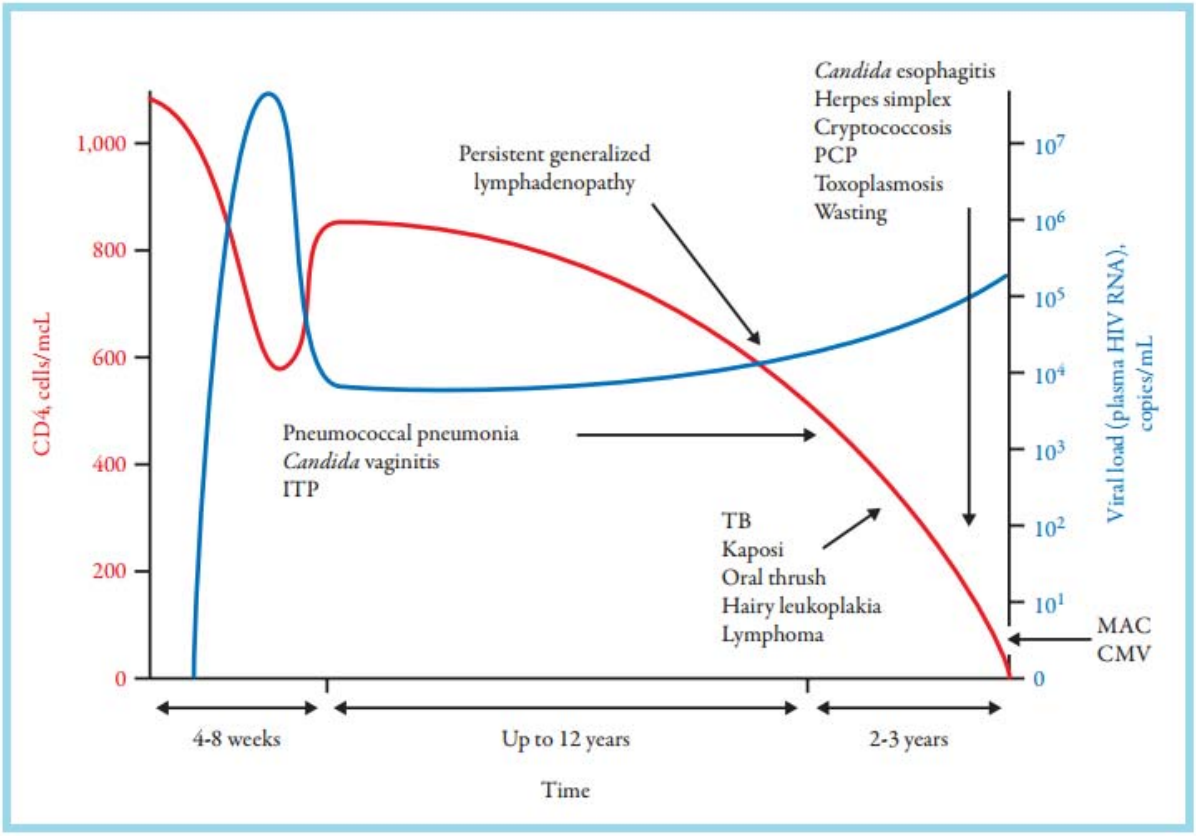
Infection by the retrovirus HIV leads to acquired immunodeficiency syndrome (AIDS). Infection may be transferred from an infected individual through exposure to body fluids including blood, semen, and breast milk. It is associated with a progressive decline in CD4+ T cell numbers. The stage of infection can be determined by measuring the patient's CD4+ T cell number and the level of HIV in the blood. HIV primarily infects CD4+ helper T cells, macrophages, and dendritic cell (antigen-presenting cells). The low level of CD4+ T cells in the blood of HIV-infected patients may be because of (1) the HIV virus killing infected CD4+ T cells directly, (2) increased rates of apoptosis in infected CD4+ T cells, or (3) CD8+ cytotoxic lymphocytes recognizing and killing CD4+ T cells after the virus has infected them. The HIV virus enters macrophages (CD4+ T cells as well), replicates in the host cells, and the new viruses are released from the host cells. Greatly reduced numbers of CD4+ T cells result in the loss of cell-mediated immunity. Without stimulation from CD4+ T helper cells, humoral immunity function is compromised. AIDS patients are vulnerable to opportunistic infections; common diseases include *Pneumocystis jiroveci pneumonia*, toxoplasmosis, and thrush. Histologically, lymph nodes in the early stage of HIV infection reveal large, irregular lymphatic nodules and an increase number of macrophages in the germinal centers.

Natural history

1. At time of primary infection, there may be seroconversion-related illness, which can include fever, maculopapular rash, malaise, myalgias, primary meningitis.
2. Usually a subsequent clinical, but not virologic, latent period of 10 years (average); many patients develop lymphadenopathy during this period
3. Eventually, fevers, mild signs, and symptoms suggestive of reduced cell-mediated immunity develop.
4. With progressive decrease of CD4 count, opportunistic infections and AIDS develop.
5. Most neurologic complications of HIV are symptomatic during latter stages of

infection; about 50% of people with HIV develop related neurologic symptoms in the course of disease.

The illnesses and conditions associated with HIV infection vary greatly depending on an individual's CD4 count and other behaviors. Figure below illustrates the natural history of HIV infection and the stages at which conditions that are commonly associated with HIV infection occur.



Natural history of human immunodefciency virus (HIV) infection:
CD4 counts, viral load, and clinical manifestations.
CMV indicates cytomegalovirus; ITP, idiopathic thrombocytopenic purpura; MAC, *Mycobacterium avium* complex; PCP, *Pneumocystis* pneumonia; TB, tuberculosis.

Questions

1. What is the most common form of opportunistic meningitis in a patient who is known to have AIDS?

2. How is cryptococcal meningitis diagnosed?

3. Is the risk of bacterial meningitis increased in AIDS patients?

4. Does HIV infect neurons?

5. What is the most common neurological complication of HIV infection/AIDS?

6. Name the HIV-associated neuropathies.

7. What is the “Sjögren’s syndrome-esque” neuropathy associated with CD8 hyperlymphocytosis?

8. What is its prognosis?

9. What is HAND, and what causes it?

10. How is HAND best treated?

11. What are the most common CNS mass lesions found in HIV+/AIDS patients?

12. For which of these is brain biopsy indicated?

13. What are the three most common focal brain lesions in human immunodeficiency virus (HIV)?

14. What modality can distinguish primary lymphoma of HIV from other focal mass lesions associated with HIV?

15. What empiric medications should be given to all HIV-positive patients with a CNS mass lesion?

16. What test can be performed on CSF to diagnose acquired immunodeficiency syndrome (AIDS) lymphoma of the CNS?

17. What are the cells of origin that are found in primary CNS lymphoma in a patient with HIV?

18. What is the most common cause of myelopathy in HIV?

19. Which parts of the spinal cord does acquired immunodeficiency syndrome-(AIDS) associated vacuolar myelopathy involve?

MCQs

1. Which of the following is the most common cause of brain abscess in patients with AIDS?
A. Tuberculosis
B. Herpes zoster
C. Cytomegalovirus
D. Toxoplasma gondii
E. Cryptococcus neoformans

2. The tumor type that is common in the brain of patients with AIDS, but otherwise extremely rare, is
A. Lymphosarcoma
B. Kaposi's sarcoma
C. Primary lymphoma
D. Metastatic lymphoma
E. Lymphocytic leukemia

3. A 32-year-old HIV positive man is noted to have forgetfulness, gait disturbance, and confusion. A lumbar puncture is performed, and the India ink preparation is positive. Which of the following is the most likely diagnosis?
A. Tuberculosis
B. Toxoplasmosis
C. Cryptococcal meningitis
D. Primary CNS lymphoma
E. HIV-associated dementia

4. A 30-year-old HIV positive man presents with a 3-week history of upper quadrantanopia, right arm weakness, and fatigue. His recent laboratory evaluation shows a CD4 count of 50 cells/mm^3. Brain MRI shows multiple areas of white matter lesions, mostly posterior, without mass effect, and nonenhancing. What is the most likely cause of this man's symptoms?
A.Tuberculosis
B.Toxoplasmosis
C. Primary CNS lymphoma
D.Cytomegalovirus (CMV) ventriculitis
E. Progressive multifocal leukoencephalopathy (PML)

5. A 28-year-old HIV positive woman presents with a several-week history of mild bifrontal headache, neck stiffness, and low-grade fevers. Also a facial palsy developed sometime before she presented. Brain MRI shows mild enhancement of the basilar cisterns. The CD4 count is 150 cells/mm^3. What organism is of particular concern in this patient and why?
A. Actinomyces
B. Toxoplasma gondii
C. Neisseria meningitidis
D. Staphylococcus aureus
E. Cryptococcus neoformans

6. What is the most common opportunistic infection in AIDS?
A. Herpes zoster
B. Toxoplasmosis
C. Cryptococcosis
D. Tuberculosis (TB)
E. Cytomegalovirus (CMV)

7. The intracranial tumor most likely to be encountered in a middle-aged man with the acquired immunodeficiency syndrome (AIDS) is:
A. Meningioma
B. Ependymoma
C. Oligodendroglioma
D. Primary CNS lymphoma
E. Glioblastoma multiforme

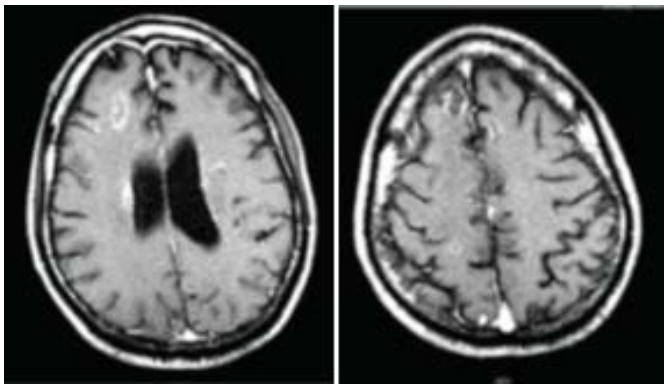
8. A patient with known HIV infection presents with seizures and two ring-enhancing brain lesions. What is the most likely diagnosis?
A. Toxoplasmosis
B. Cerebral abscess
C. Subcortical infarction
D. Cryptococcal infection
E. Primary CNS lymphoma

9. What is progressive multifocal leukoencephalopathy (PML)?
A. JC virus
B. Cytomegalovirus
C. Epstein-Barr virus

D. Herpes zoster virus
E. Cryptococcal infection

10. Which of the following is the most common neurologic complication of AIDS?
A. Dementia
B. Lymphoma
C. Myelopathy
D. Toxoplasmosis
E. Inflammatory polymyositis

11. A 28-year-old homosexual man with a history of drug and alcohol abuse was seen in a clinic complaining of new-onset headache and fatigue. He was slightly lethargic, with obvious track marks on his arms. His neurological examination was otherwise unremarkable. An MRI was obtained. Contrasted images are shown below.



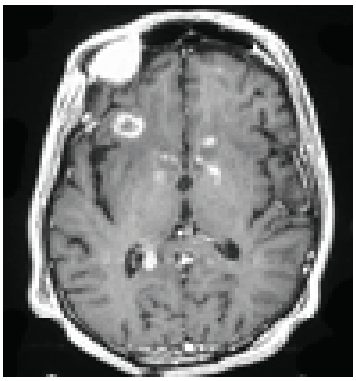
What is the least likely diagnosis?
A. Toxoplasmosis
B. Embolic infarcts
C. Cytomegalovirus
D. Cerebral abscesses
E. Cryptococcal infection

12. A 30-year-old right-handed man with known HIV infection presents to the ED with a 3-day history of progressive right hemiparesis and aphasia. MRI of the brain reveals a homogeneously enhancing left frontal lesion. There is central necrosis and mass effect in the white matter of the left cerebral hemisphere. A biopsy is performed and reveals diffuse B-cell lymphoma. Genomic information

from which of the following viruses is most likely to be found in this patients tumor cells?

A. Cytomegalovirus
B. Epstein-Barr virus
C. Herpes zoster virus
D. Herpes simplex virus
E. Cryptococcal infection

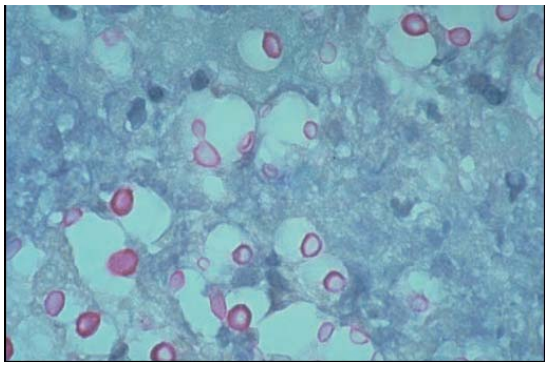
13. A 33-year-old man with the acquired immune deficiency syndrome (AIDS) develops headaches and left hemiparesis and is found to have a right frontal white matter homogeneously enhancing lesion. The most likely diagnosis is:



A. Cerebral abscess
B. Oligodendroglioma
C. Cerebral toxoplasmosis
D. Primary CNS lymphoma
E. Glioblastoma multiforme

14. A 27-year-old man presents with dementia, weakness, visual loss, and ataxia 1 year after receiving a cadaveric kidney transplant. Which of the following is the most likely cause of this patient's CNS disorder?
A. Gaucher disease
B. Adrenoleukodystrophy
C. Metachromatic leukodystrophy
D. Subacute sclerosing panencephalitis
E. Progressive multifocal leukoencephalopathy

15. A 48-year-old man with AIDS is admitted to the hospital with a headache, fever of 38.7°C, and persistent cough. His CD4 cell count is less than 500/mm^3. Lumbar puncture returns cloudy fluid, and microscopic examination shows numerous encapsulated microorganisms (shown in the image). Which of the following pathogens is the most likely cause of meningitis in this patient?



A. Aspergillus flavus
B. Toxoplasma gondii
C. Neisseria meningitidis
D. Cryptococcus neoformans
E. Mycobacterium tuberculosis

16. A 42-year-old man with AIDS dementia complex dies of respiratory insufficiency secondary to Pneumocystis carinii pneumonia. Examination of the brain at autopsy reveals mild cerebral atrophy, with dilation of the lateral ventricles. Which of the following best explains the pathogenesis of neuronal injury in this patient?
A. Apoptosis of oligodendrocytes
B. Lytic infection of neurons by HIV
C. Accumulation of lysosomal storage material
D. Release of neurotoxic cytokines from macrophages
E. Necrotizing vasculitis that results in multiple cerebral infarcts

17. A 45-year-old female patient was diagnosed with AIDS over 10 years ago. Despite receiving highly active antiretroviral therapy (HAART) that you prescribed in consultation with a specialist in infectious diseases, her most recent $CD4^+$ T cell count was 180 cells/ mm^3. You are worried about the patient's risk of acquiring an opportunistic infection and wish to begin prophylactic therapy. For which of the following opportunistic infections is this patient at risk?
A. CNS toxoplasmosis
B. Cryptococcal meningitis
C. Cytomegalovirus retinitis
D. *Pneumocystic carinii* pneumonia
E. Disseminated *Mycobacterium avium* complex infection

18. A 40-year-old man diagnosed with HIV-associated dementia is able to perform basic activities of self-care but cannot work or maintain the more demanding aspects of daily life. He is able to ambulate. In which stage of HIV-associated dementia Memorial Sloan Kettering (MSK clinical staging system) can the patient be classified?
A. Stage 0
B. Stage 1

C. Stage 2
D. Stage 3
E. Stage 4

19. Neuropsychological tests in the initial stage of AIDS dementia may show
A. Selective memory loss; impaired retrieval
B. Severe attention deficit
C. Impaired calculation
D. Language impairment
E. Preservation of manipulation of acquired knowledge

20. The most common type of peripheral neuropathy in AIDS patients is
A. Distal symmetric polyneuropathy
B. Acute inflammatory demyelinating polyneuropathy
C. Mononeuropathy multiplex
D. Autonomic neuropathy
E. Progressive polyradiculopathy

21. A 24-year-old man with a history of HIV infection consults the neurologist because of a chronic headache. Neurological examination is normal. Computed tomography (CT) scan of the head with contrast shows a ring-enhancing lesion in the left parietal area, which is confirmed by magnetic resonance imaging (MRI) of the head with gadolinium enhancement. The most appropriate diagnosis or therapeutic approach is to
A. Proceed to a biopsy to establish the diagnosis
B. Start the patient on corticosteroids
C. Start empirical antibiotic therapy
D. Start empirical antitoxoplasmosis treatment
E. Start the patient on intravenous acyclovir

22. The most frequent presenting symptom of primary central nervous system (CNS) lymphoma in HIV patients is
A. Impaired cognition
B. Seizures
C. Hemiparesis
D. Aphasia
E. Cranial nerve palsy

23. The most common cause of an intracranial space-occupying mass with contrast enhancement in AIDS patients is
A. Primary CNS lymphoma
B. Bacterial abscess
C. Fungal abscess
D. Toxoplasmosis
E. Metastatic brain tumor

24. The most frequent abnormal finding on retinal examination in AIDS patients is
A. Cotton-wool spots
B. Cytomegalovirus (CMV) retinitis
C. Optic atrophy
D. Swollen optic nerve
E. Toxoplasmal retinitis

25. The most common cause of epidural abscess in immunocompetent patients is
A. Klebsiella pneumoniae
B. Staphylococcus
C. Streptococcus
D. Fungal infection
E. Mycobacterium tuberculosis

26. A 32-year-old intravenous drug abuser presents with more than 2 weeks of left body weakness. Brain CT scan reveals several ring-enhancing lesions, and an HIV test is positive. Serological, CSF, and MRI testing support the diagnosis of *Toxoplasma gondii.* Which of the following is the best treatment for HIV associated CNS *Toxoplasma gondii?*
A. Intravenous acyclovir
B. Neurosurgical removal of the lesions
C. Oral fluconazole
D. Sulfadiazine and pyrimethamine
E. Thiabendazole

27. Which of the following is the most common cause of brain abscess in patients with AIDS?
A. *Cryptococcus neoformans*
B. *Toxoplasma gondii*
C. Tuberculosis

D. Cytomegalovirus
E. Herpes zoster

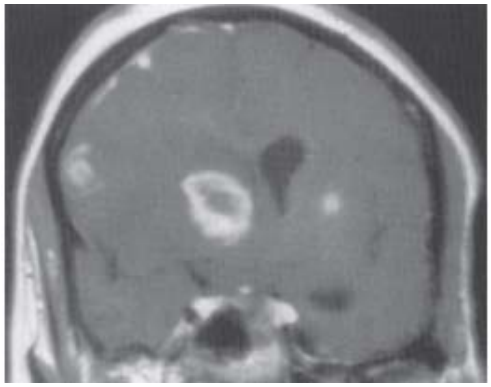
28. Both HIV and cytomegalovirus infections in the brain characteristically produce which of the following?
A. Senile plaques
B. Intraneuronal amyloid
C. Intranuclear inclusions
D. Intracytoplasmic inclusions
E. Microglial nodules

29. A 24-year-old medical student experiences an accidental needle stick from a patient known to have HIV. Which of the following is the most appropriate management?
A. Tenofovir, emtricitabine, and raltegravir
B. Tenofovir and emtricitabine
C. Abacavir
D. Reassurance

30. A 43-year-old HIV positive man presents with new onset right-sided paralysis. He recently started trimethoprim–sulfamethoxazole (TMP–SMX) for a CD4 count of 70/mm^3. The patient is afebrile and vital signs are within normal limits. Neurologic examination demonstrates hyper-reflexia, hypertonia, and positive Babinski sign on the right side. Which of the following is the most likely diagnosis in this patient?
A. Progressive multifocal leukoencephalopathy (PML)
B. Primary CNS lymphoma
C. AIDS dementia complex
D. Toxoplasmosis

31. A 45-year-old woman with a history of HIV presents to the hospital with worsening confusion, headache, and fever. She has not been to her physician for follow-up in years, and has not been compliant with her medications. She has been hospitalized twice in the past year for pneumonia. Her last CD4 count measured 6 months ago was 140/mm^3. She is admitted and found to be febrile to38.6°C. She appears lethargic and vomits several times. Her CD4 count is measured again during this hospitalization and is found to be 76/mm^3. An MRI

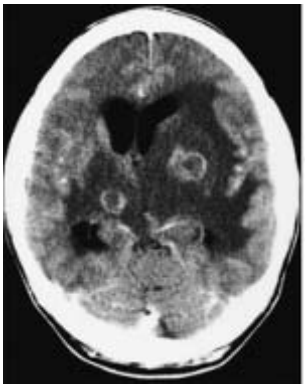
is performed, and the postcontrast T1-weighted image is shown in figure below.



Which of the following could have prevented this from happening?

A. Azithromycin prophylaxis
B. Yearly cancer surveillance
C. Trimethoprim-sulfamethoxazole prophylaxis
D. Isoniazid and pyridoxine for 9 months
E. There is no available treatment

32. The following CT scan post-contrast is taken from a lethargic 27-year-old male with AIDS who became progressively stuporous over the course of several hours. Given the CT scan and the patient's current state, what is the best approach to initial treatment?



A. Obtain an MRI scan
B. Mannitol 100 mg i.v.
C. Decadron (dexamethasone) 10 mg i.v.
D. Repeat CT scan in 6 hours

33. Directions: Match each of the following HIV opportunistic infections and neoplasms with the most likely imaging characteristic, using each answer either once, more than once, or not at all.

A. HIV encephalopathy
B. Toxoplasmosis
C. Progressive multifocal encephalopathy
D. Primary CNS lymphoma
E. Cryptococcal disease
F. Cytomegalovirus
G. None of the above

1. Lacunar infarctions resulting from “gelatinous pseudocysts”

2. Asymmetric, multifocal areas of T1 and T2 prolongation in the periventricular and/or peripheral white matter without sparing of subcortical U fibers.

3. Parieto-occipital involvement classically described, but lesions can also affect the basal ganglia, brainstem, and cerebellum.

4. Symmetric patchy or confluent areas of high signal intensity on T2-weighted images involving the centrum semiovale; frontal predominance.

5. “Eccentric target sign”.

6. Characteristic rim of generalized periventricular hyperintensity on proton density-weighted images or fluid-attenuated inversion recovery (FLAIR).

7. Ependymal enhancement often nodular and irregular.

Neurologic manifestations of AIDS

1. Name four conditions in AIDS producing focal CNS lesions.

A. t_____ toxoplasmosis

B. l_____ lymphoma

C. p_____ m _____ l _____ progressive multifocal leukoencephalopathy (PML)

D. *C*_____ *Cryptococcus*

2. Complete the following about the neurologic manifestations of AIDS:

A. What is the most common lesion causing mass effect in AIDS patients?

toxoplasmosis

B. Does this occur early or late in the course of HIV infection? late

C. Central nervous system (CNS) lymphoma is associated with what virus?

Epstein-Barr virus

D. PML is associated with what virus?

polyoma or J-C virus (not to be confused with Creutzfeldt-Jakob)

3. An imaging characteristic of toxoplasmosis in AIDS patients is

A. number multiple
B. density low
C. located basal ganglia
D. enhancement ring-"multiple enhancing lesions in the basal ganglia"

4. Complete the chart by listing the CT and MRI findings in each of the following:

A. toxoplasmosis
i. number more than 5
ii. enhance ring
iii. location basal ganglia
iv. mass effect moderate
v. miscellaneous edema
B. lymphoma
i. number less than 5
ii. enhance homogeneous
iii. location subependymal
iv. mass effect mild
v. miscellaneous may cross corpus callosum
C. PML
i. number multiple
ii. enhance no
iii. location white matter
iv. mass effect none
v. miscellaneous high on T2 and low on T1

5. Complete the following about the neurologic manifestations of AIDS:

A. treatment for toxoplasmosis
i. p_____ pyrimethamine
ii. s_____ sulfadiazine
B. How promptly should we see improvement clinically and radiologically?
2 to 3 weeks
C. If successful how long should toxoplasmosis be controlled?
for patient's lifetime if mets are continued
D. Biopsy should be considered if there is no response in _____ _____.
3 weeks (some say 7 to 10 days)

6. Complete the following about the neurologic manifestations of AIDS:

A. Can toxoplasmosis be radiologically distinguished from
i. lymphoma? no
ii. PML? usually
B. Therefore check
i. for toxo _____ _____ _____ serum toxo titers
ii. for lymphoma _____ study for LP (if no mass effect);
c_____, PCR a_____ of cytology; amplification
v_____ D_____ viral DNA

7. Considerations for performing a biopsy of a brain lesion in a HIV+ patient
A. if toxo titers are _____ negative
B. if no response to toxo meds in _____ 3 weeks
C. True or False. Biopsy is equally valuable in lesions that enhance or don't enhance.
false (more valuable in enhancing lesions to differentiate toxoplasmosis from lymphoma)
D. technique for biopsy _____ stereotactic
E. What two areas should be sampled? enhancing rim and the center
F. Positive biopsy can be expected in_____%. 96%

8. Indicate the survival times for AIDS patients with the following conditions:
A. CNS toxo _____ 15 months
B. PML _____ 15 months
C. lymphoma _____ 3 months versus 1 month without treatment
D. lymphoma in nonimmunosuppressed patient _____ 13.5 months

Answers

1. Cryptococcus.

2.

• CSF enzyme immunoassay

• Confirmatory culture

• Direct observation of the organism by India ink stain is possible in approximately 70% of cases.

3. No.

4. No.

5. Peripheral neuropathies.

6.

• Distal sensory polyneuropathy (bilateral paresthesia, numbness, and pain of the legs)

• Acute inflammatory demyelinating polyneuropathy (similar to Guillain-Barré)

• Nucleoside neuropathy (dose-dependent neurotoxicity of the Nucleoside Reverse Transcriptase Inhibitors [NRTI] drugs)

• Mononeuritis multiplex (acute sensory or motor deficit of a peripheral nerve)

• Progressive polyradiculopathy (occurs late in the illness; diagnosed by CMV in the CSF)

7. Diffuse infiltrative lymphocytosis syndrome– associated neuropathy.

8. Patients with this syndrome tend to have higher CD4 counts, fewer opportunistic infections, and better overall survival than other HIV+ patients, though some of these patients develop B cell lymphoma.

9. HIV-associated neurocognitive disorder (HAND) is a symptom of cognitive (forgetfulness, decreased concentration), behavioral (lack of spontaneity, apathy), and motor (gait instability, poor coordination) changes that arises in AIDS patients. It is thought to be mediated by HIV-infected macrophages, the cytokines they produce (including TNF-α, IL-2, IL-6), activation of NMDA receptors, and toxicity of the viral proteins gp120 and tat.

10. By antiretrovirals. Those with higher CNS penetrance (zidovudine, nevirapine, ritonavir-boosted indinavir) are thought to help the most, though this is still the subject of much debate.

11.

• Toxoplasma encephalitis

• Cytomegalovirus (CMV) encephalitis

• Progressive multifocal leukoencephalopathy (PML)

• CNS lymphomas

12.

• Toxoplasma is treated empirically with drugs; a biopsy is not indicated.

• CMV may be detected via DNA PCR of CSF or via biopsy.

• PML may require a brain biopsy for diagnosis since highly active antiretroviral therapy (HAART) reduces the levels of JC virus in the CSF (detected by DNA PCR if levels high enough).

• Lymphomas are evaluated first by testing CSF for lymphomatous cells and/or EBV DNA (by PCR) and then by brain biopsy, if CSF evaluation is negative.

13.Toxoplasmosis, primary lymphoma, and progressive multifocal leukoencephalopathy (PML).

14. A fluorine-18 fluorodeoxyglucose (18-FDG) PET scan. Lymphomas have a higher uptake than toxoplasmosis or PML.

15. A 2-week trial of toxoplasmosis medications, pyrimethamine and sulfadiazine.

16. An Epstein-Barr test of tumor cells of the CNS will be positive in AIDS lymphoma of the CNS in some cases. Primary CNS lymphoma (PCNSL) is also known as high-grade non-Hodgkin B cell lymphoma and is seen in immunocompromised patients. Chemotherapy with methotrexate can improve survival in both AIDS and non-AIDS patients. Radiotherapy is also of some benefit. Because PCNSL appears radiologically similar to toxoplasmosis, a trial of antiprotozoal medications should be done empirically before other more-invasive procedures are planned.

17. B cell origin.

18. Vacuolar myelopathy. It is prudent to obtain an MRI to exclude a mass lesion before giving this diagnosis because vacuolar myelopathy is a diagnosis of exclusion.

19. It mainly involves the posterior and lateral columns of the thoracic spinal cord.

MCQs answers

1. D. Toxoplasma gondii.
Fungal abscesses develop with unusual frequency in patients with AIDS, but T. gondii, an obligate intracellular parasite, is considerably more common than fungi as the cause of abscess formation. The fungi that do produce abscesses in persons with AIDS are most often Cryptococcus, Candida, Mucor, and Aspergillus. Mycobacteria and atypical mycobacteria are also common causes of abscess formation in some populations.

2. C. Primary lymphoma.
Kaposi's sarcoma is unusually common in patients with AIDS, but it is rarely metastatic to the brain. Metastatic lymphomas producing meningeal lymphomatosis are not especially rare in the general population, but primary lymphomas (that is, lymphomas apparently arising in the CNS) were rare before the AIDS epidemic. The primary brain lymphoma usually presents as a solitary mass and can occur anywhere in the brain, but it does have a predilection for the periventricular structures.

3. C. Cryptococcal meningitis.
India ink positive stain is highly suggestive of cryptococcal meningitis.

4. E. Progressive multifocal leukoencephalopathy (PML).
PML is an opportunistic infection caused by JC virus. Multifocal, confluent signal abnormality related to demyelination is the most typical neuroimaging characteristic. It usually occurs in late stages of HIV infection, and the prognosis is poor, with no known effective long-term treatment. CMV also tends to be pathogenic in patients with low CD4 counts, notoriously causing ventriculitis. Primary central nervous system lymphoma and cerebral toxoplasmosis can appear as mass lesions, often with enhancement.

5. E. Cryptococcus neoformans.

The subacute presentation, pattern of enhancement of the basilar cisterns, cranial nerve palsy, and underlying immunocompromised state are all indicative of infection with Cryptococcus neoformans. This is treated with amphotericin B and flucytosine; the risk of relapse can be significantly reduced by prophylaxis with fluconazole.

6. B. Toxoplasmosis.
The most common opportunistic infection in patients with AIDS is toxoplasmosis, and the most common fungal infection is cryptococcosis.

7. D. Primary CNS lymphoma.
Primary intracranial lymphomas occur with increased frequency in patients who are immunocompromised, such as recipients of organ transplants and patients with AIDS.

8. A. Cerebral toxoplasmosis.
A few clues to the diagnosis:
1) Young patients with unexplained headache, fever, seizure, neurological deficit and increased intracranial pressure.
2) CT brain shows ring enhancing lesion after IV contrast (30% unilocular but majority multilocular).
3) 75% at basal ganglia, occurs when CD4 less than 100.

9. A. JC virus.
Progressive multifocal leukoencephalopathy (PML) is an opportunistic infection caused by a polyomavirus called the JC virus (JCV). It occurs in HIV-infected patients and other immunocompromised hosts. It is characterized by patchy areas of demyelination in the white matter of the cerebral hemispheres. The clinical presentation is diverse, reflects the scattered areas of demyelination, and progresses rapidly. Motor weakness, personality changes, dementia, ataxia, and cortical blindness occur and may culminate in coma. Survival after diagnosis is often less than 6 months.

The JC virus or John Cunningham virus (JCV) is a type of human polyomavirus (formerly known as papovavirus) and is genetically similar to BK virus and SV40. It was discovered in 1971 and named after the two initials of a patient with progressive multifocal leukoencephalopathy (PML). The virus causes PML and other diseases only in cases of immunodeficiency, as in AIDS or during treatment with drugs intended to induce a state of immunosuppression

(e.g. organ transplant patients).

10. A. Dementia.
Dementia, characterized by cognitive dysfunction, behavioral disturbance, and motor impairment, occurs in one third to two thirds of patients with AIDS. Myelopathy occurs in less than 10%, inflammatory polymyositis in 20 %, toxoplasmosis in 10 %, and lymphoma in 5% of AIDS patients.

11. E. Cryptococcal infection.
This man was HIV positive, expanding the possible etiologies for his headache in association with multiple contrast-enhancing brain lesions. An infectious or neoplastic etiology should be considered in the evaluation of headache in an untreated HIV-infected individual, especially with low CD4 counts and discernible viral load. Embolic infarcts could result from bacterial endocarditis, arteritis, cocaine-induced vasospasm, or injected drug contaminants. Cerebral abscesses from multiple pathogens may be seen with HIV infection with intravenous drug abuse. Cerebral mass lesions, which may be single, but are more often multiple, are common with toxoplasmosis, cytomegalovirus infection, and CNS lymphoma. Cryptococcal infection is generally an encephalomeningitis and rarely presents with multifocal mass lesions or cryptococcomas.

12. B. Epstein-Barr virus.
Primary central nervous system (CNS) lymphoma develops in approximately 2% of patients with HIV infection, usually late in the course of infection. Unlike the lesions of immunocompetent patients with primary CNS lymphoma, the lesions in HIV-infected patients often manifest central necrosis with a ring-enhancing appearance that is difficult to distinguish from CNS infections such as toxoplasmosis. Nearly all primary CNS lymphomas in HIV infected individuals contain Epstein-Barr viral genome. Cerebrospinal fluid polymerase chain reaction is typically negative for Epstein-Barr virus. In the presence of reduced T-cell function, the Epstein-Barr-infected B cells become immortalized and are driven toward a monoclonal malignant B-cell population. Epstein-Barr viral genome is rare in primary CNS lymphoma in immunocompetent patients. Patients with primary CNS lymphoma may be treated with high-dose methotrexate and brain radiation. Unfortunately, treatment of primary CNS lymphoma in patients with HIV is rarely successful, and most patients die within 6 months of diagnosis (usually from complications of other opportunistic infections). Cytomegalovirus, herpes zoster, and herpes simplex may infect the

brain of an immunocompromised patient, but none is associated with CNS lymphoma.

13. C. Cerebral toxoplasmosis.

14. E. Progressive multifocal leukoencephalopathy (PML).
PML is a relentlessly destructive disease caused by JC virus, which principally affects the white matter in brain. Typical lesions appear as widely disseminated discrete foci of demyelination near the gray-white junction in the cerebral hemispheres and the brainstem. Most commonly, PML is a terminal complication in immunosuppressed patients, such as those treated for cancer or lupus erythematosus, organ transplant patients, and persons with AIDS. Gaucher disease (choice A), adrenoleukodystrophy (choice B) and metachromatic leukodystrophy (choice C) are caused by inborn errors of metabolism. Subacute sclerosing panencephalitis (choice D) is a chronic, lethal, viral infection of the brain caused by measles virus.

15. D. Cryptococcus neoformans.
Cryptococcal meningitis is an indolent infection in which the virulence of the causative agent marginally exceeds the resistance of the host. In most cases, it acts opportunistically in immunocompromised persons (e.g., patients who have AIDS). The organisms vary in size from 5 to 15 mm in diameter and reproduce by budding. When a drop of contaminated CSF is mixed with India ink, microscopic examination shows a clear halo about the encapsulated organism. The tissue response to C. neoformans in the meninges is typically sparse. The other choices are not typical CNS infections in patients with AIDS.

16. D. Release of neurotoxic cytokines from macrophages.
In most patients with AIDS encephalopathy, the disease is attributable to an active infection of the CNS by the virus itself. Macrophages and microglial cells in the CNS are productively infected by HIV-1. Although neurons and astrocytes may interact with the virus, they do not seem to be infected but are injured indirectly by cytokines or other neurotoxic factors released by macrophages. Dementia is the most common clinical manifestation of AIDS encephalopathy, which ranges from mild to severe cognitive impairment, with paralysis and loss of sensory functions. The other choices are not typical complications of AIDS.

17. D. Pneumocystic carinii pneumonia.

The risk of various opportunistic infections can be categorized on the basis of the patient's CD4+ T cell count. A CD4+ T cell count of less than 350 cells/ mm^3 places the patient at risk for Mycobacterium tuberculosis infection. When the CD4+ T cell count is less than 200 cells/mm^3, there is a dramatic increase in risk of P. carinii pneumonia; Kaposi sarcoma is also seen in patients with this level of immunosuppression. For patients whose CD4+ T cell counts are less than 100 cells/mm^3, CNS toxoplasmosis and cryptococcal meningitis are considerations. With very severe immunosuppression (i.e. CD4+ T cell counts of less than 50 cells/mm^3), other infections and malignancies should be considered; these include disseminated M. avium infection, cytomegalovirus retinitis, CNS lymphoma, and progressive multifocal leukoencephalopathy. This patient should receive prophylaxis for P. carinii pneumonia with trimethoprim-sulfamethoxazole.

18. C. Stage 2.

In 1988, Price and colleagues developed the following clinical staging of the severity of HIV-associated dementia:

• Stage 0: normal mental and motor function.

• Stage 0.5 (equivocal subclinical): absent, minimal, or equivocal symptoms without impairment of work or capacity to perform activities of daily life. Mild signs such as snout response, slowed ocular, or extremity movements may be present. Gait and strength are normal.

• Stage 1 (mild severity): ability to perform all but the most demanding activities of daily life with unequivocal evidence of functional intellectual or motor impairment. The patient can walk without assistance.

• Stage 2 (moderate severity): ability to perform basic activities of self-care but cannot work or maintain the more demanding aspects of daily life. The patient may ambulate independently.

• Stage 3 (severe disability): major intellectual or motor incapacity.

• Stage 4: nearly vegetative status.

19. B. Severe attention deficit.

Neuropsychological testing adds to the neurological evaluation of suspected HIV dementia by virtue of being sensitive to mild or early symptoms of HIV-related cognitive impairment. In addition to quantifying the severity of any cognitive symptoms, it can also provide information regarding the overall pattern of cognitive impairment. Attention, calculation, and language are not usually affected in HIV dementia in its initial stage, fitting with the subcortical

pattern of involvement. Impaired memory (verbal and nonverbal), impaired manipulation of acquired knowledge, memory loss selective for impaired retrieval, and deficits in psychomotor speed are characteristic of HIV dementia and are typically more severe than deficits in other cognitive domains.

20. A. Distal symmetric polyneuropathy.
Distal symmetric polyneuropathy is the most common form of peripheral neuropathy in HIV-infected patients. The proposed mechanisms of this neuropathy include direct HIV infection, injury from cytokine effects, metabolic abnormalities, or the medications used to control the HIV infection.

21. D. Start empirical antitoxoplasmosis treatment.
The presence of a ring-enhancing mass on CT scan of the head in an HIV patient should raise the possibility of CNS toxoplasmosis. The diagnostic workup should include a toxoplasmosis antibody titer of the serum and the CSF; also, if possible, a thallium SPECT study should be done to rule out a hyperactive lesion (more suggestive of lymphoma). The most appropriate therapeutic approach is to start the patient on antitoxoplasmosis therapy for 2 weeks and thereafter assess the patient clinically and radiologically. In case of improvement, the patient should be maintained on prophylactic antibiotics for life after completion of the induction therapy. If there is no improvement, stereotactic biopsy should be considered. The use of corticosteroids has not been shown to be beneficial for the treatment of CNS toxoplasmosis and may delay the diagnosis of primary CNS lymphoma. It should be used with caution and rapidly tapered.

22. A. Impaired cognition.
The most frequent presenting symptom of central nervous lymphoma is cognitive or mental status impairment, which is seen in 60% of cases. Hemiparesis or aphasia is seen in 35% of cases. Seizures are seen in 15% of cases at presentation. Cranial nerve palsy is seen in only 10% of cases at presentation.

23. D. Toxoplasmosis.
Toxoplasmosis is the most common cause of an intracranial space-occupying mass in AIDS patients, followed by primary CNS lymphoma. Toxoplasmosis lesions are most frequently found in the cerebral cortex, basal ganglia, and gray–white matter junction.

24. A. Cotton-wool spots.
The most frequent retinal lesion in AIDS patients is cotton-wool spots, seen in 75% of these cases. It is a buildup of exoplasmic material at the site of a nerve fiber layer infarct. When these spots are coupled with hemorrhage or capillary abnormalities, it is called AIDS retinopathy. Axonal loss in the optic nerve has been estimated at 40% in patients dying from AIDS in the absence of opportunistic infection of the retina. CMV retinitis may affect 25% to 35% of patients with AIDS. Toxoplasmosis retinitis, optic atrophy, and optic edema are less frequently seen.

25. B. Staphylococcus.
Staphylococcus aureus has been traditionally and remains the main pathogen in epidural abscess, accounting for over 60% of the isolates. Other gram-positive pathogens that may cause epidural abscess less frequently include Staphylococcus epidermidis, streptococci (alpha and beta hemolytic), and anaerobes. Gram-negative pathogens are increasing in frequency (second to Staphylococcus), perhaps reflecting an increasing proportion of iatrogenic infections. Myco-bacterium tuberculosis and pathogenic fungi also account for a significant percentage of cases.

26. D. Sulfadiazine and pyrimethamine.
Sulfadiazine and pyrimethamine is proper treatment for *T. gondii* infection. Neurosurgical removal of the lesions is not indicated. Oral fluconazole is a treatment for fungal infections. Intravenous acyclovir is used to treat herpes encephalitis. Thiabendazole is used to treat helminth infections.

27. B. *Toxoplasma gondii.*
Fungal abscesses develop with unusual frequency in patients with AIDS, but *T. gondii,* an obligate intracellular parasite, is considerably more common than fungi as the cause of abscess formation. The fungi that do produce abscesses in persons with AIDS are most often *Cryptococcus, Candida, Mucor,* and *Aspergillus.* Mycobacteria and atypical mycobacteria are also common causes of abscess formation in some populations.

28. E. Microglial nodules.
The microglial nodules occurring with HIV are associated with syncytial cells in the brain and spinal cord, a cell type not typically seen with cytomegalovirus

(CMV) encephalitis. Cytomegalovirus is a common CNS opportunistic agent in patients with AIDS. With HIV infection, the microglial nodules are distributed around blood vessels throughout the brain. With CMV, the nodules are more characteristically subpial and subependymal.

29. **A.** Tenofovir, emtricitabine, and raltegravir.

The risk of acquiring HIV from a needle stick is 0.3%, and the risk from mucosal contact is 0.09%. Even though the risk is low, the risk can be eliminated with postexposure prophylaxis (PEP). Currently, a three-drug regimen is recommended, and the combination of tenofovir-emtricitabine (individually or as a combination pill) and raltegravir has a low risk of adverse effcets. (B) The use of tenofovir-emtricitabine alone is thought to be less effctive than the three-drug regimen. (C) Abacavir has a high rate of life-threatening hypersensitivity reactions, so the risk would outweigh the benefi. (D) Although the patient can refuse PEP if he desires, reassurance would not be appropriate since there is a small chance that he may acquire HIV.

30. A. Progressive multifocal leukoencephalopathy (PML).
The patient in this question is likely suffering from PML, an opportunistic infection seen in immunocompromised patients that is caused by the JC virus (a human polyomavirus that has an unknown mode of transmission). This disease typically involves cortical white matter and does not produce a mass effect. Symptoms typically include hemiparesis, speech disturbances, and vision and gait changes. CT scan shows several nonenhancing cerebral demyelinating white matter lesions without any mass effect. Thre is no treatment for PML and the prognosis is poor. (B) Primary CNS lymphoma is the second most common cause of mass lesions (following toxoplasmosis) in HIV-infected patients. This involves a ring-enhancing lesion that is solitary and typically periventricular. The diagnosis is confirmed by EBV DNA in the cerebrospinal fluid (CSF). (C) AIDS dementia complex will demonstrate cortical atrophy and ventricular enlargement. (D) Toxoplasmosis is the most common ringenhancing mass lesion in HIV-infected patients. Lesions are multiple, spherical, and typically located in the basal ganglia. This is unlikely given that the patient is currently taking TMP–SMX.

31. C. Trimethoprim-sulfamethoxazole prophylaxis.

Encephalitis is the most common manifestation of *Toxoplasma gondii,* and this organism may reactivate to form CNS abscesses when the CD4 count drops

below 100 mm^3. Suspect this diagnosis in HIV patients who are not taking prophylactic antibiotics and who have multiple ring-enhancing lesions on brain imaging. The acute treatment is pyrimethamine-sulfadiazine, and patients should receive trimethoprim-sulfamethoxazole prophylaxis until they have suffient immune reconstitution on antiretroviral medications. Other important cutoff to remember for antibiotic prophylaxis of opportunistic infections are trimethoprim-sulfamethoxazole for PCP prevention when the CD4 count is <200/mm^3, and azithromycin for mycobacterium avium complex (MAC) prevention when the CD4 count is <50/mm^3. If the CD4 count rises above these thresholds for >3 to 6 months after antiretrovirals are started, antibiotic prophylaxis can be stopped.
(A) Ths patient's CD4 count is >50/mm^3, so azithromycin should not be started prophylactically. (B) HIV patients are at an increased risk of multiple cancers, including CNS lymphoma. As opposed to multiple ring-enhancing lesions on brain imaging with toxoplasmosis, CNS lymphoma will typically present as a solitary lesion that may ring-enhance, although whole tumor enhancement is more common. Also look for a positive PCR test for EBV in a CSF sample. (E) Another important item on the diffrential diagnosis is progressive multifocal leukoencephalopathy (PML) due to polyomavirus JC (JC virus), which presents with multiple lesions that do not ring-enhance. It has a very poor prognosis and there is no treatment or specific preventive strategies other than antiretrovirals. (D) Ths is the treatment for latent TB, which may cause meningitis. Patients with HIV should be screened for latent TB, bit there is no prophylactic treatment that is currently recommended to prevent TB infection.

32. C. Decadron (dexamethasone) 10 mg i.v.
The contrast CT scan reveals two ring-enhancing lesions with marked cerebral edema, located deep within the brain. Radiographically these areas appear consistent with brain abscesses most likely due to toxoplasmosis. Although most patients with intact mental status can be treated with anti-toxoplasmosis medication, the presence of severe vasogenic edema and depressed level of consciousness warrants immediate treatment with high dose corticosteroids. Mannitol can be given urgently to control generalized increased ICP but usually at starting doses of 1 g/kg with the usual initial dose given as 100 g i.v.

33. 1-E, 2-C, 3-C, 4-A, 5-B, 6-F, 7-D.

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