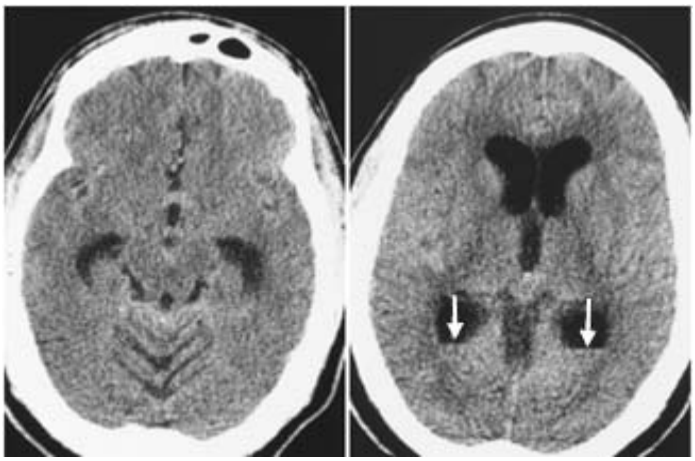
EANS/UEMS European examination in neurosurgery

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

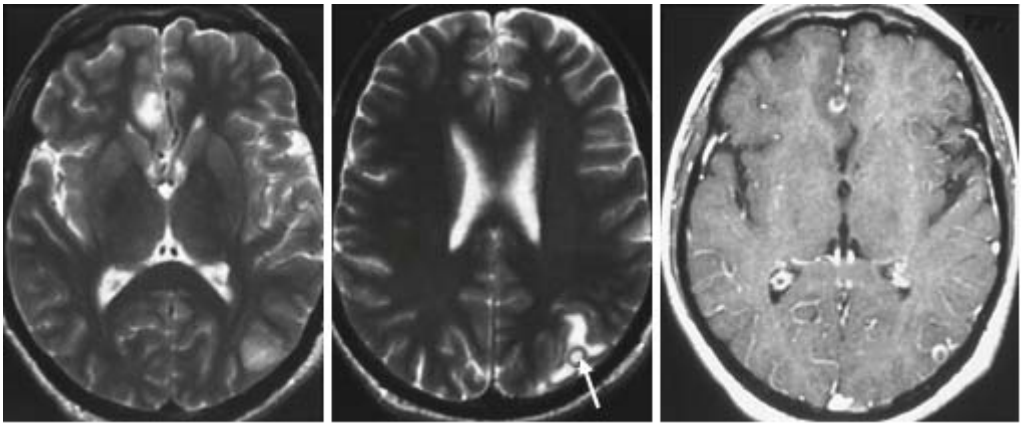
CASE HISTORIES IN NEUROINFECTIONS

Case 1



1. What are the pertinent imaging findings?
2. What are common secondary complications related to ventricloperitoneal shunts?
3. What infectious agents have a propensity to cause choroid plexitis?
4. What are common complications of meningitis?

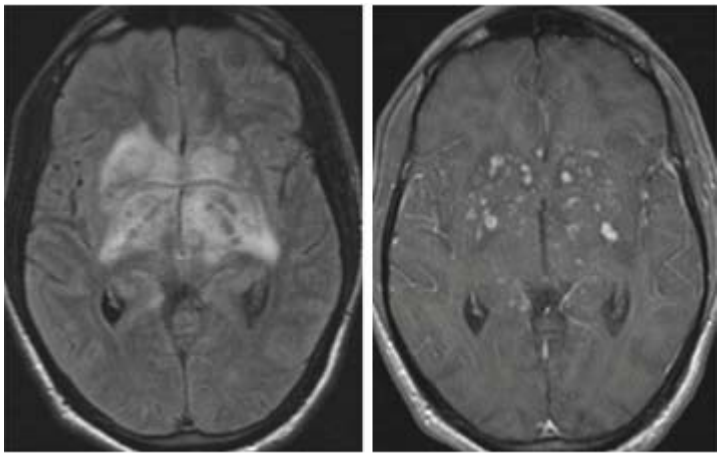
Case 2



1. What is the differential diagnosis in these cases?
2. What is the most likely diagnosis in these cases?

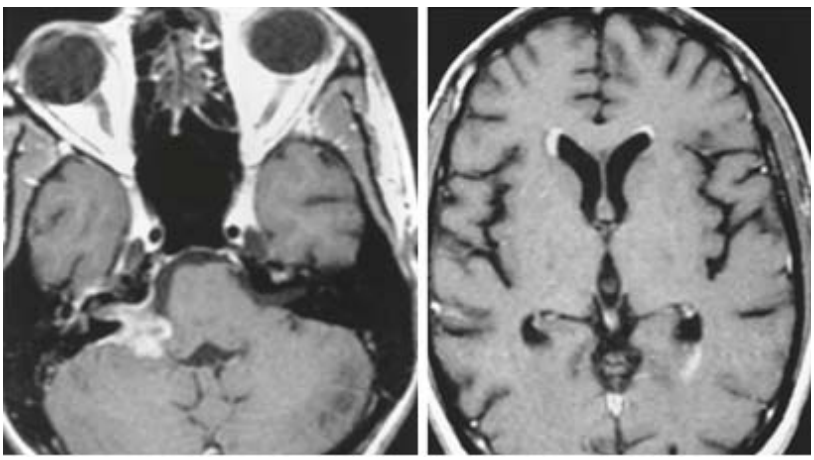
3. What is the most common clinical presentation of patients with this entity?
4. What is the most common location of intraventricular neurocysticercosis?
5. What is the most common parasitic infection of the CNS?
6. At which point in the Taenia solium life cycle do the neurological effects become apparent?
7. What is the mechanism by which the cysts may cause sudden death?

Case 3



1. What fungal infections predominantly infect immunocompromised patients?
2. What fungal infections may occur in both immunocompetent and immunocompromised patients?
3. Why is there a lower incidence of both hydrocephalus and enhancement of parenchymal lesions in immunocompromised patients with CNS infections compared with immunocompetent patients with the same infections?
4. What laboratory studies may be performed to diagnose cryptococcosis?

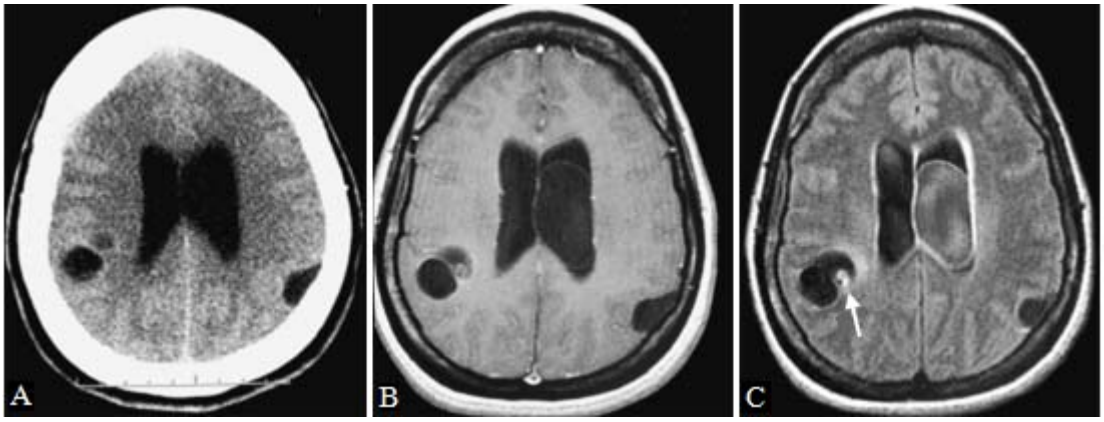
Case 4



1. What is the differential diagnosis for the findings identified on imaging?
2. What imaging findings are typical of CNS involvement in patients infected with cytomegalovirus (CMV) in utero?
3. What is the most neoplastic common cause of ependymal enhancement in the setting of AIDs infection?
4. What were the patient's acute symptoms at clinical presentation?

Case 5

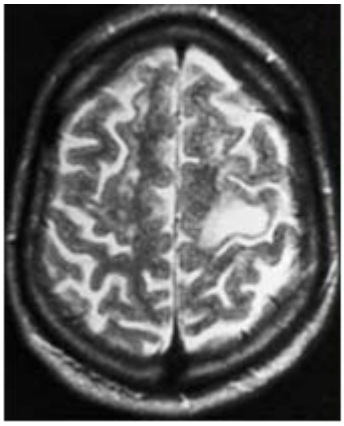
A 39-year-old Honduran female with a long history of mild, chronic headaches presents with a generalized tonic-clonic seizure. Neurologic examination was normal. Nonenhanced CT (A), T1- post-gadolinium MRI (B) and FLAIR MRI (C) were obtained.



1. What are the findings?
2. What is the likely diagnosis?

Case 6

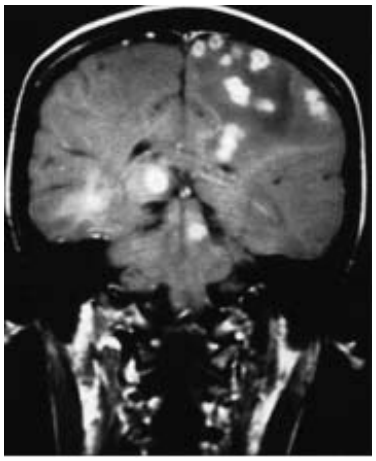
A 32-year-old homosexual male presents with a 5-week history of progressive weakness of the right arm and a 2-week history of language disturbance. On examination, he is apyrexial and general examination is normal apart from some white mucosal lesions intraorally. Neurologic examination reveals a mild expressive dysphasia and a flaccid right arm with MRC grade 3 power proximally and grade 2 distally. The MRI is shown.




1. What blood tests should be performed?
2. What is the differential diagnosis of the lesions on MRI?
3. What other investigations may be performed to confirm the diagnosis?
4. What is progressive multifocal leukoencephalopathy (PML)?

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

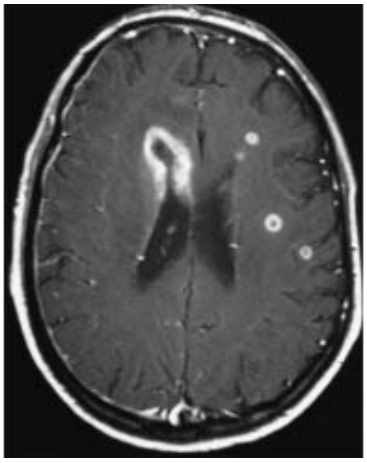
Case 7



A 26-year-old Indian female presented with a 3-month history of malaise, headache and a slowly progressive right-sided hemiparesis. A coronal gadolinium-enhanced MRI is shown.

1. What abnormalities are seen?
2. What is the most likely diagnosis?
3. What other features may be present with this diagnosis?
4. How should this patient be treated?
5. List other possible causes of the MRI appearances.

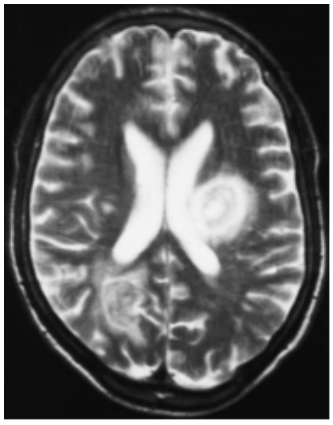
Case 8



This patient has a renal transplant, is on cyclosporin and is immunocompromised. The acute illness of confusion and fever has evolved over 1 week. The MRI is shown.

1. What is the likely diagnosis?
2. What is the treatment?
3. What is the prognosis?

Case 9

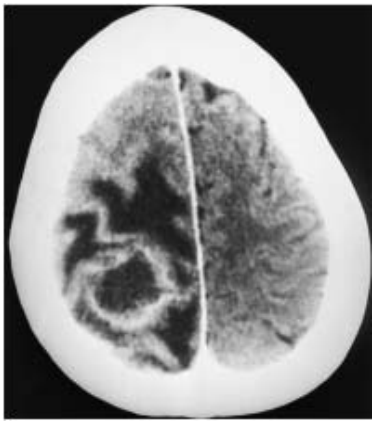


A 37-year-old HIV positive male presents with a 1-week history of headache and progressive left-sided weakness. On examination he is alert and orientated. He has a left homonymous hemianopia and pyramidal weakness affecting the left face, arm and leg with hyperreflexia and bilateral extensor plantar responses.

1. What is the differential diagnosis of the abnormality on the T2 MRI brain-scan ?
2. What blood tests and what other investigations may help in making a diagnosis?
3. How should he be managed?
4. What are the most common CNS mass lesions found in HIV+/AIDS patients?
5. For which of these is brain biopsy indicated?
6. What is the most common opportunistic infection in AIDS?

A. Herpes zoster
B. Toxoplasmosis
C. Cryptococcosis
D. Tuberculosis (TB)
E. Cytomegalovirus (CMV)

Case 10

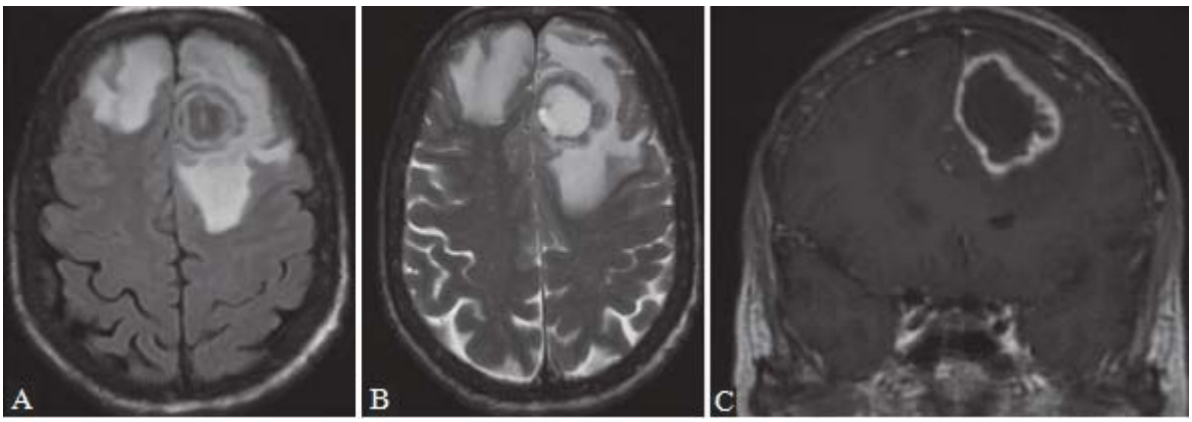


A 42-year-old female with relapsed stage IVB non-Hodgkin's lymphoma was treated with a stem cell transplant 2 months ago. She then developed focal seizures and a weakness of her left arm and increasing lethargy. She was apyrexial and did not complain of headache. A CT brain scan was performed.

1. What is the differential diagnosis?
2. What are the principles of management?

Case 11

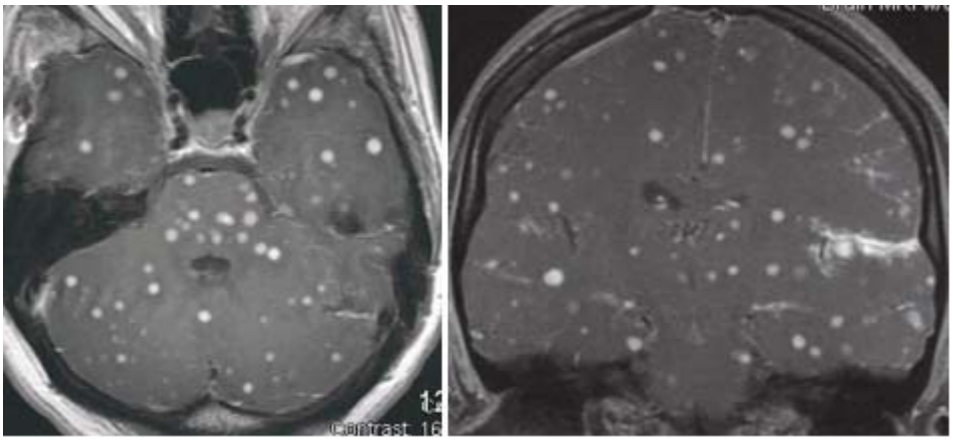
A 59-year-old female on chronic immunosuppression with mycophenolate mofetil and tacrolimus for kidney and pancreas transplant performed 7 months prior was admitted with decreased level of consciousness.



1. Describe the findings on the imaging study.
2. What is the differential diagnosis?
3. What is your diagnosis?
4. When should MRI or CT of the brain be repeated after the initial diagnosis?
5. What the treating physician needs to know?

Case 12

A 19-year-old female with weight loss, slurred speech, behavioral changes, hypersomnolence and confusion.



1. Describe the findings on the imaging study.
2. What is the differential diagnosis?
3. What is your diagnosis?
4. How often do we have to repeat the MRI of the brain during treatment?
5. What the treating physician needs to know?

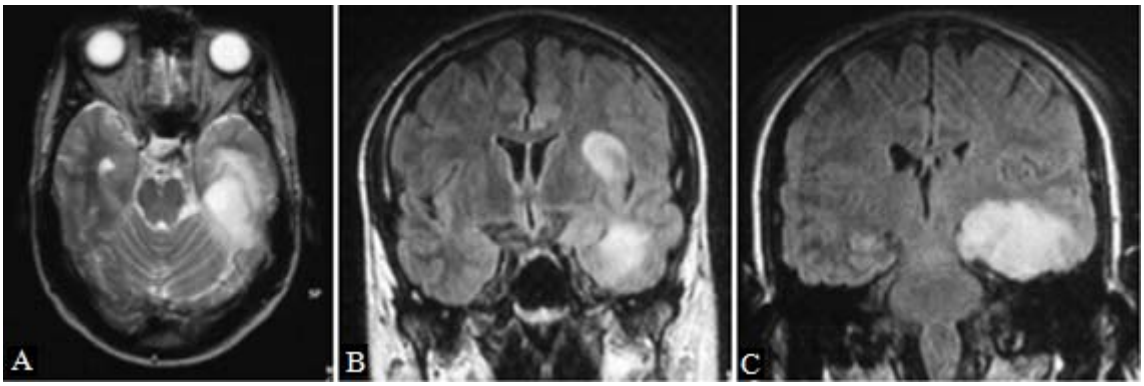
Case 13

A 29-year-old man presented with a 10-day history of sudden onset generalized headache and 2 days of depressed mood and apathy. There was no past medical history of note and he was not taking any medication. On examination, he was afebrile, the GCS was 15/15 and he was not confused (MMSE 30/30). General systems and neurological examination were unremarkable.

Investigations showed:
Hb 13g/dL, WCC 13 × 10^9/L, platelets 200 × 10^9/L.
CRP 30mg/L.
U&E and LFT normal.
CT brain: normal.
LP: normal CSF opening pressure, protein 0.8g/L, cell count 15/mm^3 (12 mononuclear cells, 3 polymorphs), glucose 2mmol/L (blood glucose 5.6mmol/L), no organisms.

Over the course of the next day he became increasingly confused and the plantar responses became extensor. On examination, the temperature was 38.7°C, blood pressure 90/60 mmHg, he was intermittently unresponsive, restless,

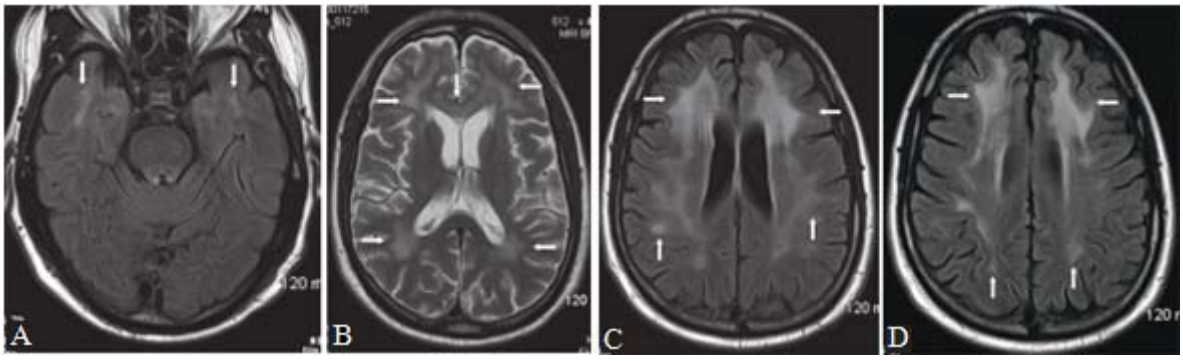
confused, and unable to follow commands, and there was a right-sided ptosis and bilateral extensor plantars. An MRI scan was performed:



1. Give the differential diagnosis you would have considered when the patient first presented, prior to the initial investigation results.
2. Describe the findings on the MRI scan.
3. What is the diagnosis and how would you confirm it?
4. How would you treat this patient?
5. What is the prognosis, and how has this changed over recent decades?

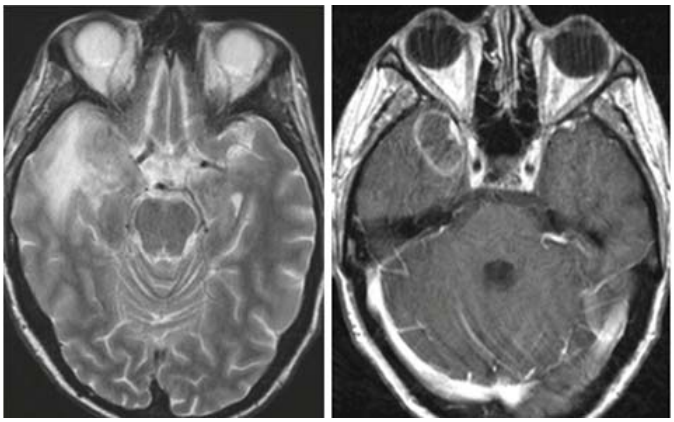
Case 14

A 54-year-old male with AIDS on antiretrovirals presenting with tremors, jerking movement of limbs, and dropping objects.



1. Describe the findings on the imaging study.
2. What is the differential diagnosis?
3. What is your diagnosis?
4. What are the risk factors for HIV encephalopathy (HIVE)?
5. What the treating physician needs to know?

Case 15



1. In differentiating a necrotic brain neoplasm from infection or abscess, which is typically associated with restricted diffusion?
2. How is Toxoplasma gondii infection transmitted?
3. In infants congenitally infected with toxoplasmosis, what are the typical neuroimaging findings?
4. In differentiating toxoplasmosis from primary CNS lymphoma, which demonstrates increased uptake on thallium-201 scintigraphy?

Answers

Case 1

Pyogenic ventriculitis with acute hydrocephalus

1. Acute hydrocephalus and pus levels layering in the lateral ventricles (arrows).
2. In addition to ventriculitis, other complications include overdrainage resulting in slit ventricle syndrome, subdural hematomas (which are frequently bilateral), and shunt malfunction.
3. Cryptococcus and Nocardia.
4. Subdural empyema, encephalitis, brain abscess, and ventriculitis with acute hydrocephalus, as in this case.

Comment

This case demonstrates acute hydrocephalus and fluid–fluid levels (arrows) within the occipital horns of the lateral ventricles, consistent with ventriculitis complicating pyogenic meningitis. Lumbar puncture yielded pus. Ventriculitis is due to the introduction of infectious organisms into the ependyma or ventricles, and may be secondary to bacteremia, extension of an intraparenchymal abscess, trauma, or surgical instrumentation (especially placement of ventricular shunts). In addition to ventriculitis, other complications of ventriculoperitoneal shunts include overdrainage resulting in slit ventricle syndrome, subdural hematomas (which are frequently bilateral), shunt malfunction, surgery-related complications, and metastases in the setting of neoplasm (such as primitive neuroectodermal tumor).

Approximately 20% of patients with pyogenic bacterial meningitis will have complications necessitating neurosurgical intervention (surgery or a ventriculostomy), even after antibiotic therapy. Such complications include subdural empyema; parenchymal brain abscess; ventriculitis with hydrocephalus, as in this case; and encephalitis. The development of such complications may correlate with inadequate treatment or with the duration of meningitis before the initiation of therapy.

Cytomegalovirus (CMV) ventriculitis is unusual, but may occur in patients with HIV infection. Most HIV-infected patients with CMV ventriculitis have already been diagnosed with an AIDS-defining condition. Pathologic findings include inflammation of the ependyma and periventricular structures, as well as ependymal necrosis with CMV intranuclear inclusion bodies. The differential

diagnosis in this patient population includes non-Hodgkin’s lymphoma.

Case 2

Cysticercosis of the Central Nervous System

1. The differential diagnosis of multiple superficial (cortical and gray–white matter junction) lesions includes a spectrum of infectious and inflammatory processes (eg, septic emboli, bacterial abscesses, cysticercosis) and metastatic disease.
2. Cysticercosis.
3. Seizures, seen in 30% to 90% of symptomatic patients. Symptoms are dependent on the stages of infestation, as well as the sites of parasitic CNS involvement. Initial cerebral infection and the mature cystic phase of infection, when the larvae are alive, are frequently asymptomatic. Patients may be most symptomatic as the larvae die because the larvae incite a significant inflammatory reaction.
4. The fourth ventricle.
5. Neurocysticercosis.
6. When the cystic larvae die in the brain.
7. When cysts in the subarachnoid space (basal cisterns and intraventricular) cause sudden obstruction of CSF outflow.

Comment

Cysticercosis is the most common parasitic infection of the CNS. It usually involves the intracranial compartment, and it may very, very, very rarely involve the spinal contents.
Cysticercosis is endemic to Central and South America, parts of Asia, Mexico, Africa, and India. The pork tapeworm (Taenia solium) is the causative agent. Humans may become the definitive host (the parasite sexually reproduces) by eating inadequately cooked pork that harbors the larvae of the pork tapeworm (cysticerci). These larvae develop into tapeworms in the small intestine that release eggs that pass into the stool. If humans ingest good or water contaminated by these ova, they may serve as an intermediate host. In the stomach, the ova release oncospheres (primary larvae), which enter the bloodstream through the gastrointestinal mucosa. These primary larvae may deposit within muscle and subcutaneous tissue, although they have a propensity to infect the CNS.

There are multiple patterns of neurocysticercosis, including the parenchymal pattern (the larvae penetrate directly into the brain), the intraventricular pattern (involves the ependyma or choroid plexus), and the subarachnoid pattern (involves the meninges). In mixed neurocysticercosis, there is involvement of the parenchyma, ventricles, or subarachnoid spaces. Patients with parenchymal involvement may present with seizures and neurologic signs (confusion, dementia, paresis, paraesthesias, visual disturbances). Intraventricular involvement may be symptomatic if there is obstructive hydrocephalus, and meningeal involvement may result in communicating hydrocephalus.

There is a spectrum of radiologic appearances, depending on the stage of disease; however, imaging findings are frequently characteristic. In the initial stages of cerebral infection, the larvae result in small, edematous lesions that are hypodense on CT and hyperintense on T2W images. The cysticerci then develop into cyst that range in size from millimeters to centimeters and contain a scolex. There may be mild surrounding edema in the brain. On the more cephalad T2W image, the left parietal lobe lesion has a characteristic appearance, with a defined capsule that has a hypointense rim and a small (1 mm), hypointense focus (arrow), representing the scolex. As the cysts die, there is an intense inflammatory reaction in the adjacent brain parenchyma that may result in prominent edema and mass effect. At this time that patients may be most symptomatic, presenting with seizures or focal neurologic signs. After years of infestation, the cysts finally collapse and often calcify. Rim enhancement has been described in as many as 38% of calcified lesions.

Case 3

Cryptococcosis

1. Candida, Aspergillus, and Mucor.
2. Cryptococcus, Coccidioides, and Histoplasma.
3. This likely reflects the inability of these patients to mount significant inflammatory and cell-mediated immune responses.
4. The diagnosis of cryptococcosis may be established by analysis of the CSF with India ink, detection of cryptococcal antigen, or positive findings on fungal cultures.

Comment

This case shows high signal intensity in the bilateral basal ganglia and thalami which is somewhat bilaterally symmetric. Buried within the flair hyperintensity are small focal regions of hypointensity within the deep gray matter with associated enhancement on the gadolinium enhanced T1-weighted image. In addition, to a lesser degree regions of parenchymal abnormality with enhancement at the gray-white matter interface in the cerebrum were also present as was mild communicating hydrocephalus [images not shown].

In this case enhancement is present. However, in patients with human immunodeficiency virus (HIV) infection, there can be a paucity of enhancement related to the inability to mount an inflammatory reaction which is related to the severity of the immunodeficient state of the patient. The CT and MR imaging findings are often nonspecific and one may not be able to distinguish among the various fungal infections, as well as toxoplasmosis and tuberculosis. Lymphoma in the setting of AIDS must also be considered.

Fungal infection in the CNS results in granulomatous changes that may affect the intracranial vasculature, meninges, and/or brain parenchyma. In patients width cryptococcosis, CT and MR imaging may be normal. Alternatively, a spectrum of imaging findings may occur, including dilated perivascular spaces; parenchymal cryptococcomas (more common in the deep gray matter of the basal ganglia and thalami than in the cerebral cortex); and, less commonly, miliary disease with parenchymal, leptomeningeal, and intraventricular nodules.

When infection spreads along the perivascular (Virchow-Robin) spaces that accompany perforating arteries, these perivascular spaces may become distended with mucoid, gelatinous material that is made by the organism’s capsule. Large accumulations of organisms and gelatinous material have been referred to as gelatinous pseudocysts. The diagnosis of CNS cryptococcosis may be established by analysis of the CSF with Indian ink, detection of cryptococcal antigen, and/or positive fungal cultures.

Case 4

Cytomegalovirus meningitis and ependymitis in a patient with AIDS

1. Infection (ventriculitis, ependymitis) and neoplasms (lymphoma or seeding from a systemic or primary brain neoplasm).

2. Bilateral ventricular subependymal calcification, ventricular enlargement, periventricular hypodensity on CT or hyperintensity on T2W MR imaging, atrophy, and migrational anomalies (pachygyria or polymicrogyria).
3. Lymphoma.
4. Sensorineural hearing loss and vertigo.

Comment

Cytomegalovirus is present in the latent form in the majority of the American population. Reactivation usually results in a subclinical or mild flu-like syndrome. In immunocompromised patients, reactivation can result in disseminated infection, usually involving the respiratory and gastrointestinal tracts; however, rarely, it can infect the nervous system. In the CNS, CMV may cause meningoencephalitis and ependymitis. Symptoms may be acute or chronic, developing over months. Patients may have fever, altered mental status, and progressive cognitive decline. Patients may also present with cranial neuropathies (as in this case). CMV polymerase chain reaction (PCR) in the CSF is sensitive and specific for the diagnosis of AIDS-related CMV infection of the CNS.

However, conventional CSF findings and neuroimaging may not adequately assess the severity of CNS CMV disease, as demonstrated at autopsy. Magnetic resonance imaging is the diagnostic study of choice in assessing immunocompromised patients suspected of having CNS infection. Imaging may show atrophy; high signal intensity in the periventricular white matter, typically not associated with significant mass effect; and retinitis (frequently seen in the AIDS population) in patients with CMV infection. Although patients with CNS infection may also have ependymal and subependymal involvement, associated imaging findings often are not present. When present, T2W signal abnormality and enhancement along the ependyma are valuable in establishing this diagnosis. Currently, the most common cause of ependymal enhancement in the setting of AIDS is lymphoma.

Case 5

CNS cysticercosis

1. The CT (A) shows enlarged lateral ventricles and several intraparenchymal and subarachnoid cysts without surrounding edema. The MR images (B, C) show an intraventricular thin-walled cyst, two parenchymal cysts at the right

parietal gray–white junction, and a left parietal subarachnoid cyst. One of the parietal cysts contains an enhancing serpiginous nodule (arrow).

2. The constellation of intraparenchymal, intraventricular, and subarachnoid thin-walled cysts in a Central American patient presenting with seizure indicates CNS cysticercosis in its vesicular form. The visualization of an enhancing intracyst nodule is diagnostic of the cysticercotic scolex in this setting. Infection of the CNS by the larval stage of the pork tapeworm, Taenia solium, results in formation of intraventricular, intraparenchymal and subarachnoid cysts. The living organism is protected from the immune system and is often asymptomatic for long periods (vesicular stage).

When the larva dies, an inflammatory reaction ensues and seizures or focal neurologic symptoms can occur. At this stage (vesiculo-nodular), peripheral edema and ring-enhancement are commonly seen on CT and MRI. Involuting cysts may show enhancement without edema (granular nodular stage). Involuted cysts eventually calcify (nodular calcified stage). FLAIR images are particularly helpful in demonstrating intraventricular cysts, since intraventricular CSF signal is suppressed whilst proteinaceous fluid remains bright.

Case 6

Progressive multifocal leukoencephalopathy (PML)

1. The white mucosal lesions could be candidiasis which is usually found in patients who are on corticosteroids (oral or inhaled), diabetics, or patients who are immunosuppressed for any reason such as infection with the HIV. An HIV blood test should be performed and if that is positive then a CD4 count and a viral load should be measured in order to obtain an idea about the degree of immunosuppression.

2. The differential diagnosis of such lesions in an HIV infected person includes PML, CMV encephalitis and HIV encephalopathy. The symptomatic lesion shown on MRI does not show mass effect or enhancement with contrast and therefore is unlikely to be due to toxoplasmosis or primary CNS lymphoma. CMV encephalitis usually presents more acutely; patients usually have evidence of CMV disease elsewhere such as a CMV retinitis, and MRI may show a periventriculitis. HIV encephalopathy presents with a subcortical dementia but no focal neurologic signs. MRI shows changes that are much more diffuse.

3. The diagnosis of PML may be confirmed by the detection of the JC virus using PCR. This has a sensitivity of around 80% and a specificity of 95%. A brain biopsy, as performed in this patient, will show the characteristic features of demyelination in association with inclusion bodies within deformed oligodendrocytes and bizarre looking astrocytes.

4. 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).

Case 7

TB

1. Multiple ring enhancing lesions in the cerebral cortices bilaterally (predominantly on the left) and one lesion in the left side of the pons. There is edema associated with the superficial left-sided cerebral lesions with effacement of the sulci and lateral ventricle on the left.

2. The most likely diagnosis is TB (multiple tuberculomas are evident).

3. Other features that may be present are: meningism, hydrocephalus, seizures, pyrexia, weight loss, night sweats, lymphadenopathy/cold abscess, previous or current pulmonary TB, SIADH, Addison’s disease picture secondary to adrenal involvement.

4. (1) Quadruple anti-tuberculous therapy with pyridoxine cover for 3 months and triple therapy continued for 1 year to 18 months. Classically, this would include isoniazid, rifampicin, pyrazinamide and either ethambutol or streptomycin; however, with more prevalent resistance other antibiotics are being increasingly used. The pyridoxine prevents the development of an isoniazid-induced peripheral neuropathy. Ethambutol can cause optic neuropathy and blindness, and regular ophthalmologic reviews are essential while on the drug. (2) Corticosteroids for 3–6 months. There is some controversy over the use of steroids. The symptoms can be exacerbated initially with steroid use.

5. Other possible causes are: cerebral metastases (although edema is usually associated with each lesion); bacterial abscesses, e.g. septicemia/endocarditis; cerebral toxoplasmosis; neurocysticercosis (the scolex of the tapeworm is usually visible in the center and inactive cysts become calcified, which would be black on MRI); cryptoccocoma – this presentation would be unusual. Usually, the picture is of meningitis with microabscess formation.

Case 8

Cerebral aspergillosis

1. The features are classical of cerebral aspergillosis with cerebral and ependymal lesions seen on MRI.
2. Systemic and intrathecal antifungal chemotherapy.
3. The prognosis is extremely poor. Eradication is usually impossible and obstructive hydrocephalus complicates management in many cases.

Case 9

Toxoplasmosis

1. The differential diagnosis in an HIV positive patient with a low CD4 count lies between toxoplasmosis, primary CNS lymphoma, and tuberculoma.

2. If the toxoplasma serology is positive, this means the patient has been exposed to the organism and is vulnerable to reactivation when immunosuppressed. Over 95% of toxoplasmosis in HIV is a reactivation rather than de novo infection. A MRI may be helpful since a single lesion on MR is

more likely to be lymphoma. More recently, thallium-201 SPECT scans have been utilized – lymphoma showing increased uptake relative to toxoplasma abscesses.

3. The standard treatment is to treat patients with anti-toxoplasma drugs such as sulphadiazine and pyrimethamine plus folinic acid for at least 2 weeks. If there is a significant response the diagnosis is one of toxoplasmosis. If the patient deteriorates a stereotactic brain biopsy should be considered. The patient continued to deteriorate. A brain biopsy showed primary CNS lymphoma.

4.
• Toxoplasma encephalitis
• Cytomegalovirus (CMV) encephalitis
• Progressive multifocal leukoencephalopathy (PML)
• CNS lymphomas.

5.
• 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.

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

Case 10

Cerebral abscess

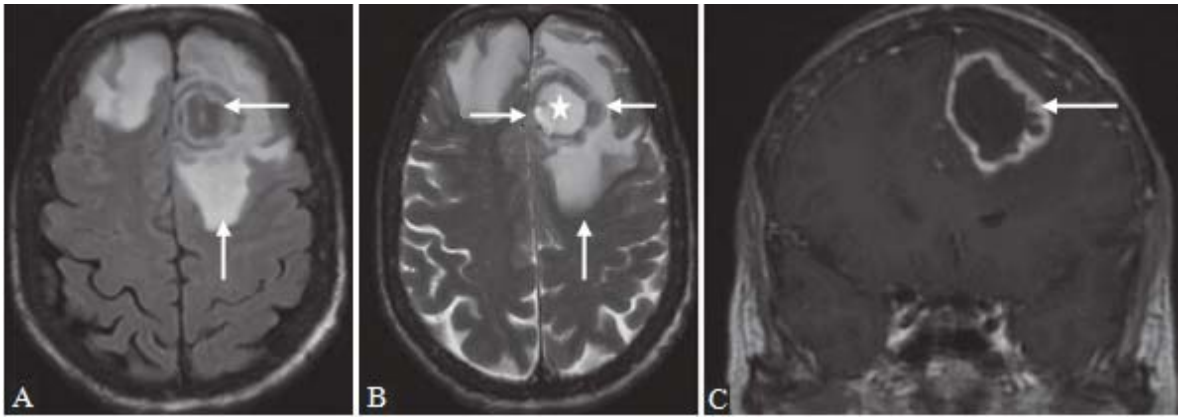
1. The scan shows a ring-enhanced mass lesion in her right frontoparietal lobe with surrounding edema. The radiologic differential diagnosis is wide but in the context of an immunosuppressed patient the most likely differentials include fungal abscess, cerebral toxoplasmosis, nocardia and bacterial abscess. Intracerebral metastases from non-Hodgkin’s lymphoma are extremely rare.

2. Broad spectrum anti-bacterial, anti-fungal and anti-protozoal cover. Do a biopsy if no improvement is observed within 1 week to guide further treatment. Perform aspiration and surgical decompression if there are symptoms and signs of rising ICP.
CNS infections are an uncommon complication of cancer and are usually seen in patients with lymphoma and leukemia, often after chemotherapy and bone marrow transplantation. The usual florid symptoms apparent in immunocompetent patients with CNS infection are not seen in these patients. In particular, headache and fever may be absent (as in this patient). Brain abscesses are usually due to fungi, nocardia or toxoplasma, i.e. a different group of pathogens compared to immunocompetent patients, and need to be covered with appropriate antibiotics. Surgical intervention should be reserved when the conscious level declines or when there is no improvement after 1 week of appropriate treatment. Often other foci of infection, e.g. lung abscesses due to nocardia, allow precise diagnosis without the need for a brain biopsy.

Case 11

Nocardiosis brain abscess

1.



(A) Axial FLAIR through the frontal lobes. There is alternating (six) layers of different intensity pattern (concentric target pattern) (transverse arrows) within the left frontal lobe lesion. There is surrounding confluent hyperintensity consistent with vasogenic edema (vertical arrow) and mass effect on surrounding structures manifested by effacement of convexity sulci.

(B) Axial T2WI through the left frontal lobe mass. There is a central high intensity core (star) with a surrounding multi-layer irregular wall; isointense to brain around the core with an outer layer of thin hyperintensity (transverse arrows) before the edema (vertical arrow).

(C) Post-contrast coronal T1WI through the left frontal mass. There is a thick irregular mural contrast enhancement (arrow).

2. Abscess (pyogenic), toxoplasmosis, aspergillosis, glioblastoma (GB), infarcts.
3. Nocardiosis brain abscess.
4. The imaging should be repeated every 2 weeks until the lesion is stable in size and imaging should be repeated if there is clinical deterioration. Drug treatment usually continues for at least 1 year.

5.
• Location and size. It is recommended that abscesses smaller than 2 cm in the presence of other extra-CNS infection could be watched if patient is stable. Abscesses larger than 2.5 cm should be excised or drained. Outcome seems better with excision.
• If a lumbar puncture (LP) is necessary, is it safe? Significant mass effect or herniation contraindicates LP.
• Brain imaging is always recommended in patients width evidence of systemic *Nocardia* infection. CNS involvement has been reported in up to 44% of cases with systemic nocardiosis.

Comment

Nocardial brain abscess could be single or multiple. MRI best depicts the geography of the lesion. The hallmark of an abscess is a round area of restricted diffusion with surrounding edema and mass effect. The restricted diffusion is ascribed to the cellularity of the pus. The typical pyogenic abscess has a smooth thin contrast-enhancing ring surrounding the pus. In this case however, the ring enhancement is thick, somewhat crenated, and irregular, and there is a multilayer wall within and surrounding the center of the abscess on FLAIR and T2WI, indicating presumably several layers of different tissues within the mass, hence their different intensities. There is a large amount of surrounding vasogenic edema. The irregularity of the enhancing wall may suggest something more sinister such as GB. However, the homogeneous restricted diffusion and the target pattern are unusual of GB. Aspergillosis on the other hand tends to show heterogeneous DWI and T2 pattern with a variable pattern of contrast enhancement with intracavitary projections.

Infarcts are usually confined to a vascular territory with ring enhancement being unusual. Clinical presentation of nocardiosis can be acute with rapid progression or insidious with subacute or chronic evolution. *Nocardia* species, aerobic fiamentous branching Gram-positive bacteria, are ubiquitous in the environment

causing human infections by direct inoculation of the skin or by inhalation. The disease is affected both immunocompetent and immunocompromised patients.

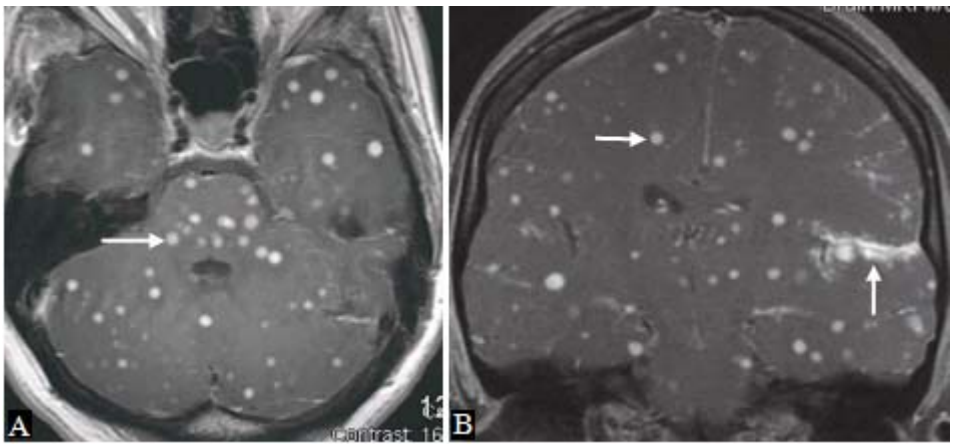
The frequency of nocardiosis among solid organ transplant recipients varies from 0% to 20%, and among allogeneic bone marrow recipients the rate is 0.3% to 1.7%. Risk factors include preexisting immunocompromised status (diabetes, alcoholism, AIDS, solid organ transplantation), chronic pulmonary disorders, graft-versushost disease, administration of high doses of steroids, high serum levels of calcineurin inhibitors (tacrolimus, cyclosporine), and cytomegalovirus disease within the preceding 6 months. Pulmonary disease is the predominant clinical presentation (40%). *Nocardia* seems to have tropism for neural tissue, central nervous system (CNS) being the most common site of infection. Clinical presentation includes headache, mental status changes, focal neurologic deficits, and seizures. Definitive diagnosis is made by bacteriologic culture following surgical evacuation of the abscesses.

Nocardia meningitis is not common and can present with or without associated brain abscess. Treatment is usually prolonged with a combination of antibiotics including trimethoprim/methoxazole as the drug of choice. Prognosis depends on the site of involvement, extent of the disease, and immune status of the host. Cure rate in patients with brain involvement is approximately 40% to 50%. Prognosis is worse in the immunocompromised and patients with multiple abscesses.

Case 12

Miliary TB of the brain

1.



(A, B) Axial post-contrast T1WI through the posterior fossa and coronal post-contrast T1WI through the sylvian fisures. There are numerous tiny nodular contrast-enhancing lesions throughout the brainstem, cerebellum, and cerebral hemispheres mainly in cortical and subcortical locations (arrows point to representative lesions). Multiple areas of leptomeningial enhancement are also demonstrated (vertical arrow).

2. Miliary tuberculosis (TB), metastases, neurocysticercosis, fungal granulomas.

3. Miliary TB of the brain.

4. Once the diagnosis is made, follow-up imaging depends on patient's response to treatment. Clinical deterioration is usually an indication for imaging. If the patient is improving, the imaging should not be repeated. Once drug treatment is completed, imaging is always necessary to confirm the status of the lesions.

5.
• Miliary TB of the brain is usually associated with tuberculous meningitis. Presence of leptomeningeal lesions indicates meningitis.
• Treatment for TB should be initiated based on clinical suspicion in the presence of miliary lesions.
• Is it safe to perform lumbar puncture (LP)? Yes, as long as there is no mass effect.

Comment

MRI is the modality of choice for evaluating brain military TB. The vasogenic edema surrounding the lesions present as multifocal smudgy hyperintensity on FLAIR and T2WI mostly in the subcortical locations in both infra- and supratentorial regions. Non-contrast T1WI shown smudgy hypointensities. Post-contrast T1WI shows nodular homogeneous enhancement usually less than 3 mm in diameter within the edema throughout the brain. Invariably there is associated leptomeningeal enhancement. Lesions are too small to characterize on DWI. Follow-up MRI showed significant progression in number and size of lesions on follow up. Tuberculous lesions may also undergo paradoxical reaction to treatment, becoming more prominent earlier or during treatment before they eventually gradually regress. Lesions are located in the cortical and subcortical regions or where end arteries are such as the brainstem or basal ganglia due to their hematogenous origin. They are usually tiny and monotonous rarely varying in size. Lesions that are close together may coalesce into bigger lesions. The monotony of the lesion size is important in differentiating these

lesions from their mimics. Presence of leptomeningial enhancement adds to the confience of the diagnosis of tuberculous meningoencephalitis. In contrast, metastases have varying sizes mostly ring enhancing with extraordinary amount of surrounding vasogenic edema. The granular nodular neurocysticercosis also tends to vary in size and may show some calcifiations.

However, treated miliary TB may also show calcifications. Fungal granulomas may show a military pattern. Presence of paramagnetic materials in the walls of fungal granuloma may result in GRE hypo/heterogeneous intensity. Clinical presentation of miliary TB is usually insidious presenting with weight loss, fever, weakness, confusion, and neurologic deficit. Initial abdominal and chest CT along with echocardiogram were negative in this patient. Bacterial blood cultures remained negative. The brain biopsy proved positive on acid fast bacilli (AFB) stain and culture for *Mycobacterium tuberculosis*. She was started on therapy with ethambutol, isoniazid, pyrazinamide, and rifampin; anti-seizure medication was added for prevention of seizures. Over the next week, her symptoms improved, and she was discharged home to complete the treatment.

Case 13

Herpes simplex encephalitis

1. The differential diagnosis is for a subacute encephalopathy and includes:
Infection: TB, HSV, cryptococcus, toxoplasma, malaria, HIV, syphilis.
Vascular disease: CVT, Cerebral vasculitis.
Neoplastic disorder.
Other: Depression, Hypothyroidism, CADASIL, MELAS, Hashimoto's encephalopathy, Drugs, Toxins e.g. mercury, Hepatic/renal failure.

The initial presenting features in this case were fairly non-specific and thus the differential diagnosis is wide. Herpes simplex encephalitis is probably the most likely cause since it produces behavioural change and headache and it is the most common cause of sporadic viral encephalitis in the industrialized world. Other viral agents should be considered in travellers and residents in other parts of the world. Non viral CNS infections that may present subacutely with altered mental state and headaches, particularly in immunosuppressed patients, are toxoplasma gondii, crytococcus neoformans, and TB. Cerebral malaria, coccidioidomycosis, and blastomycosis are possibilities in patients with recent travel to the Americas or Africa.

A space-occupying lesion particularly of the frontal lobes should be considered in view of the personality change and headache. CNS infection is high on the list of differential diagnoses despite the absence of fever at the initial presentation. CVT causes headache with or without reduced conscious level and focal neurological signs. Mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) typically causes an encephalopathy, which may initially manifest as mood change, and focal neurological signs. Hypothyroidism causes depression and apathy and there are some reports of an association with headache. Infiltrative disease of the CNS e.g. leukemia and lymphoma or malignant meningitis could cause headache and depression, likewise inflammatory CNS conditions such as cerebral vasculitis and sarcoid. Non-convulsive status epilepticus (NCSE) typically causes behavioural change and headaches are common after seizure but in this case the headaches preceded the behavioural change.

Depression, which is commonly associated with apathy, is associated with headache and other somatic complaints. Illegal drug use should be considered, particularly in younger patients where there is personality change.

2. The MRI axial T2-weighted MRI (A) and coronal FLAIR (B and C) shows extensive edema of the grey and white mater of the right insula and temporal lobe. Asymmetrical temporal lobe abnormalities are often seen in herpes simplex encephalitis on MRI but CT is less sensitive and is often normal early in the course of the disease. Temporal lobe changes are not exclusive to the diagnosis of herpes simplex encephalitis and extensive grey matter abnormalities may be seen with other encephalitides e.g. chicken pox. Temporal lobe change may also be seen in limbic encephalitis.

3. The diagnosis is herpes simplex encephalitis.

PCR for herpes simplex virus (HSV) should be performed on the CSF. EEG may provide further supporting evidence. The HSV virus invades the brain parenchyma and has a particular predilection for the temporal lobes, causing hemorrhagic necrosis. HSV-1 causes nearly all cases of HSV encephalitis in adults and oral herpes. HSV-2 causes genital disease, aseptic meningitis, and congenitally acquired neonatal encephalitis. Both types have been associated with myelitis. There is no characteristic prodromal illness, or other clinical features that distinguish herpes simplex encephalitis from other causes of encephalitis. Fever, headache, confusion, bizarre behaviour, lethargy, stupor, seizures, hyperreflexia, and mild neck-stiffness are common.

Hemiparesis (generally affecting the face and arm more than the leg), cranial nerve palsies, aphasia, and ataxia are less common. Superior quandrantanopias may occur. Infection and associated tissue injury predominantly involves the temporal and frontal brain regions and may be unilateral or bilateral. EEG may show seizure activity, sharp waves, and lateralized epileptiform discharges often localized to the frontotemporal regions. CSF shows a pleocytosis with lymphocytic predominance (5–500 cells/mm^3), moderately elevated protein (<1g/L) and normal or slightly low glucose.

In the past, brain biopsy was required to confirm the diagnosis of herpes simplex encephalitis, an invasive procedure associated with significant morbidity and mortality. More recently, PCR assay of CSF for the presence of DNA fragments to HSV has become the standard diagnostic test. In the first 4 days, PCR is positive in more than 95% of cases and remains so in 80% at one week.

Although false positive tests do occur, this is limited to around 5% in most laboratories. The EEG in herpes simplex encephalitis may show diffuse slowing, focal temporal region changes or periodic lateralized epileptiform discharge.

4. Treatment is with intravenous aciclovir. Intravenous aciclovir for 2–3 weeks should be given as soon as the diagnosis is suspected and before a definitive diagnosis is reached since early administration improves outcome. Renal function and hydration status should be monitored during treatment with aciclovir. Standard supportive therapy should be accompanied by antiepileptics if seizures occur. Use of steroids is controversial. Aciclovir resistant HSV has been described in immunocompromised patients for which foscarnet is the only treatment. Patients may relapse after completing therapy and biopsy may be necessary to distinguish ongoing viral infection from immune mediated disease.

5. The use of aciclovir has greatly reduced the mortality from 70% prior to aciclovir use to 25–30%. However, there is still significant morbidity and mortality associated with herpes simplex encephalitis. Persistent symptoms include memory impairment, poor concentration, irritability, emotional lability, and depression. Poor prognostic features include age over 30 years, presentation in coma, bilateral abnormalities on EEG, high CNS viral load, delayed treatment (4 days plus), and abnormal CT. The efficacy of steroids in herpes simplex encephalitis, principally for patients with increase intracranial pressure and edema, has not been demonstrated in randomized trials.

Case 14

HIV encephalopathy

1. (A) Axial FLAIR through the temporal lobes. There is bilateral anterior temporal lobes white matter (WM) hyperintensity (arrows). (B) Axial T2WI through the basal ganglia. There is confluent bilateral symmetrical WM hyperintensity around the frontal and occipital horns extending from the ventricular walls to the subcortical regions (arrows). The frontal WM hyperintensity extend across the genu and anterior body of the corpus callosum (vertical arrow). This T2WI captures the degree of brain volume loss which is mild in this case. (C, D). Axial FLAIR through the corona radiata and centrum semiovale, respectively. There is predominant symmetrical bilateral frontal lobes confluent WM hyperintensity extending from ventricular wall to subcortical regions (transverse arrows). The lesions are more subcortical, smudgy, and not as confluent in the parietal and occipital WM with relative sparing of the deep WM (vertical arrows). It is noted that there is no mass effect, and the post-contrast images (not shown) do not show areas of contrast enhancement.

2. Chronic small vessel ischemic changes, progressive multifocal leukoencephalopathy (PML), HIV encephalopathy (HIVE), leukodystrophy, Binswanger's disease.

3. HIV encephalopathy (HIVE).

4. Risk factors for HIVE include older age at seroconversion, female gender, duration of HIV infection, presence of a prior AIDS-defining diagnosis, low $CD4^{+}$, and low nadir CD4 count. These risk factors suggest that severe and prolonged immunosuppression may have long-lasting effects on neuropsychiatric performance regardless of subsequent viral suppression. Other factors such as high plasma HIV-RNA load, anemia, low weight, presence of hepatitis C virus, and substance abuse are associated with increase in the prevalence of neurocognitive deficits and dementia.

5.
- Pattern of WM lesions and degree of volume lots.
- Other associated abnormalities.
- Exclusion of opportunistic infections and neoplastic change.

Comment

Imaging features of HIVE consist of diffuse, confluent, or smudgy WM changes that are predominantly frontal with involvement of the genu of the corpus callosum but occur elsewhere in the corona radiata and centrum semiovale. These lesions are hypointense on T1WI and hyperintense on FLAIR and T2WI. They generally extend from ventricular walls to subcortical WM in the frontal lobes and around the occipital horns but are predominantly subcortical elsewhere. They are more often symmetrical without mass effect or contrast enhancement.

Unilateral lesions have been reported. Basal ganglia calcifications are seen in adults but more common in children. There is varying degrees of brain volume loss affecting both cortical and subcortical regions resulting in enlargement of the ventricles and sulci. Caudate nucleus atrophy is common. MRS shows low *N*-acetyl aspartate (NAA) peak with elevated myoinositol not only in the WM but also in the GM. Presence of lactate peak has also been noted, and this disappears following successful treatment of the encephalopathy.

CT shows corresponding non-contrastenhancing confluent hypodensity in similar locations as in MRI along with global brain volume loss. PML is usually subcortical and not necessarily bilateral. PML may contrast enhance with a T1WI cortical hyperintensity in immune reconstitution inflmmatory syndrome (IRIS). Chronic small vessel ischemic changes are usually monotonous small WM changes which may be confluent in severe cases. Binswanger disease tends to be globally confluent and not necessarily frontal predominant.

HIVE usually presents with a combination of cognitive deficit, movement disorders such as tremors, gait instability and weakness, depressive symptoms, and behavioral changes. HIVE is the result of direct HIV infection of the brain macrophages and/or microglial cells. On autopsy of AIDS patients with HIVE, demyelination, microglial nodules, multinucleated giant cells, and perivascular infiltration are described.

Diagnosis is based on neuropsychological testing of suspected individuals and exclusion of alternate conditions. Cerebrospinal fluid (CSF) studies are helpful in the diagnosis and excluding mimics such as cryptococcosis, toxoplasmosis, PML, or syphilis. Highly active antiretroviral therapy (HAART) is the primary treatment of choice, and its benefit is well documented.

Case 15

Toxoplasmosis Infection in Acquired Immunodeficiency Syndrome

1. Pyogenic brain abscess.
2. Toxoplasma can be transmitted through raw meat, milk, blood products, and cat feces, and by in utero exposure.
3. There are multiple calcifications in the basal ganglia and cortex as well as in the hydrocephalus. In severe cases, there may be microcephaly.
4. Lymphoma.

Comment

Central nervous system toxoplasmosis is caused by the intracellular protozoan Toxoplasma gondii. Toxoplasma encephalitis is most commonly seen in immunocompromised patients with impaired cellular immunity, especially in the setting of AIDS. Other immunodeficient conditions associated with increased infection includes following organ transplantation, long-term steroid therapy or chemotherapy, and impaired immunity from an underlying malignancy. In the setting of AIDS, radiologic differentiation between toxoplasmosis and lymphoma can be difficult. Both entities may have multiple lesions, and both may have solid or ring enhancement.

Toxoplasmosis has a predilection for the basal ganglia and the corticomedullary junction. Lesions are often hyperintense on T2W imaging, but vary widely in their signal characteristics. Lesions may be hemorrhagic. Findings favoring lymphoma are hyperdense masses on unenhanced CT, ependymal spread on enhanced MR imaging (rare in toxoplasmosis), and a periventricular distribution.

Distinguishing these two disease processes is important because they are treated differently. Primary lymphoma responds to radiation therapy; however, the benefit of radiation therapy is diminished when treatment is delayed, as may happen in patients first treated empirically for toxoplasmosis. Thallium-201 SPECT can be effective (sensitive and specific) in distinguishing lymphoma (takes up thallium) from toxoplasmosis (normally does not take up thallium). Positron emission tomography has been shown to be useful in the accurate differentiation of hypometabolic toxoplasmosis lesions versus metabolically active lymphoma.

Diffusion-weighted imaging with apparent diffusion coefficient (ADC) maps has been used to distinguish these two lesions. Toxoplasmosis lesions have demonstrated significantly greater diffusion than lymphoma, with increased diffusion relative to that in normal white matter, in contrast to the restricted diffusion seen within pyogenic abscesses. Increased diffusion in toxoplasmosis lesions has been postulated to reflect relatively decreased viscosity within the central cores of the lesions, perhaps due to an impaired cellular immune response related to the immunocompromised state of these patients. Although considerable overlap of ADC ratios between 1.0 and 1.6 has been reported, ADC ratios greater that 1.6 have been associated solely with toxoplasmosis. The core of the lesion in this case demonstrates increase diffusion relative to white matter: the ADC value was 1.3. Recent investigations with perfusion MR imaging have shown decreased regional blood volumes in toxoplasmosis lesions (attributed to the avascularity of abscesses) compared with increased blood volumes in lymphoma (attributed to increased vascularity in region of metabolically active tumor).

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