CNS INFECTIONS

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1. Acute bacterial meningitis
2. Brain abscess
3. Central nervous system empyemas
4. Spinal epidural abscess
5. Tuberculosis
6. Viral meningitis
7. Viral Encephalitis
8. Progressive multifocal leukoencephalopathy (PML)

1. Acute Bacterial meningitis

Medical emergency

It is critical for all physicians to know its presentation, its initial diagnostic evaluation, and the urgency with which a potential cause of bacterial meningitis needs to be addressed

Cardinal findings: headache, fever, neck stiffness.

Patients can also be confused or have depressed level of consciousness,develop seizures , or have other focal neurological symptoms or signs, depending on the extent to which the meningeal infection or inflammatory process affects the brain parenchyma(thus causing meningoencephalitis)

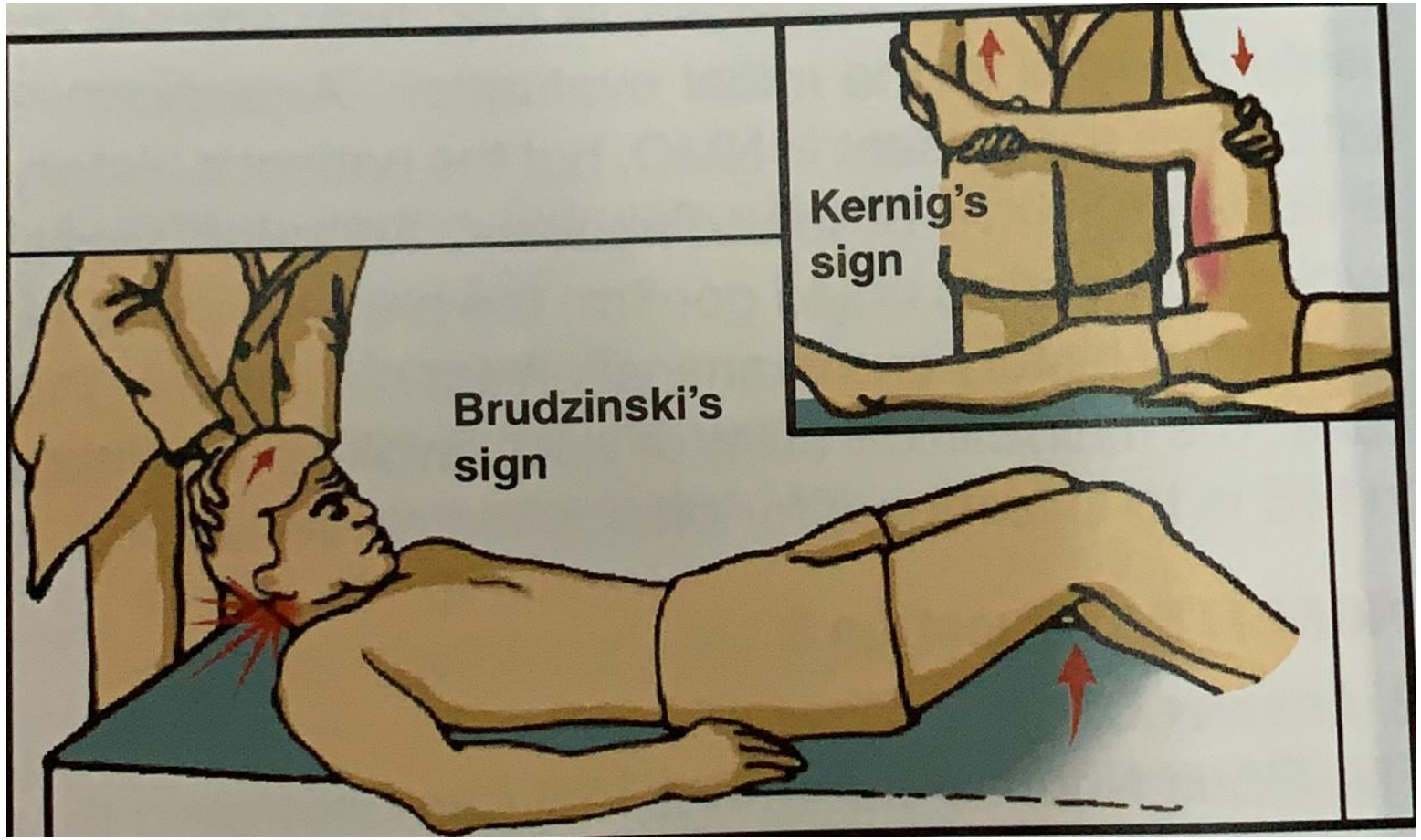
In immunosuppressed patients, as well as in the very elderly, there may be no fever, so it is vital to have a higher degree of suspicion in these populations

On examination, patients often have nuchal rigidity, that is , rigidity with flexing the neck forward

Two other physical signs, not specific to the bacterial form are:

* Kernig sign: the patient lies supine , and the knee is extended passively while the hip is flexed.If the patient is unable to extend the knee because of pain , the sign is positive

* Brudzinski sign: An involuntary flexion at the hip when the neck is flexed (figure)


Kernig's sign
Brudzinski's sign

Etiology

The most common organisms depend upon the patient's age at presentation (table)

The introduction of vaccines against Streptococcus pneumoniae

(pneumococcus), Neisseria meningitides(meningococcus) and Hemophilus influenzae has substantially reduced the incidence of bacterial meningitis in children

In most cases, bacteria reach the subarachnoid space by hematogenous spread from the respiratory tract, although bacterial meningitis can also be a direct sequela of traumatic or mechanical invasion of the subarachnoid space, such as after neurosurgical procedures or open head injury

It is also possible to have direct infiltration of the subarachnoid space from parameningeal foci , such as the sinuses

TABLE 21–1. Common Causes of Meningitis by Age, and Empiric Antibiotic Treatment

Age	Bacterial	Empiric Treatments
0–3 mo	—Group B Streptococcus —*Streptococcus pneumonia* —*Listeria monocytogenes* —*Escherichia coli*	Ampicillin + cefotaxime OR ampicillin + an aminoglycoside
3–24 mo	—*S. pneumonia* —*Neisseria meningitides* —*Haemophilus influenza type B* —Group B Streptococcus	Vancomycin + a third-generation cephalosporin
2–18 y	—*N. meningitides* —*S. pneumonia*	Vancomycin + a third-generation cephalosporin
Older adults	—*S. pneumonia* —*N. meningitides* —*H influenza, type B* —Group B Streptococcus —*L. monocytogenes*	Vancomycin + ampicillin + a third-generation cephalosporin

Diagnostic workup

The critical test in the diagnosis of acute bacterial meningitis is CSF analysis from a lumbar puncture(LP)

Because of the concern that LP may precipitate brain herniation in the presence of a focal intracranial mass with increased intracranial pressure, CT Brain should be performed before LP when papilledema is present on funduscopic examination or if there is any focal sign on neurologic examination suggesting the possibility of an intracranial lesion

Many neurologists advocate CT Brain prior to LP under any circumstances with an acute presentation

The characteristic CSF profile in acute bacterial meningitis includes an elevated white blood cell(WBC) count, with a predominance of polymorphonuclear leukocytes(generally never acceptable in a CSF sample), elevated protein and low glucose (less than 40 mg/dL) or less than 2/3 of a simultaneous measured serum glucose level(table)

The differential on the CSF WBC count must be interpreted with caution early in the course of meningitis because patients with bacterial meningitis may present initially with a lymphocytic predominance

Patients with viral meningitis may also have a neutrophil predominance early in the course

Severely immunosuppressed patients with pancytopenia may also not have classic CSF patterns

CSF Gram stain can demonstrate the bacteria and narrow the differential diagnosis of causative organisms

CSF cultures in acute bacterial meningitis can often identify the specific organism, which can then be tested for antibiotic sensitivity

Because of the potentially life-threatening nature of acute bacterial meningitis , a prolonged delay in obtaining CSF may necessitate the institution of empiric antibiotic coverage prior to LP -using antibiotics that are effective against the most likely organisms, at doses that ensure adequate penetration in the subarachnoid space, or

“meningitis doses”

In this case, CSF cultures may not grow organisms if they were not obtained until well after antibiotic therapy was begun, and it may be necessary to complete an entire course of empiric therapy

TABLE 21-2. Common Cerebrospinal Fluid Patterns in Different Forms of Meningitis

	Bacterial	Viral	Fungal	TB
Opening pressure	Elevated	Normal	May be normal or elevated	May be normal or elevated
WBC	≥100 cells/μL	<100 cells/μL	<500 cells/μL	<500 cells/μL
Cell type	*Polymorphonucleocytes*	Lymphocytes	Lymphocytes	Lymphocytes
Glucose	Low	May be normal	Low	Low
Protein	Elevated	Elevated	Elevated	Elevated

Treatment

Appropriate antibiotic therapy needs to be administered promptly upon the diagnosis of acute bacterial meningitis , with specific drugs initially chosen on the basis of the most likely organisms, and subsequently modified on the basis of Gram stain or culture results

(table)

In addition to the antibiotic therapy, some adjunctive therapies may also be helpful in certain situations

Corticosteroids are often used in children in an attempt to prevent some long-term complications of acute bacterial meningitis, such as deafness

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Prevention

* Chemoprophylaxis : Rifampicin or ciprofloxacin is indicated for household contacts in meningococcal meningitis

* Immunization against H. influenzae infection (using H. influenzae type B vaccine) is recommended routinely for children at the ages of 2,3, and 4 months, and has greatly reduced the incidence of meningitis caused by this organism

2.Brain abscess

Brain abscesses typically present much like any focal intracranial lesion, with headache, focal neurologic signs(that depend on the location of the abscess), seizures ,and potentially, signs of increased intracranial pressure.

Fever may be present, but this is not invariable

Etiology

*Solitary brain abscesses often arise from invasion of the intracranial space from neighboring sites of infection, such as the sinuses, or from direct open trauma or mechanical instrumentation

The first stage of brain abscess development is often cerebritis in which there is an active infection in the brain but not yet walled off

If there are no contraindications for LP, CSF studies are abnormal, and imaging studies or EEG or both may also be abnormal

In the second stage, the infection becomes organized and walled off to form a classical abscess

*Multiple brain abscesses are typically the result of hematogenous dissemination , such as from infective bacterial endocarditis, or with immunocompromised states

Responsible organisms depend on the etiology: respiratory pathogens may invade from the sinuses; abscesses from trauma or instrumentation are often skin flora; multiple abscesses are often caused by organisms that cause infective bacterial endocarditis

Most abscesses contain multiple organisms, often a mixture of aerobic and anaerobic pathogens(table)

TABLE 21–3. Causes of Brain Abscesses

Source of Infection	Bacterial Causes
Traumatic brain injury	*Staphylococcus aureus* *Staphylococcus epidermidis* *Pseudomonas aeruginosa* *Enterobacter* species
Neurosurgery	*Staphylococcus aureus* *Staphylococcus epidermidis* *Pseudomonas aeruginosa* *Propionibacterium acnes* *Streptococcus* species
Hematogenous spread	*Staphylococcus aureus* *Streptococcus viridans* *Klebsiella pneumoniae*
Ear	*Proteus mirabilis* *Streptococcus milleri* group organisms *Streptococcus pneumonia*
Dental	*Streptococcus* species *Bacteroides fragilisus*

Diagnostic workup

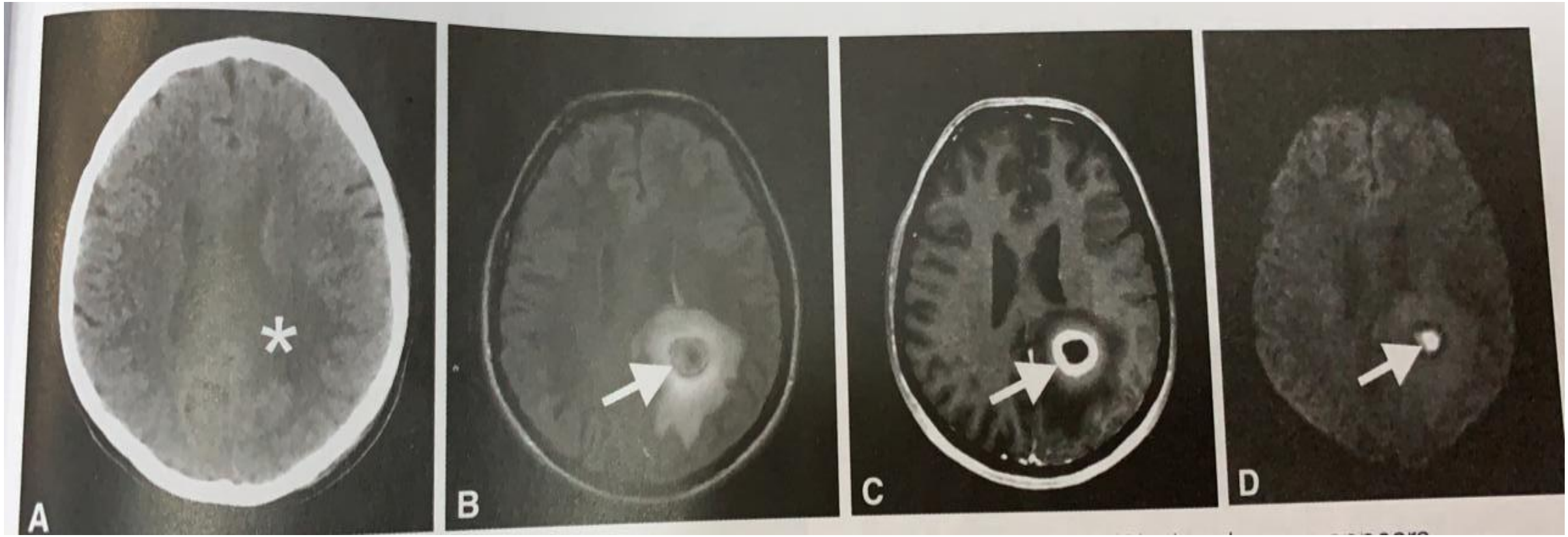
The diagnosis is usually made by neuroimaging

CT or MRI brain with intravenous contrast agents will usually demonstrate a mass lesion , often surrounded by " ring enhancement" and signs of central necrosis within the brain parenchyma (figure)

There may be surrounding edema

At the top of the radiologic differential diagnosis are malignant neoplastic lesions, which often have a similar ring enhancing mass appearance

Sometimes single photon emission computed tomography(SPECT) scanning can help differentiate a neoplastic process from an abscess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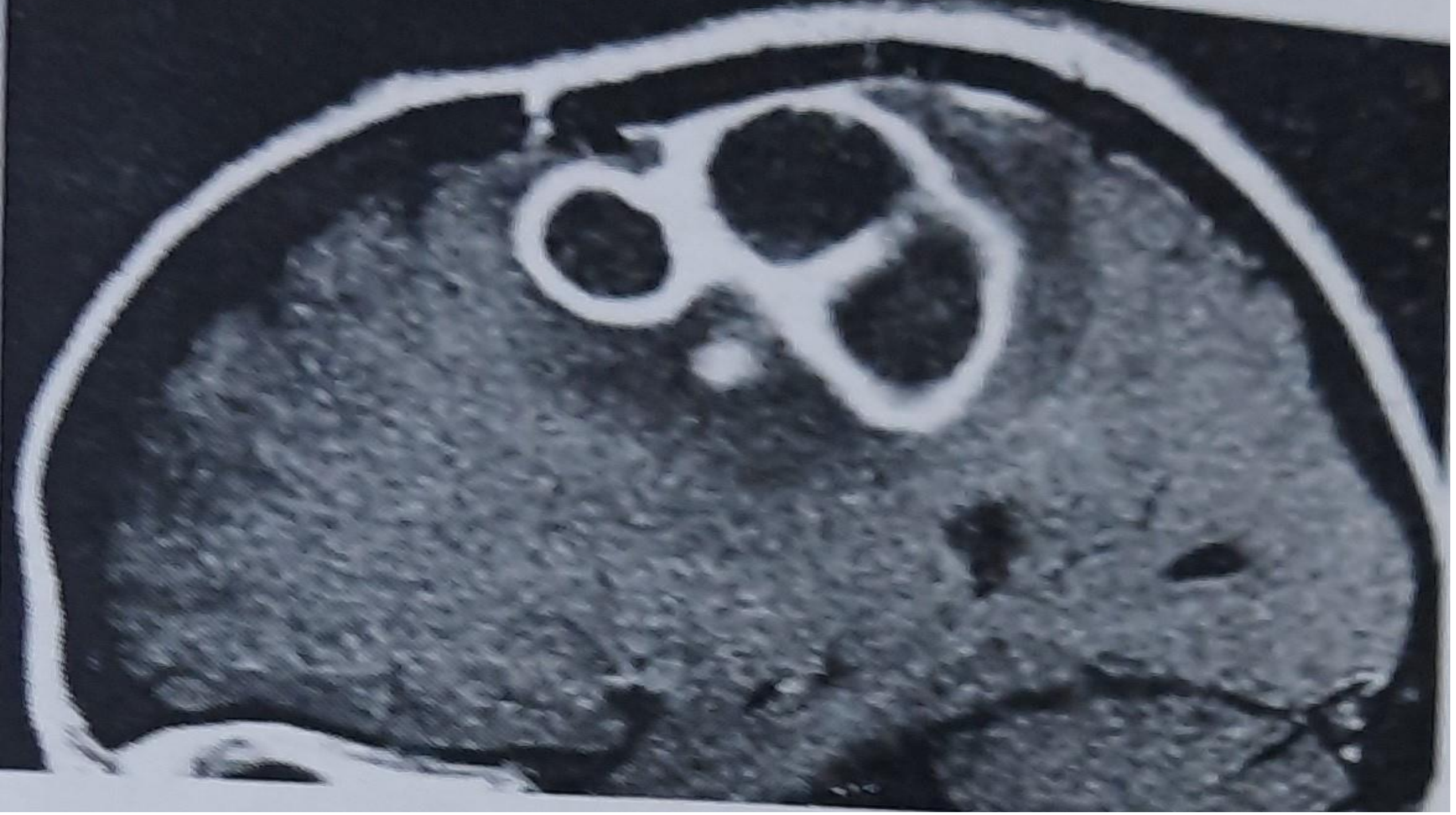


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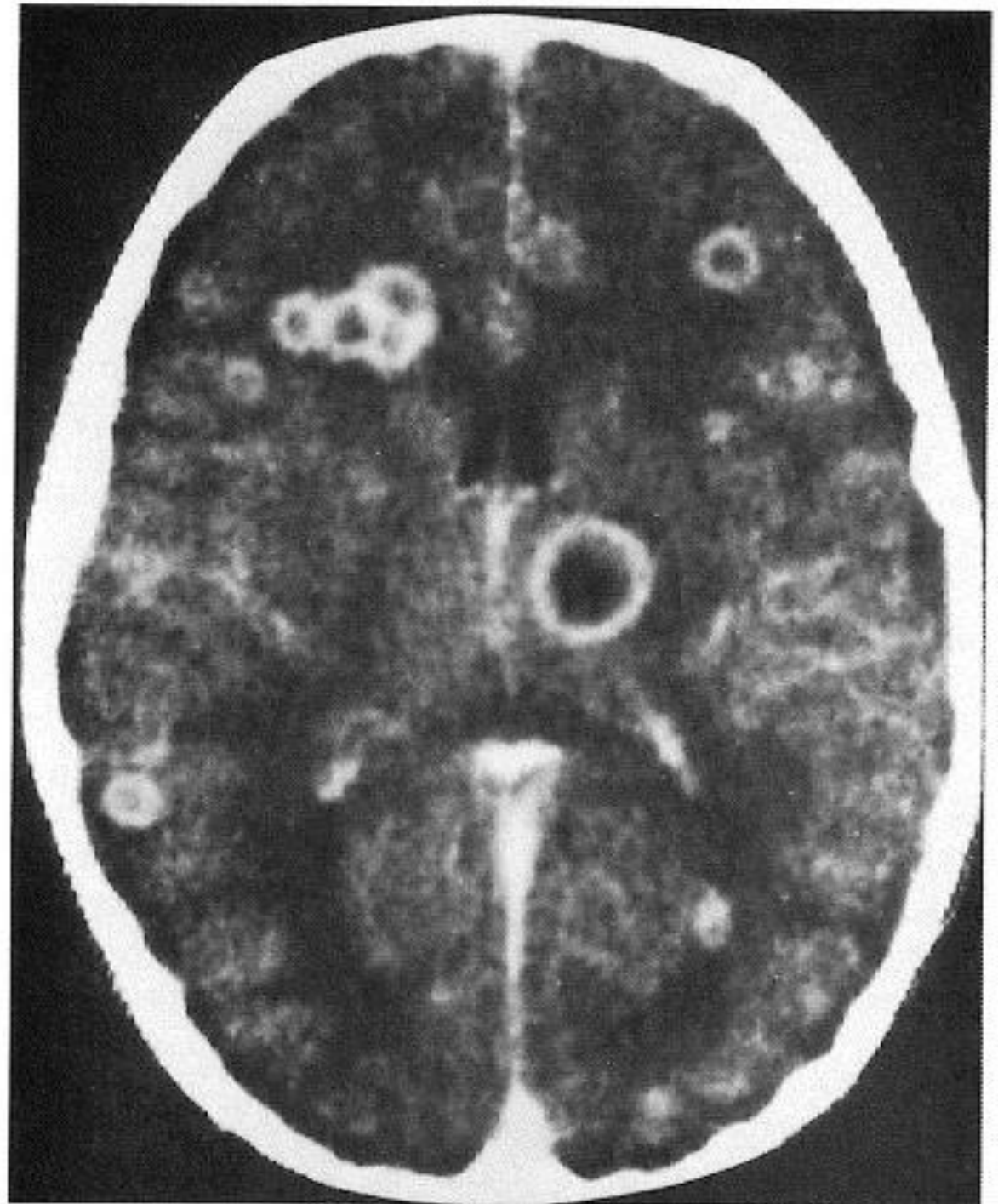
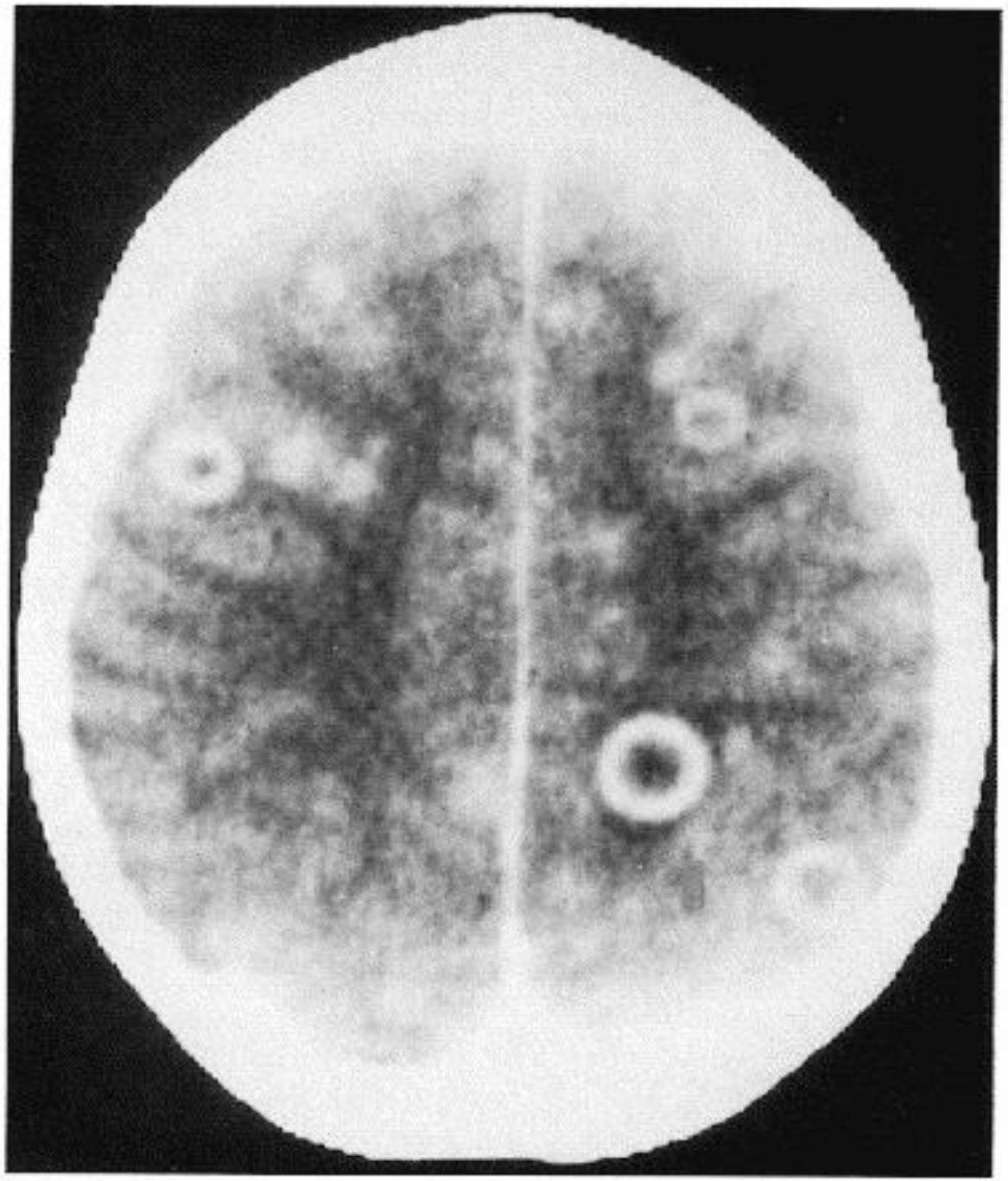




Depending on the source of the infection, blood cultures may identify the responsible organisms, but neurosurgical drainage is often necessary for definitive pathogen identification

Treatment

Prolonged courses of intravenous antibiotics , either chosen empirically for broad-spectrum coverage of aerobic and anaerobic organisms or tailored specifically on the basis of culture results, are the mainstay of treatment for brain abscesses

If the lesion does not respond to antibiotics, surgical drainage may be required

If the lesion causes mass effect and the patient is at risk of herniation, surgical drainage may also be necessary

3. Central nervous system empyemas

Collection of pus, known as **empyemas**, can occur in the central nervous system (CNS) as in other tissues

CNS empyemas most commonly occur in the subdural or epidural spaces

One must have a high degree of clinical suspicion because the empyema may be difficult to differentiate from a subdural hematoma on a CT Brain scan.

Consequently, these lesions are missed frequently

Patients may present with fever and headache

The infection typically arises from direct spread from an adjacent tissue (sinus, bone, or skin) or hematogenous spread(figure)

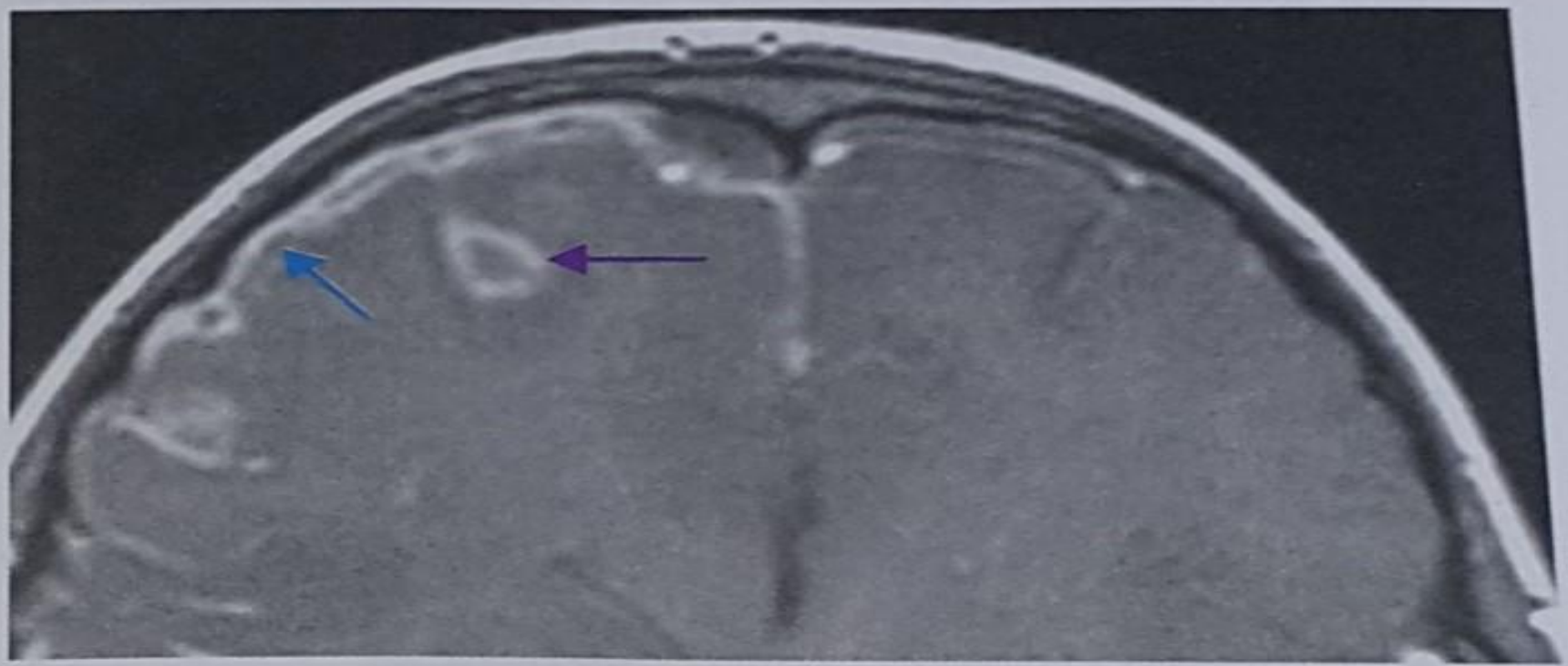


FIGURE 21-3. Frontal sinusitis with intracranial empyema. T1-weighted, contrast-enhanced image confirming likely subcortical infarction. Blue arrow: empyema. Violet arrow: subcortical infarct.(Reprinted with permission from Mancuso AA. *Head and Neck Radiology*. 1st ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2010. Figure 13.16.)

4. Spinal epidural abscess

*Clinical findings

Spinal epidural abscesses typically present with the combination of neck or back pain and focal neurologic signs consistent with spinal cord compression or cauda equina involvement, depending on the spinal level of the abscess

For thoracic or lumbar abscesses, clinical signs may include leg weakness, sensory loss with a discernible sensory level on examination, and urinary and sexual dysfunction

Cervical abscesses may present with the same symptoms as those at lower levels, but the arms may be involved as well, resulting in arm weakness or sensory symptoms there, or both

Fever is not necessarily present

Symptoms may come on acutely or more insidiously; an acute rapid presentation raises concern for a spinal cord infarction

* Etiology

Spinal epidural abscesses can be sequelae of spinal instrumentation, including epidural or spinal anesthesia or spine surgery

In these cases, the responsible organisms are often skin pathogens such as staphylococcal species

Abscesses can also be the result of spread from more anterior infections, including vertebral body osteomyelitis or diskitis

* Diagnostic work-up

If there is a clinical suspicion on the basis of history and exam, spine imaging should be obtained urgently because an intraspinal lesion such as an epidural abscess can cause cord compression with resulting paralysis

In general, the administration of contrast (with either CT or MRI) can help demonstrate the enhancing nature of spinal epidural abscesses (figure)

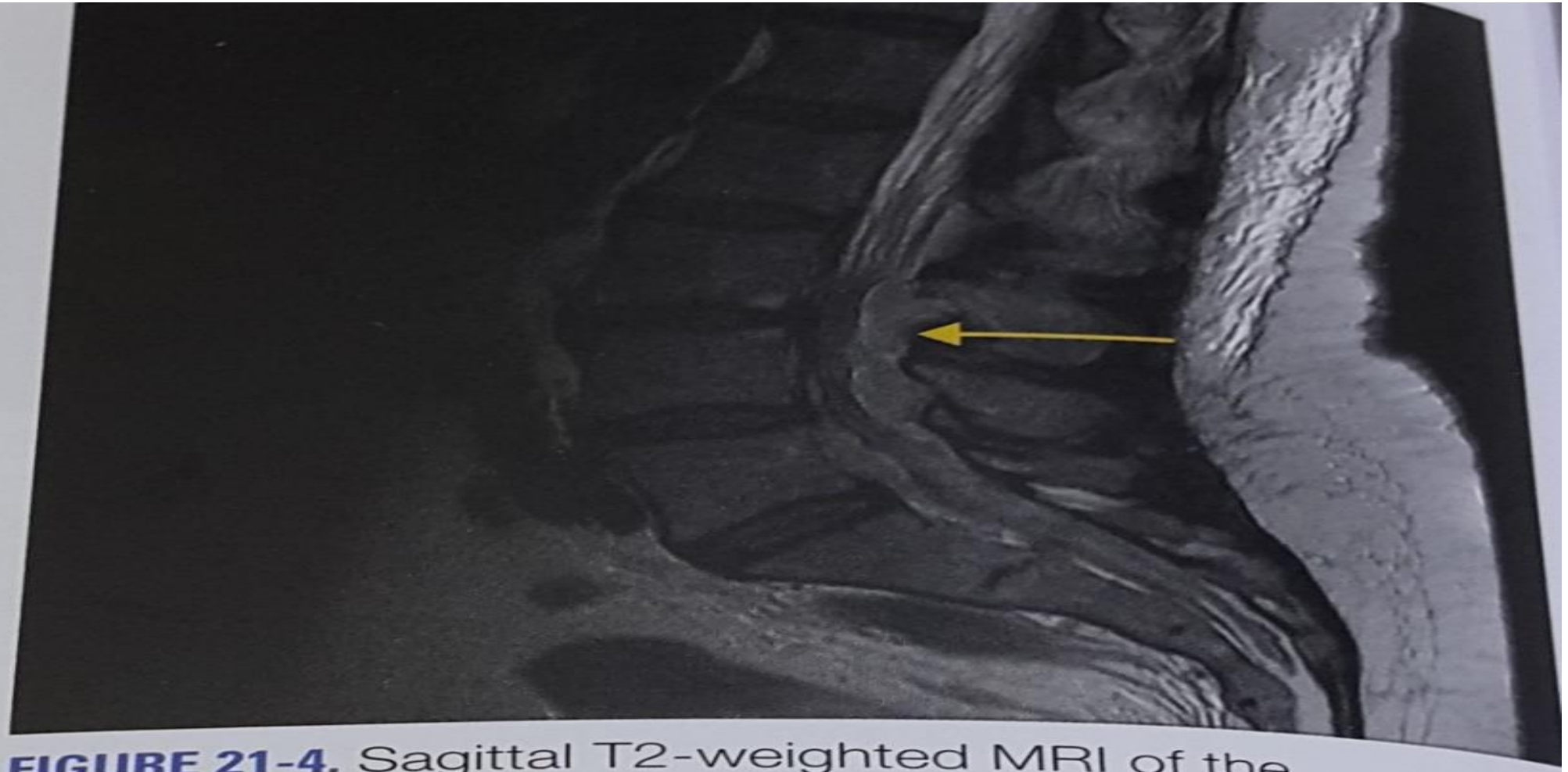


FIGURE 21-4. Sagittal T2-weighted MRI of the lumbosacral spine demonstrating a large spinal epidural abscess (orange arrow). [MRI, magnetic resonance imaging.] (Reprinted with permission from Rathmell JP. *Atlas of Image-Guided Intervention in Regional Anesthesia and Pain Medicine*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011. Figure 5.27B.)

Lumbar puncture is contraindicated in most situations before the anatomic extent of the lesion is defined clearly by imaging, because there is a theoretical possibility of seeding the subarachnoid space with bacteria using the spinal needle

As with intracranial abscesses, blood cultures can sometimes demonstrate the responsible organisms, but in many cases, radiologically guided biopsy or surgical drainage for microbiologic studies is necessary

* Treatment

Prolonged courses of intravenous antibiotics are the mainstay of treatment for spinal epidural abscesses, although in some cases neurosurgical drainage is necessary

When a clinical syndrome of acute cord compression or cauda equina involvement is present, surgical decompression may be required urgently

5. TUBERCULOSIS

One third of the global population is infected with tuberculosis

In the United States, it is less common(3 cases per 100000 people)

Mycobacterium tuberculosis affects the nervous system in several ways: tuberculous meningitis, intracranial tuberculomas, and Pott's disease (tuberculoma of the spine)

A) Tuberculous meningitis

Tuberculous meningitis arises from hematogenous dissemination of mycobacteria from a pulmonary source

A number of features distinguish tuberculous meningitis from acute pyogenic bacterial meningitis

First, meningitis caused by M. tuberculosis has a predilection for affecting the basal meninges(those at the base of the brain) and thus present with cranial nerve palsies in addition to the usual features of acute bacterial meningitis

A basal meningitis can also lead to hydrocephalus or brain infarctions from inflammation affecting cerebral vessels

Second, tuberculous meningitis tends to have a more subacute or chronic, insidious presentation than acute bacterial meningitis, so a prolonged prodrome of malaise and fairly nonspecific constitutional symptoms may precede the appearance of frank neck pain or stiffness

Finally, the CSF profile in tuberculous meningitis typically demonstrates a leukocytosis with lymphocytic predominance , rather than polymorphonuclear predominance (except initially), and the CSF glucose is often very low (previous table)

Acid-fast bacilli staining of the CSF can identify mycobacterial infection, but culture of this organism takes weeks to grow, and some never become positive

Fortunately, polymerase chain reaction (PCR) testing of mycobacterial antigens is available

The treatment of tuberculous meningitis requires a regimen of multiple antituberculous drugs that penetrate the intrathecal space effectively, usually with isoniazid(INH) , rifampin, pyrazinamide, and streptomycin

B) Intracranial tuberculoma

Tuberculomas are mass lesions caused by M. tuberculosis infection

Although uncommon in the United States , tuberculomas are one of the most common focal brain lesions in the developing world

Typically, they present with features that would be expected for any inflammatory mass lesion within the brain, including headache, focal neurologic symptoms and signs, and seizures

They can calcify, be variably enhancing on radiologic studies with contrast, and sometimes be associated with hydrocephalus

The radiologic differential diagnosis typically includes brain tumor, bacterial abscess, or cysticercosis

Appropriate treatment includes prolonged courses of antituberculous therapy and neurosurgical intervention if needed

C) Pott's disease

Pott's disease, or tuberculosis of the spine, typically presents with neurologic symptoms and signs when a vertebral body infection extends into the epidural space, leading to subacute spinal cord or cauda equina compression, depending on the level of involvement

Fever and back pain are common

Spread through disk spaces to adjacent vertebral bodies often suggests Pott's disease, usually differentiating it from metastatic cancer(figure)

Treatment includes antituberculous drugs and spine stabilization procedures if necessary

FIGURE 21-5. Tuberculous spondylitis (Pott's disease). A vertebral body is almost completely replaced by tuberculous tissue. Note the preservation of the intervertebral disks. (Reprinted with permission from Rubin R, Strayer DS, Rubin E. *Rubin's Pathology*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2011. Figure 26.22.)

6. Viral meningitis

Commonly caused by enteroviruses , such as Cocksackie virus, or arboviruses, such as West Nile virus

Clinically, the presentation may be very similar to that of acute bacterial meningitis, and it is mainly the latter that needs to be considered and ruled out immediately, even if viral meningitis is suspected to be more likely

The CSF profile differs from that of acute bacterial meningitis, in that viral meningitis usually features a lymphocytic predominance of WBCs

(except initially, when polymorphonuclear leukocytes can be present) and an elevated protein without a concomitant significant lowering of CSF glucose(table on a previous slide)

Gram stain and bacterial culture of CSF are, of course, unrevealing

Testing the blood and CSF for virus-specific serologies and PCR assays can help identify the responsible virus

Treatment generally involves just supportive care, unless herpes simplex virus (HSV) 1 is suspected

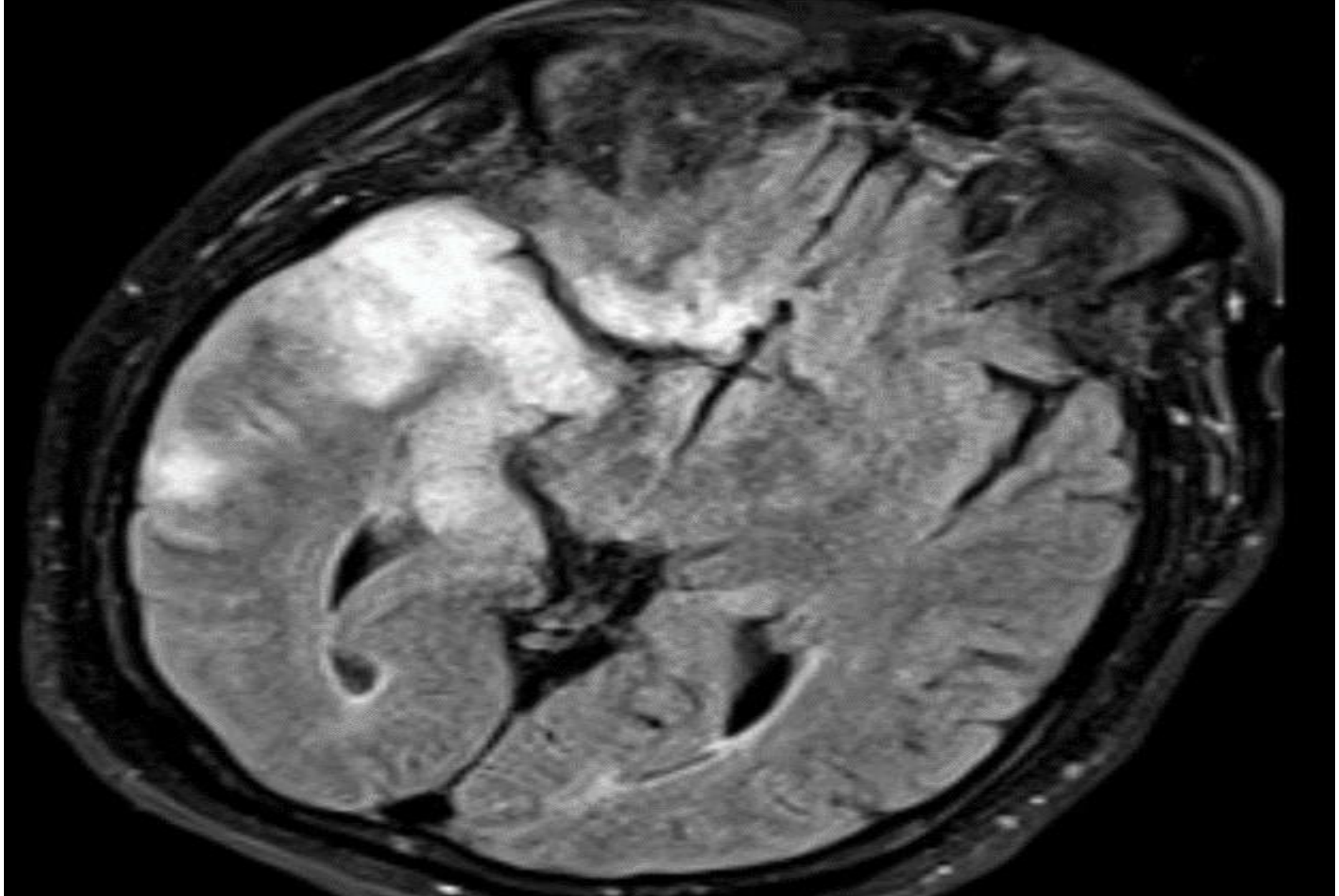
7. Viral encephalitis

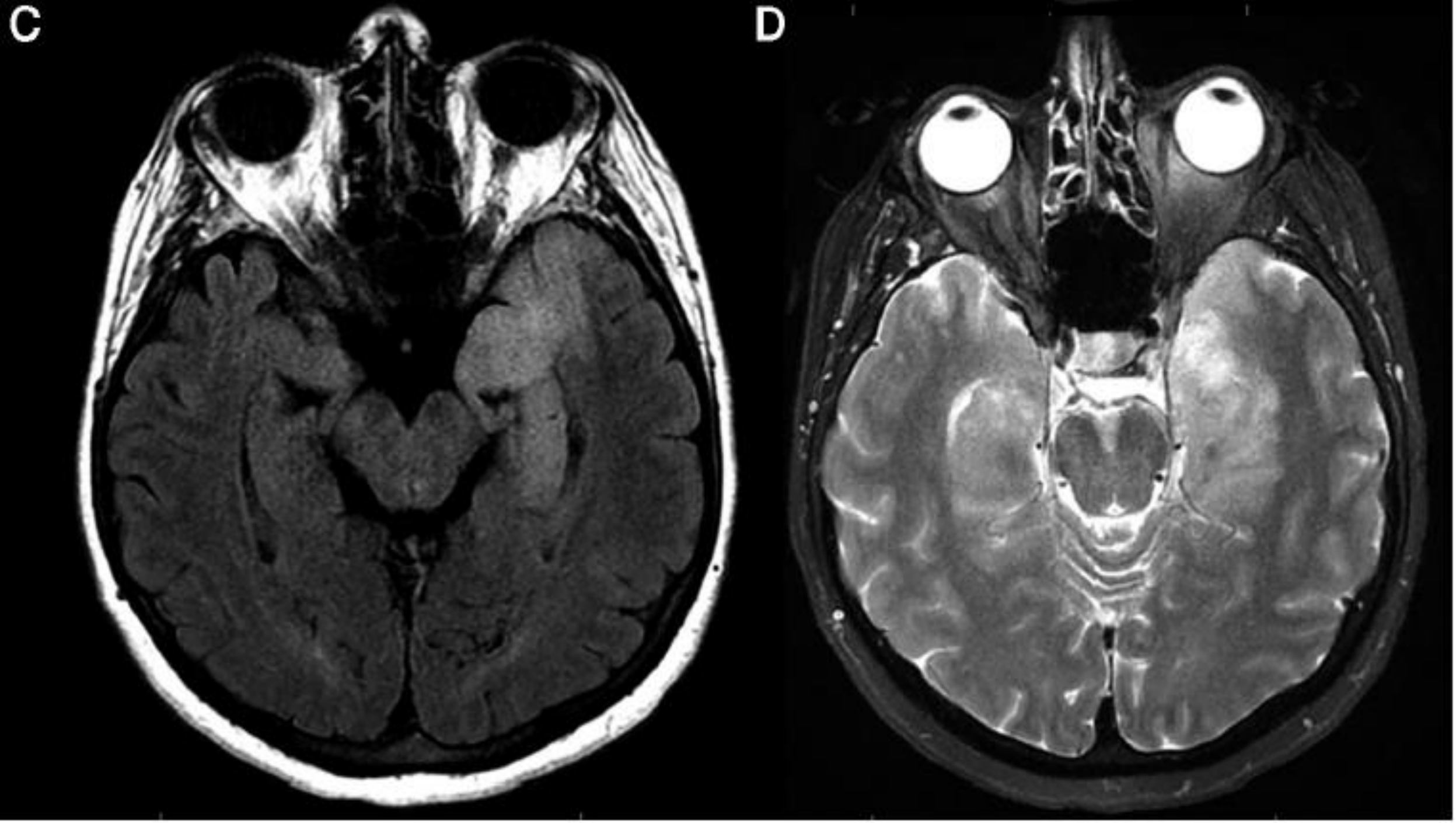
Viral encephalitis , which affects the brain parenchyma itself, usually presents with headache, fever, altered consciousness or behavior, and often seizures, focal neurologic abnormalities, or both

Although most viruses causing encephalitis have no specific anti-infective therapy available,encephalitis caused by HSV 1 leads to some distinct clinical features and warrants specific , emergency therapy

HSV 1 encephalitis has a predilection for the base of the brain, specifically including the medial temporal lobes, and orbitofrontal regions of the cortex (figure)

FIGURE 21-9. MRI findings in HSV encephalitis. T2-weighted coronal MRI demonstrating predominantly right mesial temporal hyperintensity and swelling in presumed HSV1 encephalitis. [HSV, herpes simplex virus; MRI, magnetic resonance imaging.] (Reprinted with permission from Wyllie E. Wyllie's *Treatment of Epilepsys*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2015. Figure 32-3a.)

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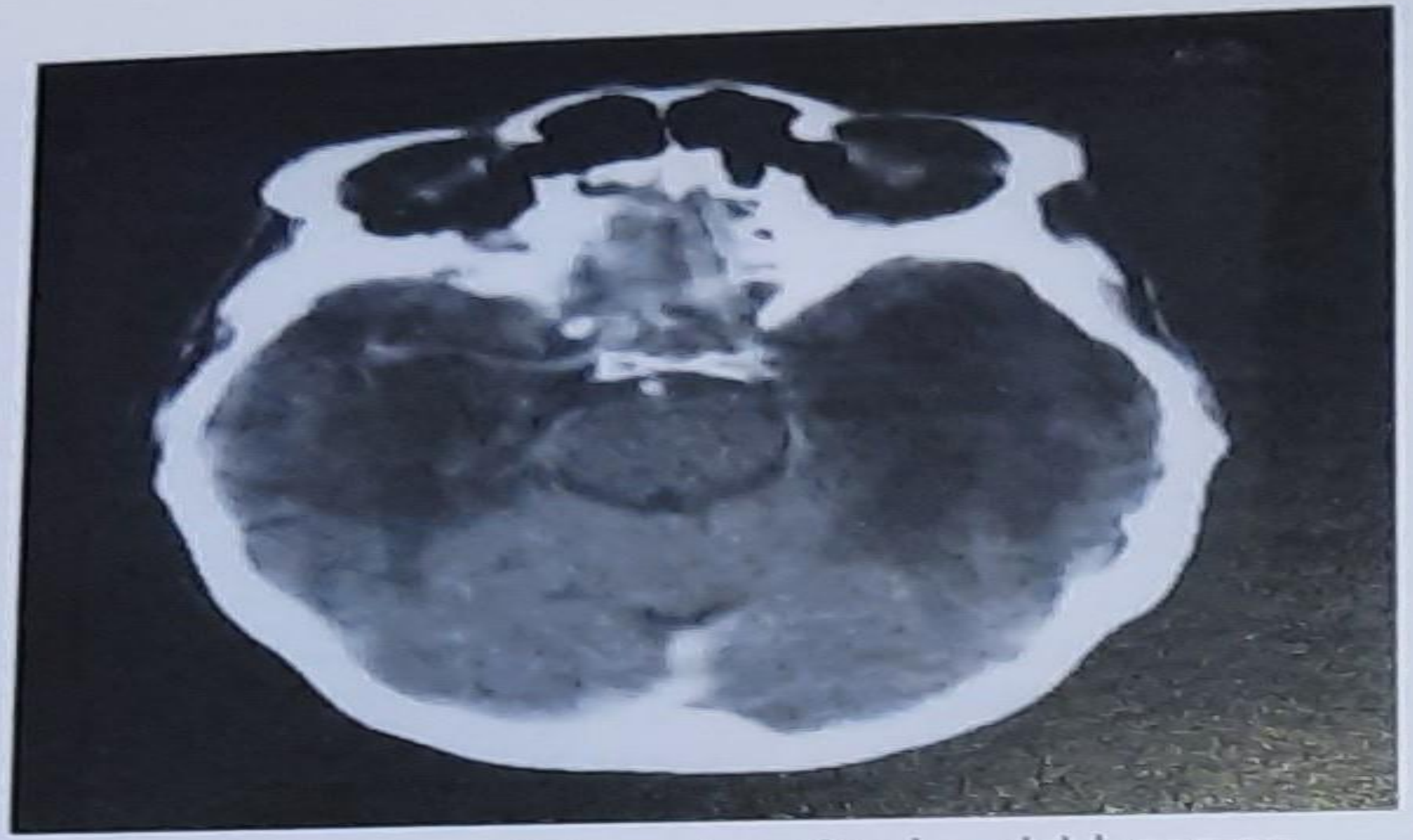

Limbic dysfunctions, including complex partial seizures of mesial temporal lobe origin, olfactory hallucinations, and memory disturbances(including sometimes profound anterograde amnesia and some degree of retrograde amnesia) , are common parts of the clinical presentation

The CSF in HSV 1 encephalitis often demonstrates an elevated red blood cell count in addition to leukocytosis(and thus needs to be distinguished from traumatic LP results)

A CSF PCR test is available for HSV 1

EEG recording may demonstrate periodic epileptiform discharges over one or both temporal regions, particularly after several days of infection

HSV 1 encephalitis is treated with a prolonged course of intravenous acyclovir

This drug can be started empirically if there is initial clinical or laboratory-supported suspicion for HSV 1 encephalitis, while awaiting results of the more definitive CSF PCR test to return, which can take several days

Other causes of viral encephalitis are managed with supportive care, including analgesics for headache and anticonvulsants for seizures, as appropriate

8. Progressive multifocal leukoencephalopathy

Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease of the CNS caused by infection of oligodendrocytes by the John Cunningham (JC) virus

JC virus is a ubiquitous polyomavirus for which most humans are seropositive because they were exposed early in life

The virus becomes activated and causes PML in the context of immune suppression such as from HIV or with immunomodulatory treatment for illnesses such as multiple sclerosis(Natalizumab) and Crohn disease

The presentation may be insidious, and patients may present with cognitive dysfunction, encephalopathy, ataxia, visual symptoms or weakness, depending on the cerebral territories involved

MRI of the brain shows patchy nonenhancing foci of T2 hyperintensity within the subcortical white matter (figure)

Treatment in HIV patients involves antiretroviral therapy and supportive therapy when appropriate

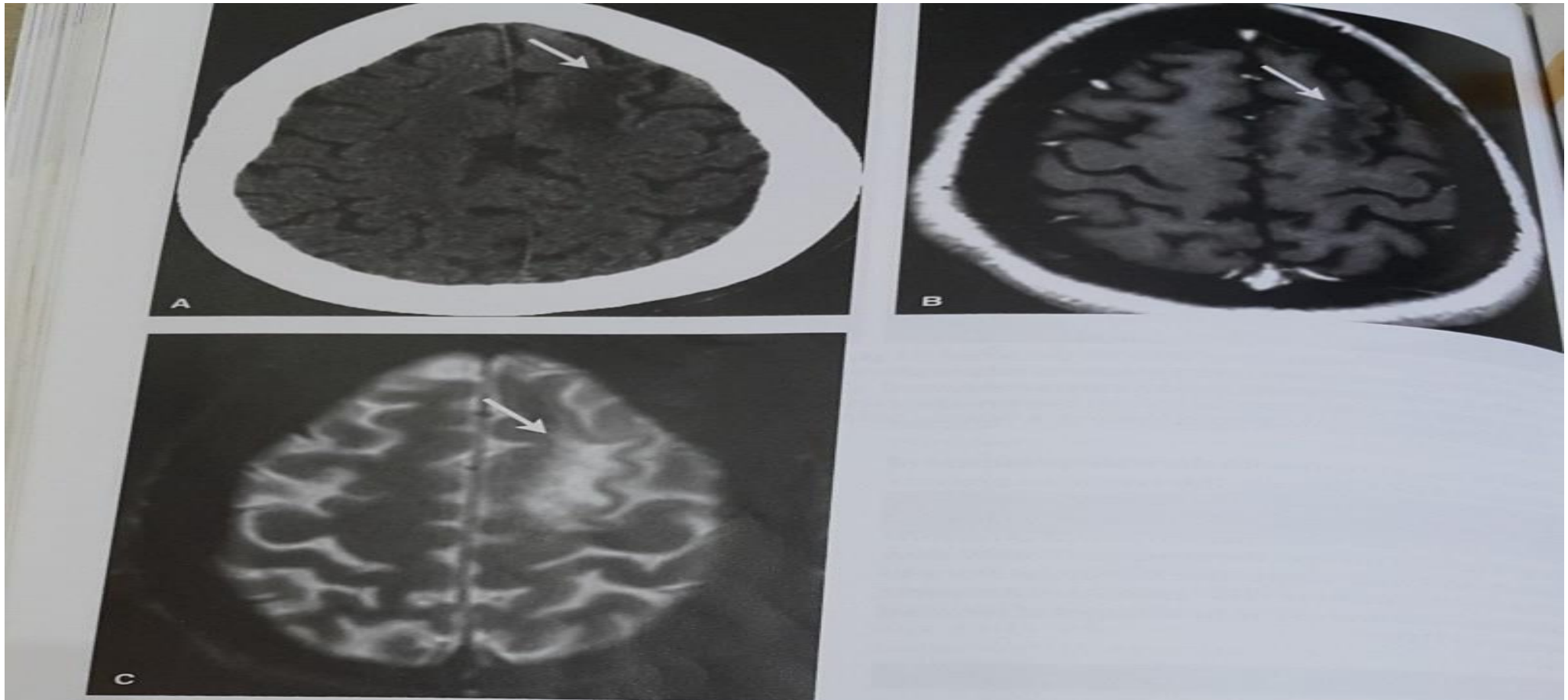

FIGURE 21-12. *Progressive multifocal leukoencephalopathy:* **(A)** axial CT; **(B)** postcontrast T1-weighted MRI; **(C)** *T2-weighted MRI. Images show a subcortical focus of abnormality within the high left frontal lobe (arrows), corresponding to the motor association region. The characteristic features of this demyelinating process inclu minimal to no mass effect, even when very large, and essentially no contrast enhancement or hemorrhage. A low T-cell count reflecting an immunocompromised status is also key to the diagnosis. In an immunocompete patient, differential diagnostic considerations for this type of lesion include posterior reversible encephalopath syndrome, which can have a similar appearance. [CT, computed tomography; MRI, magnetic resonance ima (Reprinted with permission from Brant WE, Helms C. Fundamentals of Diagnostic Radiology. 4th ed. Philadel PA: Lippincott Williams & Wilkins; 2012. Figure 7.14.)*