Review Article

Neurosurgical infections

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Abstract

The central nervous system is a very delicate and vulnerable organ which enjoys protection by layers of coverings. It is described as an immunological vacuum, and when afflicted by infections the outcome is most often devastating. Factors leading to compromise of the host defense play a major role in establishing neurosurgical infections. A number of such factors can either be avoided or minimized. Over the past decades, these infections have been fatal. However, more recently, the advent of newer more effective antibiotics, improved bacteriological studies, advanced imaging facilities, and meticulous surgical techniques have turned around the outcomes. This article will review infections of the central nervous system of neurosurgical significance.
Keywords: Neurosurgical; Infections; Bacterial; Fungal; Viral; Parasitic

Introduction

The practice of medicine has been greatly advanced by the technological improvements of the last century. The treatment of neurosurgical infections has particularly improved dramatically. The development of newer antibiotics ,advances in bacteriology and imaging, and precision in surgical procedures have transformed diseases that were previously associated with high mortality into entities that routinely have complete cures. Two main factors, among others, have significantly influenced the natural history of neurosurgical infections. These factors are the host defenses and the antibiotic characteristics.

Host Defenses

In the central nervous system, host defenses comprise two main categories: the anatomical barrier and the immunologic response to microbial invasion.
 The anatomical barriers include skin, subcutaneous tissue, bones of the skull , spinal column and the meninges, guard against microbial penetration. When any of these protective barriers is breached by surgery , trauma and congenital defects, the risk of infection rises significantly.

The immunologic response to invasion by microbes involves three components: humoral response, cellular response, and complement system. These mechanisms are normally absent in the central nervous system (CNS) in the absence of microbial provocation. The CNS has in fact been considered an immunologic vacuum that is slow in the recruitment of systemic host defenses in confronting any microbial penetration. This characteristic permits a small number of organisms the ability to invade, multiply quickly , and harm the host with an attendant higher mortality compared to infections in other parts of the body. It is documented that there is no evidence of antibacterial activity in the cerebrospinal fluid (CSF) as would be found elsewhere in the body [1, 2] and the immunoglobulin levels in the CNS are characteristically low. The 1gG and 1gA CNS levels are 0.5% of serum, and 1gM levels are less than 0.1% [3].   In purulent meningitis the levels of immunoglobulins are low and rise slowly.
In the normal state, usually there are no polymorphonuclear leukocytes circulating in the CSF and there are no phagocytes seen on antigen

presentation. Phagocytic cells migrate into the CSF in in the absence of opsonizing antibodies. It is known that infected CSF is chemotactic for polymorphonuclear leukocytes but the beneficial effect of leukocytes in CSF is still unclear. Two studies describing the role of leucocytes in CSF present conflicting results: in one study bacterial meningitis with low CSF leukocyte was associated with high mortality , and in another study there was high CSF leucocytes and bacterial proliferation progressed unhindered . The later point is explained by the lack of complement and opsonizing antibodies necessary to enhance opsonophagocytic activity and bacterial killing. Worthy of note o is the fact that polymorphonuclear leukocyte diapedesis(migration) is sluggish (14 – 16 hours), giving room for the initial invading bacteria to proliferate unhindered.

Infection may establish itself due to the low levels of Complement concentrations in normal CSF. This localized complement deficiency is further worsened by the presence of leukocyte proteases, released during meningitis and will lead to degradation of complement components.   Further deficiency of complement components in the CSF is influenced by the variable permeability of the blood-brain barrier (BBB), enhanced clearance from CSF, and decreased production within the CNS.

Infection of the CNS may be due to some host factors. These factors include acquired immunodeficiency syndromes, other T-cell defects, asplenia, hypogammaglobulinaemia, and leukopaenia,

Antibiotics and the central nervous system

The blood-brain barrier (BBB) separates the intravascular compartment from the CSF, thereby restricting efflux of substances, including antibiotics into the CSF. The BBB is commonly divided into blood-brain and blood-CSF barriers.[4]

Most antibiotics penetrate the BBB poorly. However, permeability increases significantly in the presence of bacterial meningitis by disrupting tight junctions between endothelial cells and increasing the number of pinocytic vesicles.   Consequently, antibiotic penetration into CSF increases significantly. Besides the BBB, a number of characteristics of the drug molecule are among important factors affecting CSF antibiotic concentration. These include molecular weight, lipid solubility, degree of ionization, serum protein binding, and the mode of removal of the drug from CSF.

Since most antibiotics penetrate the CSF by passive diffusion across the BBB, small molecules with simple structure and low molecular weight achieve higher CSF levels than do large, complex molecules. Lipophilic drugs (e.g. chloramphenicol, sulfonamides, and rifampicin) will penetrate well into CSF even in

response to infection or injury, but they are inefficient the absence of meningeal inflammation. Some drugs with lower lipid solubility that are usually highly ionized at physiological pH e.g. most β-lactam penetrate the BBB poorly in the absence of meningeal inflammation. Molecules with high serum protein binding (> 90%) enter the CSF with difficulty as only the free molecules can enter the CSF with significant ease. Finally, some antibiotics may be removed from CSF to the blood by an active transport "pump" mechanism in the choroid plexus (e.g. penicillins, cephalosporins),.   This mechanism is energy dependent and is inhibited by conditions such as meningitis and uraemia.[4, 5]

Scalp infections

The scalp is a common site for infection. The danger of its infection stems from its closeness to the skull and brain, and the possibility of spreading disease.

Scalp anatomy has an important bearing on understanding the outcome of scalp infections. Of its five layers (skin, connective tissue, galea aponeurotica, loose connective tissue, and pericranium), the first three move as a unit. Access of bacteria to the subgaleal space may permit extensive spread of infection and may produce osteomyelitis, epidural or subdural infection, or brain abscess via the diploic or emissary veins of the skull.

The vascular supply of the scalp is abundant, conferring a natural resistance to infection, but also providing a potential route for haematogenous seeding from other locations. Also the extensive anastomosis of vessels of the scalp, face and neck allow retrograde extension of scalp infection. Lymphatic channels form a rich network in the neighbourhood of the vertex. Enlargement and tenderness of the lymph nodes may indicate an unrecognized scalp infection.

Spontaneous scalp infections

Spontaneous scalp infections are rare, produced by almost any type of pyogenic bacterium, virus and fungus. Non healing ulcers and chronic sinus tracts should be suspected of harbouring infection. Alopecia or scalp thickening may precede frank scalp infection.[6] Therefore, preoperative evaluation of a craniotomy patient should include scalp examination. Any evidence of infection should delay the procedure as possible.

Carbuncle:

Many patients present with a carbuncle which is a type of a simple staphylococcal folliculitis. It a deeply infiltrating lesion situated in the thick, inelastic skin such as in the region of the occiput.[7] It begins as a very tender nodule that enlarges over 5

days after which it discharges pus. Central ulceration develops to involve the full thickness of the scalp. Treatment consists of surgical drainage and culture of drained pus. A broad spectrum antibiotics should be commenced before culture results are obtained.

Atypical organisms may be the cause and so cultures for aerobic and anaerobic bacteria and fungi, as well as biopsy of the adjacent scalp should be obtained following debridement.[8]

Necrotizing fascitis

It is a rapidly progressive, highly destructive rapidly,fatal bacterial invasion of the subcutaneous and subgaleal spaces. Spread is limited by the scalp attachments: the supra orbital ridges anteriorly, and the occipital protuberance posteriorly. It commonly occurs spontaneously, following minor trauma, and may present following craniotomy. There is a diffuse patch or erythema and progresses and rapidly undermines the scalp with widespread necrosis and usually, associated with severe toxaemia. There is sloughing and ulceration due to vascular thrombosis in the subcutaneous tissue and deep dermis . The entire calvaria may be denuded as the pericranium becomes incorporated into a layer of thick fibrous tissue. Bacteriology shows multiple organisms, often staphylococcus epidermidis, staphylococcus aureus, and streptococcus spp.   Immediate generous débridement, with copious antibiotic irrigation of the subgaleal space is advocated. Multiple postoperative inspections and débridement are usually necessary with a planned second-look operation after the first 24 hours. Split skin grafting can then be applied after two weeks.   Systemic toxicity must be treated aggressively. Mortality may be from multiple organ failure but commonly there is septic shock , cardiac failure and respiratory failure . Hyperbaric oxygen may help in the treatment of necrotising fascitis.

Infection in Scalp Lacerations

Most scalp wounds heal satisfactorily, even those that are grossly contaminated at the time of closure. Any delay in débridement increases the risk of infection. Unfortunately, minor scalp wounds are usually ignored, and these may result in serious infections[9].

Certain principles are to be followed. The entire scalp must be inspected thoroughly and cleansed to remove debris. The depth of the would must be checked for skull penetration. Any CSF leak should be noted and a skull fracture with dural tear suspected. Because the scalp is highly mobile, a skull fracture may be beyond the limits of the wound. The wound must be thoroughly cleaned with a sterile solution and foreign material and devitalized tissue removed.
Lacerations that do not sever the aponeurotic layer do not gape, and can easily be re-approximated. Lacerations through the galea result in a wide separation and require suturing of the galea as well as the skin. Tetanus prophylaxis should be administered.

Osteomyelitis Of The Skull

Osteomyelitis of the skull is a relatively rare disease. However, the proximity of the brain and the propensity to formation of epidural abscess necessitates prompt diagnosis and definitive early treatment. The skull infection originates from three key sources : (a) Paranasal sinusitis, mastoiditis, or otitis; by direct spread (b) haematogenous spread secondary to bacteraemia or fungaemia; (c) penetrating trauma or craniotomy.

War wounds tend to be more extensive and contaminated than civilian wounds, but principles of treatment are same .

Pain and swelling at the wound site should subside within a few days of closure. Clinical manifestation of traumatic wound infection may become apparent within days to months after closure.When an infected scalp wound is suspected, treatment should be immediate.[9]   The wound is opened, all purulent material evacuated and suture materials removed, and devitalized tissue excised.   To ensure satisfactory recovery of the exposed skull, the wound should be closed loosely over a drain, which should be removed within 24 to 48 hours. A single layered closure with an inert suture material, followed by a gentle compressive dressing to obliterate any dead space, are applied[9].
Staphylococcus species are the commonest culprits, and appropriate systemic antibiotics should be started before culture result is obtained.   Persistence of infection after adequate treatment should suggest subgaleal spread, underlying osteomyelitis, or erroneous identification of the offending organism. Signs of meningeal irritation, seizures, new focal neurologic deficits, or a decreased level of consciousness may signal penetration of the infection beyond the galea, which warrants a lumbar puncture and a further investigation including a contrast enhanced CT scan and MRI.

Craniotomy infections

Most recent studies report risk of infection of 1 to 3%, although re-operation on glioma patients is associated with rates as high as 11%.[10] This increased risk may be attributed to reopening of surgical wounds and prior irradiation of the scalp.   Other factors contributing to the risk of infection after craniotomy include long duration of surgery, multiple incisions, placement of a drain , foreign body, the presence of a CSF leak, and immunosuppression of the patient.[11]
Treatment   consists of systemic antibiotics and surgical débridement.   The risk of spreading superficial infection to the deeper layers after craniotomy is sufficiently serious to warrant antibiotic administration even before cultures are obtained. Early detection of a craniotomy flap infection is important by looking out for the local and systemic signs of infection. Once infection is identified, the wound must be opened. All purulent material and

visible sutures should be removed, followed by mechanical débridement and irrigation. Dura should not be violated unless subdural infection is suspected. The standard technique is removal of an infected bone flap to prevent it being a nidus for chronic infection. A subsequent cranioplasty is then done later.

Contiguous spread

The contiguous spread of infection from frontal sinusitis is the most frequent source of skull osteomyelitis. Invasion of the skull by the direct spread of infective organisms occurs via the diploic veins. The diploic space communicates freely with the valveless veins of the mucous membranes of the frontal sinuses, so septic emboli can translocate easily to the dura. The arterial blood supply to the inner table of the skull is diminished and retrograde thrombosis can occur, creating an avascular outer table. When the pericranium is elevated from the underlying bone by a process of necrosis and suppuration, swelling and oedema occur, commonly referred to as pott's puffy tumour. Other symptoms of osteomyelitis include pain, erythema, and fever. Patients with intracranial extension may present with seizures, neurological deficits or persistent headaches.[12]

Staphylococcus is the single most important pathogen in osteomyelitis of the skull. [12] Systemic antibiotics have not eliminated the need for surgery in the treatment of osteomyelitis associated with sinusitis. A wide craniectomy of all necrotic bone to the freely bleeding bone edge must be ensured. Involved sinuses and associated empyema should be drained and frontal sinuses exenterated when they communicate with the intracranial space. The dura should be left intact whenever possible.[11,12]

Haematogenous Skull Osteomyelitis

Reports of osteomyelitis of haematogenous origin are rare. Syphilitic and typhoid osteomyelitis are extinct in most developed countries, but very occasionally occur in developing countries. Disseminated coccidiodomycosis, a fungus, frequently involves bone by haematogenous spread.[13] The presentation is that of small cystic areas of skull destruction with a significant risk of meningeal spread. Extensive bone debridement is successful in the treatment of disseminated coccidiodomycosis by decreasing the antigen load in the immunosuppressed patient.[13]

## Postoperative Osteomyelitis of the Skull.

Osteomyelitis may follow craniotomy or trauma . The presence of a compound fracture significantly increases the risk of osteomyelitis as does inadequate initial treatment.[14]

Craniofacial reconstruction, is considered a clean procedure, may presents a significant risk of osteomyelitis because there may be ; violation of mucosal barriers so opening the oronasal cavity to the cranium and bone grafting is often required. Risk of infection can be minimized by the use of staged procedures. Incisions and bone grafts should be limited whenever possible[14]
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Diagnosis of skull Osteomyelitis.

Diagnosis of osteomyelitis is mainly clinical, manifesting as pain, swelling, and fluctuance. X-ray and radionuclide imaging may help to confirm or localize the infection. Radiographic evidence is seen only after 30 to 50% of bone is demineralised, and thus may be absent in the acute phase of osteomyelitis.[15] The pattern is that of a moth-eaten appearance due to avascular necrosis. Chronic osteomyelitis is identified by the presence of radiopaque sequestra (calcified necrotic bone). CT scan has the same lag phase behind the acute osteolytic changes (Fig. 1) but is still superior to x-rays in imaging skull base and identifying intracranial empyema or abscess.

Radionuclide scans using technetium – 99m and Gallium – 67 are more sensitive than x-ray and CT scan.[15] Other diagnostic studies such as leukocyte count, and erythrocyte sedimentation rate, are normal too often to be of diagnostic value. However, when elevated, they may be useful indicators of treatment efficacy, if followed serially.
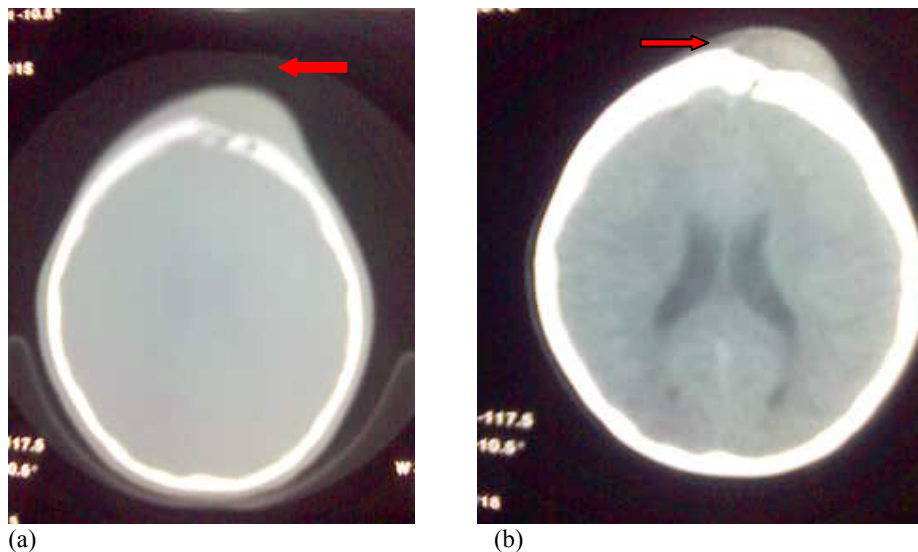
(a)   (b)

(Fig. 1) Bone window (a) and plain (b) CT images demonstrating moth eaten appearance of chronic osteomyelitis on the frontal bone with overlying soft tissue swelling- Pott's Puffy tumour. See spear

Antibiotics in the treatment of Osteomyelitis of the Skull.

The major effect of antibiotics has been on the adequate treatment of sinus infection, with resultant decrease in the risk of osteomyelitis. Staph. spp and possibly methicillin – resistant staph spp must be taken into account. Immunosuppression may lead to fungal involvement. Salmonella is common with haemoglobinopathies; pseudomonas in drug addicts and diabetic patients; Escherichia coli, in neonates. The antibiotics are adjusted when culture results are available. Generally, 1 to 2 weeks of intravenous antibiotic therapy followed by 6 to 12 weeks of oral therapy is recommended. Resolution of infection can be documented by a serial gallium nucleotide scans (where available), and a normal ESR value

Bacterial Meningitis

Most cases of meningitis are caused by bacterial or viral infection of the leptomeninges and CSF, but the list of other causes is extensive. This disease is associated with significant morbidity and mortality, but currently there is improved survival of patients with bacterial meningitis, owing to major advances in antimicrobial therapy.
Atypical and new bacterial forms causing meningitis are encountered in patients with infection following craniotomy , shunt placemment and in immunosuppressive conditions These present new challenges in management and the outcome is less predictable..[1,2,3]

Causative organisms

The incidence of the leading causes of bacterial meningitis varies strikingly with age of the patient. This relationship is so important that it must always be taken into account when planning the therapy of patients with bacterial meningitis. The table below gives a summary.

Table 1 - Common bacteria causing meningitis

Organisms	Ages			
	a	b	c	d
Str agalctiae (grp	+++	+	-	-
Bacilli -ve	+++	+	+	+
L monocytogenes	++	+	+	+
H influenzae	++++	+	+	
Str pneumoniae	++	+	+++	+++
N Meningitidis	-	+++	++	++
S aureus	+	+	+	+
S. epidermidis	+	+	+	+

A=0-1mo b= 1mo-4yr c=4-30yr d=>30Yr

Infections following neurosurgical procedures, are quite different from those found in other situations..[16] Staphylococcus aureus may be involved in postoperative meningitis but gram-negative bacilli are also regularly encountered in these patients. Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus spp., Enterobacter spp, and Acinetobacter spp are regularly isolated. When a CSF leak is present, Streptococcus pneumoniae is the commonest organism. When a ventricular shunt is present, staphylococcus epidermidis is the leading cause of infection, followed by diphtheroids such as propionibacterium acnes. This unique distribution of causative organisms requires an approach to therapy that is quite different from that used in non-neurosurgical patients.[10,16]

Pathology

Grossly, post mortem brain specimen is frequently swollen, sometimes with evidence of herniation. The sulci may be obliterated following cortical oedema.

Pus may be found in sulci and major fissures, often in contact with veins and venous sinuses. Exudates may surround the base of the brain or the cerebellum and dorsum of the spinal cord.

Associated findings may include subdural effusions, subdural empyema, venous sinus thromboses, cortical infarctions and secondary hydrocephalus. Small perivascular collections of inflammatory cells may occur within the brain itself.

Microscopy reveals purulent inflammation of the leptomeninges with dilated thrombosed veins and a variable amount of haemorrhage. The superficial layers of the cerebral cortex may be inflamed, and perivascular collections of leukocytes may be found deeper in the brain. Organisms, often in large numbers, may be identified by special stains. In viral meningitis frank pus does not form and the inflammatory cells are primarily mononuclear. In cases of chronic meningitis from tuberculosis or cryptococcosis, the exudate is also primarily mononuclear, sometimes with granulomas.[17]

Clinical features

Bacterial meningitis may be preceded by symptoms of upper respiratory tract infection. The typical manifestations include high fever, severe headache, photophobia, neck stiffness, nausea, vomiting, and anorexia. Back pain, myalgia and altered consciousness are frequent.

The patient is acutely ill, with fever often above 39°c. There may be petechial rash. There may be evidence of portal of entry such as otitis media, sinusitis, mastoiditis, orbital cellulitis, and bacterial endocarditis. Signs of meningeal inflammation (kernig's and Brudzinski's) are present. Cranial nerve abnormalities occur in 10% of cases, mainly transient CrN VI palsy. Papilloedema is not common. In advanced cases with raised intracranial pressure the pupillary signs of tentorial herniation may be present. In premature infants and neonates the manifestation may be atypical with absent neck stiffness and low or normal temperature.

The post neurosurgical patient with bacterial meningitis may also have atypical features. Nuchal rigidity, headache, and altered consciousness are less reliable as diagnostic features because they may also be caused by the recent operation. Body temperature of above 38% in the post operative period should suggest the possibility of meningitis.

Diagnosis

The diagnosis of meningitis is based mainly on examination of the CSF. The more important tests are summarized below.

Table 2 - Diagnostic tests on CSF sample for acute bacterial meningitis.

Tests	Findings
Standard tests	
Cell count	usually >500 cells/mm^3, with predominance of polymorphonuclear leukocytes.
Protein level	usually >100 mg/ell
Glucose level	usually < 40mg/dl; CSF: serum ratio usually < 0.4
Gram's stain	For common pathogens, positive in 70 – 80%; for gram-negative bacilli positive in 50%.
Counterimmuno electrophoresis or Coagglutination	Positive in 70-80% of cases; helpful in patients taking antibiotics and for early identification of organisms.
Supplementary Tests	
Lactic acid level	usually ≥ 35 mg/dl
Limulus lysate assay	+ve in meningitis caused by gram-negative bacilli.
India ink preparation :	positive for cryt. neoformans
Slide agglutination	+ve for cryptococcal antigen
Wet mount	" for amoeba

Complications

Bacterial meningitis is associated with many complications some of which may be life threatening by themselves. These include cerebral edema,

seizures, venous thrombosis, brain abscess, subdural effusion, subdural empyema, shock and persistent or recurrent fever.

Treatment

The principles of treatment are, to provide adequate supportive care through the critical period of illness, and to eradicate the organism with appropriate antibiotic therapy.

Supportive measures include prevention of shock and cellular oedema by strict fluid input and output, adequate control of respiration, control of seizures and control of raised intracranial pressure.

With regards to specific antibacterial therapy, the ideal antibiotic for this serious infection should have the characteristics of good CSF penetration, bactericidal activity in the CSF, and proven efficacy in clinical practice. Because there is no room for error in the early period of treatment, high dose parenteral antibiotic therapy should be used in all cases.

Brain Abscess

A brain abscess is a localized suppurative process within the brain parenchyma caused by a wide variety of bacteria, fungi, and protozoa. Despite advances in diagnosis and antibiotic therapy, the incidence of brain abscess does not appear to be changing and may in fact be increasing. Computerized tomography (CT) has become indispensable in determining the location, size and pattern of contrast enhancement of the lesion. In the past few decades, there has been a steep rise in the number of immunosuppressed patients and a concomitant rise in brain abscess caused by opportunistic organisms, which present diagnostic and therapeutic challenges.[18]

Pathogenesis

Predisposing factors and sources

Majority of brain abscesses arise by direct spread from paranasal sinuses, middle ear, or mastoid infections. Infection can spread from the paranasal sinuses by way of retrograde thrombophlebitis through the valveless diploic veins to either the frontal

or the temporal lobe. A single abscess is usually formed, located superficially in the brain near the site of the primary infection. Frontal sinusitis can result in a brain abscess in the anterior or inferior portions of the frontal lobe; sphenoid sinusitis, an abscess in either the frontal or the temporal lobe; maxillary sinusitis, an abscess in the temporal lobe; and ethmoidal sinusitis, an abscess on the frontal lobe. Dehiscence of the posterior table of the frontal sinus, either from trauma or osteitis, provides an important avenue for direct extension of infection into the brain.[18]

Metastatic brain abscesses arise by haematogenous dissemination of infection from a primary site that is remote from the brain. The abscesses that form are frequently multiple and occur at the junction of white and gray matter. The incidence of matastatic brain abscess in each part of the brain is proportional to its regional blood flow, therefore, most common in the distribution of the middle cerebral artery (primarily the parietal lobe) but can also be found in more unusual locations such as the cerebellum and brain stem.[18]

Apart from 20-37% of patients whose primary site is unknown,[19] the commoner sites include skin pustules, dental or tonsilar abscesses, chronic pulmonary infections, osteomyelitis, septicaemia, and bacterial endocarditis. Craniocerebral trauma is a well known predisposing factor to brain abscess, especially if there are retained foreign bodies such as bone fragments or an overlying wound infection. Brain abscesses seldom occur from bullet injuries, because the clinging debris is often sterilized by the heat of the metal. Additionally, basal skull fractures with CSF leak can predispose to meningitis and brain abscess. Previous craniotomy and shunt catheters are also a known cause.

The incidence of brain abscess is increased many folds in immunocompromised patients, who include those with diabetes, tuberculosis, sarcoidosis, those on anticancer chemotherapy, organ transplant recipients, those on prolonged broad spectrum antibiotic therapy, and patients with acquired immunodeficiency syndrome. They usually suffer opportunistic infections that are of low virulence and pathogenicity to humans such as fungi, parasites and unusual bacteria.[18,19]

Histogenesis

The CNS is vulnerable to destruction by infectious processes and is incapable of mounting a significant defense by itself. A gliotic zone develops slowly around a site of infection and does little to limit the spread of infection. Early cerebritis (days 1 to 3) demonstrate a local inflammatory response surrounding the adventitia of blood vessels. The cerebritis is associated with the development of oedema and the beginning of a central necrotic region. In the late cerebritis stage (days 4 to 9) the most

important histological changes take place. Oedema reaches its maximum with the increase in size of the necrotic center and the formation of pus. A reticulin network is set down around the periphery of the zone of inflammation by fibroblasts that serves as the precursor to the collagen capsule. Early capsule formation (days 10 to 13) occurs when the collagen network is consolidated and the necrotic center is isolated from the adjacent parenchyma. This process is the most crucial in order to protect the surrounding

tissue from injury. In the late capsule formation (day 14 and later) the abscess has five distinct regions: (1) a necrotic center, (2) a peripheral zone of inflammatory cells and fibroblasts, (3) Collagen capsule, (4) zone of neovascularity, and (5) zone of reactive gliosis with oedema[18]

Various factors influence the rate and extent of capsular formation, which include the causative organism, the origin of infection, the host's immune competence, and use of antibiotics and corticosteroids.[19]

Clinical features

The clinical presentation of patients with brain abscess can be protean and depends on the location, size, number of the lesions, virulence of the causative organism, host immune status, associated oedema, and degree of intracranial hypertension. Abscesses, being acute inflammatory processes, usually present with a short clinical course. The short history is the main clinical deference with other intracranial mass lesions. Symptoms present within 2 weeks.

The main symptom is headache that is constant and recalcitrant. When associated with raised intracranial pressure (ICP) there will be nausea and vomiting.
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The raised ICP when accompanied by mass effect can cause an alteration in level of consciousness, an important prognostic factor. Focal neurologic deficits are location dependent and include hemiparesis, aphasia, visual field cuts, nystagmus, and ataxia. Seizures present in about half the cases preoperatively. Fever is usually low grade. Menigismus and papilloedema are not very uncommon features. Sudden deterioration may suggest uncal or tonsilar herniation, or even subarachnoid or intraventricular rupture.

Laboratory analysis is of little value in the diagnosis. Lumbar puncture is contraindicated. CSF and haematologic findings are nonspecific.

Radiologic evaluation

Computed tomography is the most important factor in improving the prognosis of brain abscess, along with development of antibiotics. CT classically shows a smooth thin regular contrast enhanced wall with a central region of hypodensity (fig. 2). The ventricular side of the wall is usually thinner. MRI is still being evaluated in the diagnosis of cerebral abscess, but it gives images similar to CT
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(a)

(b)

(c)

(d)

Fig. 2. CT scan images showing smooth, thin, regular contrast enhanced wall with a hypodense centre, surrounded by oedema. Cerebral abscess of the frontal (a and b) and parietal (c) lobes. Note the aerocoele in (b), depicting the previous aspiration site, and the multiple cerebral abscesses in (d).

Management Of Cerebral Abscess

Non-operative treatment

The choice of antibiotics for any bacterial abscess depends on the causative organism, penetration of the antibiotic into the abscess cavity, its bactericidal or bacteristatic capacity, and its bacteriological spectrum. The size of the abscess cavity is also important. Abscesses greater than 2.5cm in diameter seldom respond to antibiotic therapy. Once tissue has been obtained empirical antibiotics are initiated, and directed at the most likely organisms even before definitive culture results are available. It is advocated that because of the existence of stereotaxic operative techniques, rarely should lesions be treated with antibiotics before cerebral tissue is obtained, except in the presence of uncontrollable bleeding diathesis or a lesion smaller than 1.5cm in a neurologically intact patient with a clear source of infection. In the case of multiple abscesses, antibiotics can be used as sole treatment for lesions smaller than 2.5cm if cultures from one of the abscesses have yielded a causative organism.

Operative treatment

The operative management of cerebral abscesses is based on two separate procedures: aspiration with the help of stereotaxic guidance or complete excision.[18,19,20]

Aspiration has produced excellent result as it allows for precise localization and decompression of abscess cavity with minimal tissue damage. This is of great advantage when dealing with deeply seated lesions, with those in eloquent areas, or with multiple abscesses. It can be done under local anaesthesia, hence reducing the surgical risk.[20] In the cerebritis stage when an open procedure may cause significant neurological deficit, a needle biopsy can retrieve tissue for culture. Antibiotic use alone is often curative at this stage.

Excision is indicated in certain circumstances. Post traumatic abscesses associated with retained foreign bodies can only be approached in this fashion because a cure can be effected only after complete removal of foreign material. In an abscess following a CSF leak, abscess excision combined with leak repair is mandated. Fungal abscesses are often only cured through total excision. Cerebellar abscesses should be explored through craniectomy, because any failure of treatment can be rapidly fatal.

Management of Multiple Abscesses.

The following are recommendations by Manelak and Resenblum[21] as regards the management of multiple abscesses.

1. If multiple ring enhancing lesions are found, emergent surgery for all abscesses greater than 2.5cm in diameter or for those causing marked mass effect should be undertaken either by excision or preferably by stereotaxic aspiration.
2. If all abscesses are less than 2.5cm and are not causing mass effect, then the largest abscess should be aspirated for microbiological identification.
3. Antibiotics should be withheld until pathological material is obtained for culture.
4. Broad-spectrum antibiotics should be used until culture results are available and the antibiotics can be adequately tailored to these results. Afterwards, antibiotics are continued for minimum of 6 to 8 weeks and in the immunocompromised often more than 1 year.
5. Post operatively, CT scan or MRI should be performed weekly or at any sign of deterioration. Repeated surgical drainage should be undertaken if;

   (a) there is an enlargement of an abscess after 2 weeks of treatment or after clinical deterioration or
   (b) there is failure of an abscess to diminish in size after 4 weeks of antibiotic therapy.

Use of Corticosteroids

The use of corticosteroids in the treatment of cerebral abscess is disputed. Most surgeons believe that its use should be primarily in clinical situations when the cerebral oedema and the mass effect created by it are significantly debilitating or pose imminent danger to the patient's survival.

Follow up

It is paramount for all patients with cerebral abscess to undergo serial radiography to evaluate the resolution of the initial process. Weekly studies should be done during the course of antibiotic therapy, and 1 week afterwards then followed 1 month later, then every 2 months until the process has resolved. MRI has not shown any significant advantage over CT scan, and it is only logical to use the same modality throughout the course of any given patient.

Complications

The first most dreaded complication of cerebral abscess is herniation secondary to mass effect. This is avoided by identifying such patients before they have deep changes in their mentation. If these changes do occur, drainage of the abscess cavity

should promptly reduce the mass effect. Also use of corticosteroids is indicated here.

The second most dreaded complication is abscess rupture into the ventricle and subarachnoid space, a condition that in the past was considered universally fatal. It is now treated with ventricular drainage and systemic and intraventricular antibiotics. It remains a curable but serious complication.

Prognosis

The single most important factor affecting outcome is the preoperative neurological findings. The mortality ranges from 0-21% in alert patients to 60% in those with signs of herniation, and to 89% in those with coma. But recently with introduction of CT scan, improved bacteriological techniques, more versatile antibiotics, and stereotaxic surgery most major centers report a mortality of less than 10%.

The morbidities are mainly focal neurologic deficit, cognitive impairment, and seizures. These are also on the decline because of the above mentioned factors.

Intracranial Epidural Abscess

Aetiopathogenesis of Intracranial Epidural Abscess

Intracranial epidural abscesses are rarely encountered in neurosurgical practice. They mostly occur as complications of sinusitis. Septic thrombophlebitis, or direct infection to the epidural space, may occur secondary to sinusitis, leading to an epidural abscess. The abscess is limited by the dural attachment at suture lines along the base of the skull and the inferior sagittal sinus.[22]

Prognosis

Intracranial epidural abscesses unassociated with subdural empyema or intracerebral infections carry an excellent prognosis, particularly when detected early and radical resection of the purulent material has been performed.

Subdural Empyema

Subdural empyema connotes diffusion of pus over the cerebral convexity, subfrontal space, sylvian fissure, and interhemispheric region. This spread often leads to bilateral infection.

Most commonly, intracranial epidural abscesses develop secondary to foreign body implantation by trauma, adjacent osteomyelitis or post operative neurosurgical or otolaryngological complications, or sequel to sinusitis or mastoiditis. Other less common factors include orbital suppurations, congenital dermal sinuses, and sagittal sinus phlebitis. Abscesses following sinusitis are caused by streptococci whereas S. aureus and S. epidermidis follow trauma. Other unusual organisms have also been associated with abscesses, such as Actinomyces and Arachnia propionica.

Clinical features and Diagnosis

A preceding history of trauma, paranasal sinusitis, mastoiditis, or otolaryngological or neurosurgical procedure is usually obtained. There may be headache at the overlying area of infection, periorbital swelling or a chronic draining sinus along an incision line. A patient with a suspected epidural empyema who develops progressive deterioration in level of consciousness, a focal neurological deficit, and/ or seizure should be evaluated urgently for an associated subdural empyema (a more dreaded complication of epidural abscess).

Treatment

The hallmark of treatment are prompt recognition of the features, early evacuation of abscess, and resection of potentially infected bone. Broad spectrum antibiotics are given empirically pending bacteriological diagnosis. Prophylactic anticonvulsants and corticosteroids may not be necessary unless in the presence of a subdural empyema.

The dura must not be violated except with radiologic evidence of an associated subdural empyema, as seen in 20% of cases.[22, 23]

The most life threatening subdural empyema is the spontaneous or acute variety. It is commonly related to paranasal sinusitis, ear infection and haematogenous disease.

Subacute subdural empyema uncommonly follows trauma, and caused by staphylococcus, serratia and diphtheroids. It is generally walled off and responds well to appropriate treatment.

Chronic subdural empyema, or infected subdural effusion has been seen mainly in infants. Hemophilus Influenza is the common offending organism.

Clinical Presentation

Acute subdural empyema presents with headache, altered sensorium, focal neurological deficit, seizures, pyrexia, nausea and vomiting. A history of paranasal sinusitis and ear suppuration may be evident. Once a focal deficit or altered sensorium develops, the neurological deterioration rapidly progresses to a devastating outcome if the empyema is not treated radically.

Subacute subdural empyema commonly follows a burr hole infection. It may also follow an infected craniotomy or trauma. The incision usually shows evidence of infection. There may be low-grade fever and meningismus. A focal neurologic deficit, a significant alteration of mental state, and seizures are less likely. The empyema is commonly walled off by adhesions and is limited to the surgical site. This has a good prognosis.

Chronic subdural empyema presents with pyrexia, irritability, and lethargy in infants. Seizures, a full or tense anterior fontanelle, and a progressive increase in head circumference are common. Past history of meningitis is commonly obtained in these children.

Diagnosis

CT and MRI are now the 'gold standard' in diagnosis of subdural empyema. CSF examination and skull x-rays are often of limited value.

CT usually demonstrates paranasal sinusitis, an epidural collection, and skull changes of osteomyelitis. The subdural empyema appears as a hypodense and diffuse collection which may be associated with mass effect and surrounding parenchymal oedema.

T1- weighted MRI images demonstrate diffuse low signal extradural collections and a relative high signal on T2-weighted images. Enhanced T1-weighted axial images reveal a peripheral ring enhancement.

Initial Treatment

A satisfying outcome in subdural empyema depends on prompt intervention. It is fatal, with a mortality of 42% in comatose patients, and 6 to 14% in awake to moderately lethargic patients. Once diagnosis is established, administration of anticonvulsants is recommended due to high likelihood of seizures. Antibiotics are instituted empirically pending culture results.

Surgical Management

It is recommended to approach a subdural empyema via an appropriate craniotomy, coupled with gentle suction and copious antibiotic irrigation. Dura should be meticulously closed and the bone flap replaced after thorough cleaning. Serial follow-up CT scans are recommended for early identification of residual or recurrent collections. Parenteral antibiotics are continued for 4 to 12 weeks, depending on response.

Subacute subdural empyema is managed by re-exploration of surgical site, antibiotic irrigation and excision of loculating membranes.

Chronic subdural empyema is managed through burr hole evacuation, copious antibiotic irrigation and the use of drain.[23]

Granulomatous Disorders Of The Central Nervous System

Chronic granulomatous disorders of the CNS are relatively uncommon and hence usually present diagnostic difficulties especially to the unwary.

Tuberculosis

Over the past 50 years, vigorous public health control measures and the availability of anti tuberculosis chemotherapy have reduced greatly the prevalence of pulmonary tuberculosis world wide, especially in the developed world. Incidence rates vary widely between countries in inverse relation to socioeconomic conditions. However, the advent of HIV has worsened the incidence recently, especially in HIV endemic areas.

Although the incidence of pulmonary tuberculosis (TB) has declined in the US, the number of extrapulmonary TB cases, including TB infections of the CNS has remained constant at approximately 4000 new cases per year. TB meningitis accounts for approximately 15% of extrapulmonary cases or about 0.7 % of all clinical TB in the US.[24]

CNS TB comprises three clinical categories: Meningoencephalitis, intracranial tuberculoma, and spinal tuberculous arachnoiditis (Pott's disease). Each category has its variable manifestation.

Diagnosis.

The patient with TB meningoencephalitis usually presents with malaise, lassitude, low-grade fever, intermittent headache, and often a personality change. This may progress to meningismus, vomiting, confusion, cranial nerve palsies, and signs of upper motor neuron lesion. In untreated cases death may ensue in 5 – 7 weeks.

The clinical diagnosis of TB meningitis begins with high index of suspicion. Delay in diagnosis and treatment negatively influences the prospect for recovery with minimal neurological sequelae.

A positive tuberculin skin test may be of some diagnostic importance. However, a negative is of no significance as false negative results are seen in a variety of situations. Mild anaemia may be present. Full blood count and even Erythrocyte sedimentation rate are usually normal.

Blood chemistry is usually normal except in the presence of syndrome of inappropriate ADH secretion, which has been observed in a minority of cases of miliary tuberculosis complicated by meningitis.

The classic CSF findings are elevated protein levels, a decreased glucose concentration, and lymphocytosis. Repeated (serial) CSF examinations give better results. Cultures of CSF will be positive in 80% of cases, but if the patient is to survive, therapeutic

decisions will have to be made long before the results of the culture are available.

Neuroradiological Findings

CT scan or MRI are the current imaging modalities of choice in the diagnosis and treatment of TB of the CNS. They allow the assessment of the developments in the clinical course, evaluation of hydrocephalus and ventriculomegaly associated with basilar meningitis of CNS Tuberculosis. Enhanced CT or MRI in cases of miliary TB with no clinical meningitis have revealed multiple small lesions compatible with tuberculoma.[25] Tuberculoma, tuberculous brain abscess, and focal tuberculosis meningoencephalitis are either closely related processes or different stages of the same process.

Pathology of Tuberculosis

At autopsy, the brains of patients dying with TB meningitis reveal thickening and fibrosis of the arachnoid, especially over the base of the brain. Small tubercles may be seen. In pyogenic meningitis, cerebral infarction may be seen due to intraluminal thrombosis of major cerebral vessels.
On microscopy, the meninges show caseating granuloma, and partial destruction of cranial nerves. Typical tubercles consisting of a central area of caseous necrosis surrounded by epithelioid macrophages and lymphocytes with prominent langhan's giant cells are seen in active TB meningitis.

Surgical Treatment

Surgical decompression of the ventricular system in cases of hydrocephalus with raised intracranial pressure, should not be delayed in patients with progressive neurological impairment. Decompression is achieved readily by ventriculostomy or ventricular shunting. Laminectomy and abscess drainage, on the other hand, can be done to decompress spinal lesion.

Cryptococcosis

Cryptococcosis is a systemic fungal disease of man and animals caused by Cryptococcus neoformans. CNS infection commonly manifests as meningitis. While modern treatment has improved the prognosis considerably, CNS cryptococcosis is increasing due to the ever rising population of immunocompromised subjects. C. neoformans has a world wide distribution and, at present, four subtypes designated A to D are recognized. All the serotypes are believed to be equally virulent.[26]

The intense fibrosis that occurs in TB meningitis may lead to obliteration of the subarachnoid space and subsequent hydrocephalus.

Treatment and outcome

The most important principle of therapy is that it should be initiated on the basis of strong suspicion and not delayed until proof has been obtained. The outcome is usually good when therapy is initiated before development of focal neurological deficit or significant alteration of consciousness.

Medical Therapy

The medical treatment requires a multidrug therapy, consisting of 3 to 4 anti tuberculous drugs. Isoniazid remains the cornerstone of treatment as it has good CSF penetration even without meningeal inflammation. Current recommended regimens for treatment employ the use of drugs such as isoniazid, rifampicin, ethambutol and pyrazinamide.[24] Corticosteroids administration may give dramatic response in patients with rapidly deteriorating mental status, increased intracranial pressure, cerebral oedema, focal neurologic signs, spinal block, hydrocephalus, and basilar optochiasmatic pachymeningitis. The decision to employ corticosteroids should rest on a strong presumptive or positive diagnosis. Their use in uncertain cases can be especially devastating if the patient has fungal meningitis, and the benefits of steroids must be judged against this possibility.[24]

Following inhalation of the organism primary pulmonary infection and subsequent dissemination may occur if the host defenses allow. On dissemination, C neoformans invades multiple organ systems, with a predilection for the CNS. Cryptococcosis of the CNS manifests as one or more of the following syndromes: Chronic meningitis, encephalitis, or cryptococcomas. Immunosuppressive therapies and diseases act as predisposing factors.[26]

Cryptococcomas are not very common and present as focal neurologic abnormalities including hemiparesis, hemianopsia, and focal seizures. If spinal cord is involved, there may be quadriparesis or paraparesis.
Headache (75%) and mental status changes (50%) are the commonest presentations in cases of meningitis and meningoencephalitis. Nausea, vomiting, pain and nuchal rigidity also occur. As many as 15% have no symptoms referable to the nervous system and yet have infection. As a result it is important to perform a lumbar puncture in suspected cases.[26]

Clinical Diagnosis

With the exception of isolated cryptococcoma without meningeal involvement C. neoformans of the CNS is diagnosed by CSF examination. However, lumbar puncture should not be done in the presence of features of raised intracranial pressure until the presence of an intracranial mass is ruled out, preferably by CT scan.

Lumbar Puncture reveals elevated intracranial pressure, lymphocytic pleocytosis, elevated protein level and reduced CSF glucose. India stain is positive in 75% of cases of meningitis and CSF culture positive in 90% of cases. Other tests include cryptococcal antigen titre, which may be elevated.[26] The radiologic findings in CNS cryptococcosis are non specific. All patients should undergo CT or MRI to diagnose cryptococcomas as well as detect hydrocephalus. On CT cryptococcomas appear as homogeneously enhanced lesion, that are isodense or lucent before contrast infusion. CT findings may show no abnormalities in meningoencephalitis.[18]

Pathology

The meninges are thickened. Small cysts are located within the cortex and deeper. There is little or no surrounding inflammatory reaction or gliosis. In areas of inflammation there are lymphocytes, plasma cells, eosinophils, and multinucleated giant cells. India ink demonstrates the capsule clearly.

Medical Treatment

Combination therapy of Amphotericin B with 5-flurocytosine gives a favourable response. Intrathecal amphotericin B is reserved for cases of relapse or the critically ill.

Surgical treatment

Craniotomy and resection of the granulomatous mass is the ideal in patients with mass effect. Hydrocephalus may also require surgical intervention. Neurosurgical assistance may also be required to insert ventricular access device (Ommaya reservoir) to instill antifungal drugs and obtain CSF for repeated analysis.

Other granulomatous CNS disorders include Aspergilosis, blastomycosis, Histoplasmosis, Sarcoidosis, Brucellosis, sporotrichosis, and Leprosy.

Fungal Infections Of The Central Nervous System

Most fungal infections of the CNS of utmost neurosurgical importance have been mentioned under granulomatous CNS disorders. However, other fungal infections worthy of mention are candidiasis, Histoplasmosis, Coccidiodomycosis, blastomycosis and narcodiosis.

Parasitic Infections Of The Central Nervous System

The parasites that most commonly cause human disease are nematodes and protozoa. They are usually localized in certain organs of the body, but in the present of background malnutrition or immunosuppression they become disseminated disease, with some having special predilection to the CNS.

Cerebral Amoebiasis

Entamoeba histolytica, a motile histotoxic protozoon, is the causative agent of cerebral amoebiasis, which primarily afflicts young men. It is a relatively rare complication of intestinal amoebiasis, which is endemic in Africa, Latin America, South East Asia and Mexico. CNS infection is thought to result from haematogenous spread from the gastrointestinal tract. It results in multiple, poorly demarcated necrotic lesions located at the gray-white mater junction. Occasionally, amoebae can be identified within these lesions. They present with focal neurological deficits, raised intracranial pressure, seizures, and meningismus. Most patients have liver abscesses. Diagnosis is established by recovering the organism from the gastrointestinal tract or liver, or with serological tests.

CT images of the brain show focal hypodense lesions consistent with cerebritis early in the disease and one or more ring enhancing lesions with surrounding oedema later.[27] Treatment is with metronidazole and aspiration of large cerebral abscesses.

Echinococcosis

Echinococcosis, or hydatid disease is caused by the tape worm Echinococcus granulosus and is endemic in the Mediterranean area, South Africa and parts of South America. Canines, the definitive hosts, harbour the adult warm in their small intestine. Humans, intermediate hosts, ingest the egg via faecooral route, which hatch, releasing the larvae (oncosphere). These penetrate the gut wall and spread primarily to the liver and lungs.

CNS involvement occurs in less than 2% of cases. The larvae forms a primary cyst which enlarges at a rate of 1 to 5 cm per year. Primary cysts of the brain are usually single, but occasionally multiple.

CNS hydatid disease manifests depending on the location and size of the cyst and include raised intracranial pressure, seizures, and focal neurological deficit.

Diagnosis is usually established by serological tests. ELISA is sensitive but not specific. The double-diffusion test in agar, using arc-5 antigen from sheep hydatid fluid, is more specific. On CT, hydatid cysts may be unilocular or multilocular. Unilocular cysts are usually large, spherical and no surrounding oedema. They often lie adjacent to the

inner table of the skull, with density similar to that of CSF. The cyst wall does not enhance, though calcified in 20 to 40% of cases. Multiloculated cysts may be clustered or scattered and often associated with oedema and contrast enhancement of the cyst wall. The finding of multiple small low density, secondary cysts within a primary cyst is pathognomonic of cerebral hydatid disease. MRI shows the primary cyst as a well defined lesion with signal intensity similar to that of CSF in both T1, and T2 weighted images.

The primary treatment of CNS hydatid cyst is surgical excision of the intact cyst. Care must be taken not to spill the contents into the surgical field. If the cyst cannot be removed injection of 20% saline, formalin, cetrimide, or silver nitrate kills the protoscoleces. Long term therapy with albendazole is also effective.

Toxoplasmosis

Toxoplasmosis is caused by Toxoplasma gondii, an obligate intracellular pathogen. It has a worldwide distribution especially in areas where cats are used as pets, or where improperly cooked meat is consumed. Infection can also follow transfusion with contaminated blood products. The organism can survive up to 50 days in refrigerated anticoagulated blood. Fetal infection can occur from acute material infection especially during first trimester.

T. gondi exists in three forms: trophozoites, tissue cysts, and oocysts. Lymphnodes, skeletal muscle, myocardium, retina, placenta, and brain are the usual target organs.

CNS infection is accompanied by mononuclear cell infiltrate and microglial module formation. It can be associated with focal or diffuse necrotizing encephalitis, meningitis, or abscesses. In the immunocompromised, lesions tend to develop in the basal ganglia, white matter, or gray-white interface.

CNS involvement is rare, and usually seen in the immunocompromised patient. It is the commonest cause of encephalitis and brain abscesses in AIDS patients, and manifests as headache, altered consciousness, seizures and focal neurological deficits.

Congenital toxoplasmosis produces widespread inflammation and necrosis. Necrotic areas are most prevalent in periventricular and periaqueductal regions. Other manifestations include cortical atrophy, ventriculomegaly, and intracranial calcifications. Victims suffer seizures, severe developmental delays and cerebral palsy.

Toxoplasmosis is best diagnosed using one of several serological tests, including Sabin-Feldman dye test, indirect fluorescent dye test for IgG, and DS-1gM-ELISA. On CT there may be one or more rounded isodense or hypodense lesions with ring enhancement,

but immunocompromised patients show no enhancement. MRI is more sensitive.

Biopsy of an intracranial lesion may be required to establish a diagnosis. The treatment include a combination of folate antagonists pyrimethamine and sulfadiazine. Response to therapy can be monitored with serial MRIs, which should show a decrease in oedema, mass effect, and the number and size of enhancing lesions within 2 to 4 weeks of therapy.[28]

Other parasites of neurosurgical importance include cysticercosis, schistosomiasis, Trypanosomiasis, Trichinosis, and Plasmodium spp(cerebral malaria).

Viral Infections Of The Central Nervous System

Human Immunodeficiency Virus Type 1

Over 50% of patients infected with Human Immunodeficiency virus type 1 (HIV-1), the agent of the acquired immunodeficiency syndrome (AIDS), will develop symptomatic neurological disease. In some autopsy series, neuropathologies are found in over 90% of cases.

The spectrum of neurological disorders that complicate HIV-1 infection is extremely wide. The illnesses can be classified as those due to the infection, and those that arise as a consequence of immunosuppression. The precise mechanism by which the virus produces the primary neurologic disorders has not been fully understood. The common disorders include encephalopathy, myelopathy, peripheral neuropathy, and inflammatory myopathy. Secondary neurologic diseases include cerebral toxoplasmosis and cryptococcal meningitis particularly, and neoplasms such as primary CNS lymphoma.[29]

Primary HIV 1 Related Neurological Disease.

HIV-1 Meningitis.

Meningitis is frequently associated with HIV-1 infection. Since clinical features are nonspecific, careful microbiological and cytological studies of the CSF are required to establish the diagnosis. When evidenced only by CSF pleocytosis, HIV-1 itself is perhaps the commonest cause of meningitis in infected patients. Other common causes of meningitis include Cryptococcosis, tuberculosis, syphilis, and lymphoma.

HIV-1 Encephalopathy.

The incidence of HIV-1 encephalopathy has been about 16-30%. An apparent decline may be the result of effective antiretroviral therapy. However, the

incidence at autopsy is also varied between 17% and 70%.

The pathology is characterized by brain atrophy with sulcal widening, ventricular dilatation, meningeal fibrosis, white matter pallor, diffuse astrocytosis, and multinucleate giant cells.

The encephalopathy typically sets in during moments of advanced immunosuppression and intercurrent systemic disease. It manifests with disturbance in intellect, fatigue, malaise, forgetfulness, incoordination and gait disturbance.

CSF studies show mononuclear pleocytosis with a low count and elevated protein. The main value of brain imaging is to rule out other neurological disorders. CT and MRI show cerebral atrophy. There may be diffuse, patchy or punctate white matter disorders.

Zidovudine has been confirmed to be beneficial in the treatment of HIV-1 encephalopathy.[29, 30]

HIV-1 Associated Myelopathy

HIV-1 associated myelopathy is a unique degeneration of the spinal cord seen at autopsy in more than 20% of cases. It begins insidiously and is characterized by leg weakness, gait impairment, paraesthesia, vague leg discomfort, and bladder and bowel incontinence. The disorder typically occurs with advanced immunosuppression. Patients have spastic paraparesis, lower extremity hypereflexi (except when diminished as a result of concomitant peripheral neuropathy), gait ataxia, and impaired sensation. Usually, the lower extremities, are symmetrically involved. Other HIV-1 related afflictions of the spinal cord include acute myelopathy, spinal myoclonus, and a relapsing remitting myelopathy.
Histology reveals loss of myelin and spongy degeneration, particularly in the dorsal and lateral columns. Microglial nodules and HIV-1 multinucleate giant cells are also seen.
No treatment has been demonstrated unequivocally to be of value in vacuolar myelopathy.

Secondary (Opportunistic) HIV-1 Related Neurological Diseases.

Viral Infections

Progressive multifocal leukoencephalopathy
This is caused by JC virus, a papovirus. It stays latent in the reticuloendothelial system in 75% of the population, and is reactivated at the time of immunosuppression. Once the infection is established in the brain, oligodendrocytes and astrocytes become infected. . Limb weakness, cognitive dysfunction, visual loss, gait disturbance, speech and language defects, and headache are the presenting symptoms.
Histology reveals demyelination, giant astrocytes with pleomorphic hyperchromatic nuclei, and oligodendrocytes containing large abnormal nuclei. CT reveals nonenhancing hypodense white matter lesion without mass effect in the centrum semiovale, usually in the parieto-occipital region, and the cerebellum. MRI is very sensitive. CSF studies may not be very helpful. Brain biopsy may be employed to confirm diagnosis.
Zidovudine, cytosine arabinoside and interferon-alpha have been proposed as therapies. Survival time ranges 0.3 to 18 months.

Cytomegalovirus.

Human cytomegalovirus (CMV) is a ubiquitous, enveloped, DNA – containing herpes virus that infects leukocytes during primary infection of healthy young adults. It then remains latent and reactivated only during periods of immunosuppression. A single patient may harbour multiple strains of the virus.
Microscopic lesions include microglial nodules and inclusions in the brain tissues. Guancyclovir is shown to be effective in the treatment of disseminated CMV, but it is associated with neutropaenia.[30]

Fungal, Protozoal, and Bacterial infections

Fungal infections associated with HIV-1 infection include cryptococcal meningitis, candidiasis, coccidiodomycosis and histoplasmosis.
Toxoplasmosis is a common protozoa associated with HIV-1 infection. Common secondary bacterial infections include mycobacterial infections, neurosyphylis, Listeria monocytogenes, and Norcadia astroides infections.

Neoplasms associated with HIV-1 infection.

The advent of HIV-1 infection has increased the incidence of CNS lymphomas dramatically. Systemic lymphoma metastatic to the CNS, and primary CNS lymphoma are the commonest neoplasms associated with HIV-1 infection.
The role of the neurosurgeon include shunting for hydrocephalus, implantation of reservoirs for intrathecal chemotherapy decompression procedures for intraspinal neoplasms, and also brain biopsy to establish definitive diagnosis.[29, 30]

Other Viral Infections Of The Central Nervous System

Herpes Simplex Virus

This is one of the herpes viruses. Herpes simplex virus type 1 (HSV-1) is a ubiquitous agent against which approximately 90% of adult population have developed antibodies. It is usually acquired through nonsexual activity. This is in contrast to the Herpes simplex virus type 2 (HSV-2) acquired through sexual activity. Infection of herpes simplex virus is through intimate, personal contacts, and acquired from virus shed at a mucosal surface or another peripheral site. Following viral replication at the primary site, it is

transmitted by retrograde axonal flow via the peripheral nerves to sensory ganglia where latency is established. The virus may be reactivated by mechanical trauma, exposure to cold, sunlight, wind, menstruation or emotional stress. Once reactivated the virus travels along dermatomes to produce lesion on ocular, genital or cutaneous sites. It becomes localized and heals in the immunocompetent, and may become disseminated in the immunocompromised patient.[30]

Herpes simplex virus Type 1 – Encephalitis

Herpes simplex virus encephalitis is caused by type 1 virus in 95% of adult cases. It is an acute haemorrhagic necrotizing encephalitis associated with severe morbidity. The disease is mainly localized to the subfrontal and medial temporal lobes, explained by entry of the virus via the olfactory mucosa, and spread along the olfactory bulb and nerve. It is characterized by acute onset headache, behavioural changes, focal neurologic signs, seizures, and coma. 70% of untreated cases die and survivors often have severe neurological sequelae.

There are usually electroencephalographic changes. CT is normal in the initial stage, and abnormalities are indicative of poor prognosis , which is characterized by areas of haemorrhage in the temporal or frontal region. MRI is most sensitive for early diagnosis, showing selective temporal lobe gray matter oedema and thickening, and in the later stage, haemorrhages, and encephalomalacia. CSF studies show non specific changes.

With the advent of relatively nontoxic and effective antiviral agent to treat HSV encephalitis, the trend is now to treat empirically with acylovir rather than perform brain biopsy. However, there may be indications for intracranial pressure monitoring in patients with severe encephalitis.

Herpes Simplex Virus Type 2

Aseptic meningitis caused primarily by HSV-2 has been associated with genital herpes virus infection in immunocompetent patients. It presents with a self limited meningeal irritation, fever, headache, vomiting, photophobia, and nuchal rigidity. Signs of encephalitic illness are rarely present. CSF findings include elevated intracranial pressure, lymphocytic pleocytosis, elevated protein content, and moderate hypoglycorrhachia. Infectious virus can be isolated from CSF.

Creutzfeldt – Jakob Disease.

Creuztfeldt-Jakob disease (CJD) is one of the diseases caused by the "unconventional" viruses. It has three distinct manifestations; the sporadic cases, the familial cases, and those from iatrogenic transmission. The incidence for sporadic cases is 1 per million. The familial type is linked to gene mutation on chromosome 20. Direct inoculation is the only proven way of disease transmission. The initial rise in incidence of the disease following the use of growth hormone extracted from cadaveric pituitary gland has been reduced since introduction of a recombinant source. Corneal transplant, placement of deep electroencephalogram electrodes into the brain, use of infected neurosurgical instruments, and dural grafts have all been implicated in disease transmission.

The patients present with higher cortical dysfunction, dementia, behavioural and sleep disturbance, intellectual decline, and myoclonic jerks. Following accidental transmission incubation period is 4 months to 2 years, but up to 30 years has been reported. Once symptoms and signs appear, most patients live 6 to 12 months. No treatment is known.
Electroencephalogic changes (repetitive, high-voltage, triphasic-sharp discharges with a periodicity of 1 to 2 seconds) in a patient with dementia and myoclonus, give the presumptive diagnosis of CJD. CT and MRI images are nonspecific.[30, 31]
Brain biopsy could help provide the classic histological picture of all spongiform encephalopathies: loss of neurons, neuronal vacuolation, astrogliosis, and absence of inflammatory response. Although brain biopsy remains the best diagnostic tool for most atypical dementias, including CJD, this approach merits very careful consideration because there is no known treatment for CJD, and decontamination of surgical instruments requires special protocols.

Conclusion

Neurosurgical infections are caused by a variety of organisms ranging from bacterial, fungal, viral to parasitic. The modes of presentation in most of these infections are similar, but yet each has its subtle distinct fingerprint, which requires knowledge, diligence, and meticulousness to diagnose. Prompt diagnosis and active early treatment are the hallmarks of a satisfactory outcome.

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