*VIRAL MENINGOENCEPHALITIS Viral meningoencephalitis is the most common cause of CNS infection. Et.  Enteroviruses are the most common cause of viral meningo-*

*encephalitis. It spread directly from person to person with incubation period of ≈ 5 days and the disease ranges from mild, self-limited illness to severe encephalitis resulting in death or significant sequelae. Parechoviruses may be an important cause of aseptic meningitis or*

*encephalitis in infants; its manifestations are similar to that of the*

*enteroviruses with the exception of more severe MRI lesions of cerebral*

*cortex and at times an absence of CSF pleocytosis.  Herpes simplex virus type 1 (HSV-1) is an important cause of severe,*

*sporadic encephalitis. Brain involvement usually is focal with progression to coma and death in many cases without antiviral therapy.  Herpes simplex virus type 2 (HSV-2) may cause severe encephalitis*

*with diffuse brain involvement in neonates who usually contract the*

*virus from their mothers at delivery.  Varicella-zoster virus (VZV) may cause CNS infection (especially cerebellar ataxia) in associated with chickenpox.  Cytomegalovirus (CMV) infection of the CNS may be part of congenital*

*infection or disseminated disease in immunocompromised hosts, but infection does not occur in normal infants and children.  Epstein-Barr virus (EBV) has been associated with myriad (numerous) CNS syndromes e.g. Alice in Wonderland syndrome.*

*Measles virus can cause acute, subacute or subacute sclerosing parencephalitis (SSPE).  Mumps virus meningoencephalitis is mild, however deafness may occur.  Rabies virus cause the most severe encephalitis that is always fatal.*

*Arboviruses are arthropod-borne agents, responsible for some cases during summer months. West Nile virus is common in some areas of the world. Meningoencephalitis may occasionally caused by respiratory viruses or it may follow live virus vaccins.*

*Path. Neurologic damage is caused by direct invasion and destruction of neural tissues by actively multiplying viruses or by host reaction to viral*

*antigens. A marked degree of demyelination with preservation of neurons and their axons represent "postinfectious" or "allergic"*

*encephalitis. Most viruses cause diffuse encephalitis; whereas HSV-1 cause severe focal encephalitis in the temporal lobe. Rabies virus is mainly affect the*

*basal ganglia.*

*C.M. The clinical course resulting from infection with the same pathogen is widely variable. Some children may appear initially mildly affected, only to lapse into coma and die suddenly. In others, the illness may be*

*very severe followed by complete recovery. The onset of illness is generally acute. The presenting manifestations in older children are headache & hyperesthesia; whereas in infants,*

*irritability & lethargy. Other manifestations include: fever, nausea, vomiting, photophobia, pain in neck, back and legs, mental dullness progressing to stupor in combination with bizarre movements and convulsions. There also may be focal neurologic signs, unprovoked emotional outbursts & loss of bowel and bladder control. Enteroviruses may cause anterior horn cell injury and acute flaccid paralysis. Exanthemas (skin rash) may precede or accompany the CNS signs, especially with echoviruses, coxsackieviruses, VZV, measles, rubella. Cx. Guillain-Barre syndrome, Transverse myelitis, Hemiplegia, and*

*Cerebellar ataxia. D.Dx. Include many infectious & non- infectious CNS diseases. Inv. CSF exam; see the table above.*

 *Serology of blood may be useful in determining the etiology of some*

*viral CNS infection e.g. arboviral infection, but it is of no value in Enteroviruses.  EEG show diffuse slow wave activity.  CT & MRI show swelling of brain parenchyma.*

*Note: HSV encephalitis is suggested by focal seizures & focal finding on EEG, CT, or MRI especially if involve the temporal lobe. Rx. HSV encephalitis is treated with IV Acyclovir, 10 mg/kg every 8 hr*

*by infusion over 1 hr for 2-3 wk. Otherwise, Rx of viral*

*meningoencephalitis is supportive (although some literatures suggest Pleconril for enteroviral infection). Mild disease may require only symptomatic relief. More severe disease may require hospitalization and intensive care.*

 *Headache and hyperesthesia are treated with rest, non–aspirin-*

*containing analgesics & reduction in room light, noise, and visitors.  Pain may require codeine, morphine (but better avoided).  Fever; acetaminophen.*

 *Vomiting; phenothiazine.*

 *Poor oral intake; IV fluids same of that in bacterial meningitis. TPN may be required in prolonged coma.  Anticipate and be prepared to manage; convulsions, cerebral edema, inadequate respiratory exchange, ARDS, disturbed fluid and electrolyte*

*balance (commonly due to SIADH), aspiration and asphyxia, cardiac or*

*respiratory arrest of central origin. ↑ ICP should be closely monitored (better by pressure transducer in the epidural space) & managed accordingly. Pg. Most children recover completely from viral infections of the CNS, especially those due to enteroviruses, whereas others have high*

*mortality rate e.g. rabies & HSV, or have severe sequelae e.g. intellectual, motor, psychiatric, epileptic, visual, or auditory. Therefore, neurodevelopmental and audiologic evaluations should be part of the*

*routine follow-up.*

*Pv. Isolation of cases, vaccination is available for some viruses e.g. rabies, varicella, & measles with control of vector for some viral*

*infections e.g. arboviruses.*

*TUBERCULOUS MENINGITIS Tuberculosis of the CNS is the most serious Cx in children and is fatal*

*without prompt and appropriate Rx. TB meningitis complicates ≈ 0.3% of untreated TB infections in children and most common between 6 mo & 4 yr of age. Occasionally, it occurs many years after the infection. Et. TB meningitis usually arises from the formation of a metastatic*

*caseous lesion in the cerebral cortex or meninges that develops during the lympho-hematogenous dissemination of the primary infection.*

*This initial lesion increases in size and discharges small numbers of tubercle bacilli into the subarachnoid space. The resulting gelatinous exudate infiltrates the corticomeningeal blood vessels, producing inflammation, obstruction, and subsequent infarction of cerebral cortex. The brain stem is often the site of greatest involvement, which usually → dysfunction of cranial nerves III, VI, and VII. The exudate also interferes with the normal flow of CSF → communicating hydrocephalus. Profound abnormalities in electrolyte metabolism due to salt wasting or SIADH may occur. Note: TB meningitis is not necessarily associated with an obvious pulmonary*

*disease.*

*C.M. The clinical progression of TB meningitis may be rapid or gradual. Rapid progression tends to occur more often in infants and young children, who can experience symptoms for only several days before the*

*onset of acute hydrocephalus, seizures, and cerebral edema. More commonly, the signs and symptoms progress slowly over several*

*weeks which can be divided into 3 stages:- 1st stage typically lasts 1-2 wk and is characterized by nonspecific*

*symptoms e.g. fever, headache, irritability, drowsiness, and malaise. Focal*

*neurologic signs are absent, but infants can experience a stagnation or*

*loss of the developmental milestones. 2nd stage usually begins more abruptly. The most common features are lethargy, nuchal rigidity, seizures, positive Kernig and Brudzinski signs, hypertonia, vomiting, cranial nerve palsies, and other focal neurologic*

*signs*

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*The accelerating clinical illness usually correlates with the development of hydrocephalus, ↑ ICP, and vasculitis. Some children have no evidence*

*of meningeal irritation but can have signs of encephalitis e.g. disorientation, movement disorders, or speech impairment. 3rd stage is marked by coma, hemiplegia or paraplegia, decerebrate*

*posturing, hypertension, deterioration of vital signs, and eventually death. Inv. The Dx of TB meningitis can be difficult early in its course, requiring a high degree of suspicion because TST is nonreactive in up to 50% of cases, and 20-50% of children have normal CXR.*

*The most important laboratory test for the diagnosis is examination*

*and culture of lumbar CSF. (see CSF profile of TB in the table above).*

*Although the lumbar CSF is grossly abnormal, ventricular CSF can have*

*normal chemistries and cell counts because this fluid is obtained from a site proximal to the inflammation and obstruction. During early stage I, the CSF can resemble that of viral aseptic meningitis but eventually progress to the more-severe CSF profile over several weeks. The success of the microscopic examination of acid-fast-stained CSF and mycobacterial culture is related directly to the volume of CSF sample.*

*When 5-10 mL of lumbar CSF is obtained, the acid-fast stain of the CSF sediment is positive in up to 30% of cases and the culture is positive in*

*50-70% of cases. Cultures of other fluids e.g. gastric aspirates or urine can also help to confirm the Dx. CT or MRI of brain is normal during early stages of TB menigitis, but as the*

*disease progress, basilar enhancement and communicating hydrocephalus with signs of cerebral edema or early focal ischemia are the most common findings. Rx. Prompt Anti-TB with corticosteroids therapy (see Rx of TB, chapter 11). It is sometimes imperative that antituberculosis Rx be considered for any child who develops basilar meningitis with hydrocephalus, cranial nerve palsy, or stroke without apparent etiology, especially if an adult with chronic cough is in contact with the child, even if the adult is not diagnosed yet with TB!. Ventriculo-peritoneal shunting may be required for hydrocephalus*

*Pg. It correlates most closely with the clinical stage of illness at the*

*time Rx is initiated. The majority of patients in the 1st stage have an excellent outcome, whereas most patients in the 3rd stage who survive have permanent disabilities including: blindness, deafness, paraplegia, diabetes insipidus, or mental retardation. The prognosis for young infants is generally worse than for older children. Tuberculoma is another manifestation of CNS tuberculosis, a tumor-*

*like mass resulting from aggregation of caseous tubercles that usually manifests clinically as a brain tumor. Tuberculomas account for up to 40% of brain tumors in some areas of the world. In children they are often infratentorial, located at the base of the brain near the cerebellum. Lesions are most often singular but may be multiple. It can develop*

*before or during therapy of TB meningitis. The most common symptoms are headache, fever, and convulsions.*

*The TST is usually reactive, but the CXR is usually normal. CT or MRI of brain usually shows a discrete lesions with significant amount of surrounding edema. Contrast medium enhancement is often impressive and can result in a ring-like lesion. Surgical excision is sometimes necessary to distinguish tuberculoma*

*from other brain tumors. However, surgical removal is not necessary because most tuberculomas resolve with medical Rx by antiTB & corticosteroids.*

*GUILLAIN-BARRE SYNDROME Et. GBS usually follows nonspecific gastrointestinal or respiratory infection by ≈ 10 days. This include nonspecific viral infections, bacterial*

*infection e.g. Campylobacter jejuni, H. pylori, & M. pneumonia; or vaccines*

*e.g. rabies, influenza, & meningococcus. Path. GBS is an autoimmune disorder often considered as*

*postinfectious polyneuropathy due to demyelination & sometimes axonal degeneration involving mainly motor nerves, but sometimes also sensory and autonomic nerves. C.M. GBS affects people of all ages. The classic disease pattern called Landry ascending paralysis; initial symptoms include numbness and*

*paresthesia followed by symmetrical weakness in the lower limbs &*

*progressively involves trunk, upper limbs and finally the bulbar muscles (which occur in ≈ half of cases). Asymmetrical weakness occurs in ≈ 9% of cases. Onset usually gradual over days or weeks or may be abrupt → pain & tenderness of muscles initially then flaccid tetraplegia & respiratory muscles paralysis within 24hr. Dysphagia and facial weakness are often impending signs of respiratory failure and also they interfere with eating and ↑ the risk of aspiration. Some patients may exhibit symptoms of viral meningo-*

*encephalitis & others may have papilledema. Sensory nerves involvement → paresthesia; whereas autonomic*

*nervous system involvement → variation of BP or HR e.g. postural hypotension, episodes of bradycardia or asystole, as well as urinary incontinence or retention. ॐ Types (variants) of GBS:- 1. Classic type " Landry ascending paralysis" is the most common. 2. Miller-Fisher syndrome is characterized by ataxia, areflexia, &*

*ophthalmoplegia (mostly due to 6th cranial nerve involvement). 3. Chronic Relapsing (unremitting) Polyradiculoneuropathy is recur intermittently or do not improve for a period of months or years. 4. Congenital GBS is rare, improve gradually & do not require Rx.*

*D.Dx. Spinal cord lesions, Peripheral Neuropathies (toxic, infections, inborn errors of metabolism), or Neuromuscular junction disorders. Inv.  CSF protein ↑ > twice of the upper limit of normal, other profiles are normal except WBC are <10/mm3. This dissociation between high CSF protein and lack of cellular response is diagnostic of GBS.  NCV of motor nerves is greatly ↓, whereas in sensory nerves is slow.  EMG show features of acute denervation of muscle.  MRI (with enhancement) shows thickening of cauda equine & intrathecal nerve roots in >90% of cases; it also may be used to exclude other D.Dx.  CK level is normal or mildly ↑.*

*Serologic tests; Antiganglioside antibodies are mainly ↑ with axonal neuropathy.  Biopsy of nerve or muscle is usually not required. Rx.*

*Patients with slowly progressive disease may simply be observed in hospital for spontaneous remission with supportive therapy e.g. feeding, hydration, Px of bed sores & DVT, Rx of secondary infections, &*

*Rx of neuropathic pain by gabapentin or carbamazepine.  Patients initially presented with rapidly progressive disease should be*

*admitted to the ICU for observation & stabilization; in addition to the supportive care, patients should be given the following:-  IVIG in dose 0.4 g/kg/day for 5 consecutive days or 1 g/kg/day for 2 consecutive days.  Alternative is Plasmapheresis +/_ Immunosuppressives.*

*Note: Corticosteroids are ineffective in GBS.  Respiratory monitoring is mandatory by PEFR or PEEP with intervention by ETT & artificial ventilation if there is respiratory failure.  Cardiovascular monitoring by continuous measurement of HR & BP with insertion of a temporary pacemaker if required.*

*Patients with Chronic Relapsing Polyradiculoneuropathy may be*

*treated with IVIG (which can be given subcutaneously), plasma*

***exchange (upto 10 times daily), immunosuppressives, or high-dose pulsed IV methylprednisolone. Pg. GBS is usually a benign disease, and spontaneous recovery begins***

***within 2-3 wk. Most patients regain full muscular strength, although some are left with residual weakness (especially with axonal***

***neuropathy).***

***Improvement usually follows a gradient inverse to the direction of involvement. Tendon reflexes are the 1st lost (although 10% may have normal reflexes) & usually the last one to recover. Long-term outcome after complete recovery may be easy fatigability; only ≈ 7% of patients suffer from relapse.***

***Factors associated with poor prognosis include: maximum disability at the time of presentation, cranial nerve involvement, & endotracheal***

***intubation. Death may occur in GBS due to either respiratory failure or***

***cardiovascular Cxs.***