Neuropathology of Central Nervous System Infections

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Disclosures

• I have no relevant financial relationships to disclose
Learning Objectives

• Identify the morphological appearances of the various infectious agents that affect the Central Nervous System (CNS).

• Formulate diagnostic hypotheses of CNS infections according to the topography and morphological presentations of the lesions.

• Propose diagnoses of CNS infections taking into account the immunological state of the patient.
Etiology

Bacterial:

Fungal:

Parasitic: Protozoal:

Metazoal (Helminths): Cestodes:

Nematodes:

Trematodes:

Viral:
Etiology

Bacterial: Pyogenic (Gram + / -), Tuberculosis, Syphilis

Fungal: Cryptococcosis, Histoplasmosis, Mucormycosis, Aspergillosis, Paracoccidioidomycosis

Parasitic: Protozoa: Toxoplasmosis, Trypanosomiasis, Malaria, Amebiasis

   Helminths: Cestodes: Cysticercosis
   Nematodes: Strongyloidiasis
   Trematodes: Schistosomiasis

Viral: Arboviroses (Dengue, Zika), CMV, Herpes, HIV, HTLV1, Measles, Poliomyelitis, PML, Rabies.
Morphological Presentations of the Lesions

- Meningitis
- Encephalitis/Myelitis (Polio, Leuko)
- Encephalopathy/Myelopathy

- Space occupying lesions “Pseudo-tumors”
  - Abscesses
  - Granulomatous lesions
  - Non-granulomatous (necrotizing) lesions
  - Cystic lesions
  - Calcified lesions

- Vasculitis/Infarct/Hemorrhage

- Congenital Infections / Malformations
Morphological Presentations x Etiology x Host

One single agent can present with various morphological patterns (e.g. Tuberculosis, Toxoplasmosis, Cryptococcosis).

Relationship with the immunological state of the host (e.g. Cryptococcosis, Toxoplasmosis, Tuberculosis).

Relationship with the age of the host (e.g. etiology of bacterial meningitis).

Acute, sub-acute, chronic, post-infectious (e.g. Pyogenic, Dengue, Measles...
Neisseria meningitidis (Gram -) Hyper acute meningitis
Waterhouse-Friderichsen syndrome
Sub-acute / Chronic stages
COMPLICATIONS

• Ventriculitis
• Hydrocephalus
• Infarct (vasculitis, thrombosis)
• Abscess (micro-abscesses)
Ventriculitis, hydrocephalus
Venous congestion, inflammation, may cause thrombosis and venous infarct
Microabscess and large abscess
Pyogenic Abscess

Hematogenic origin
Abscesses – Surgical specimens
Pyogenic Abscess

Granulation Tissue

Fibrous wall
Pyogenic contents rich in PMN neutrophils

Gram + cocci
Less frequent bacterial abscess

Courtesy of Dr. T Freire
Filaments Grocott and Gram (+)

Diagnosis - Nocardia
TUBERCULOSIS

• Still a major health problem
• Endemic in developing countries with a large population, crowding and poverty
• Cerebral Tuberculosis
  • Tuberculous meningitis
  • Tuberculoma
  • Tuberculous abscess
Tuberculous Meningitis
Granuloma and vasculitis (infarct)
Tuberculoma
Abscess in an immunodeficient young male
Tuberculous Abscess

Ziehl Nielsen staining shows numerous acid fast bacilli
Syphilis

Meningovascular
Goma
Tabes dorsalis
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Cryptococcosis

Meningitis
(Immunodeficient)
Grocott Metenamine Silver

*Courtesy of Dr. F. Andreiuolo
47-year-old HIV+ man – Clinoid tumor
Large septate and branching hyphae - Mucormycosis
Histoplasmosis

- Histoplasma capsulatum
- Inhaled in infected dust contaminated by chicken, bird or bat excreta
- Lungs are primarily infected, but also mouth, digestive tract and skin
- Frequent involvement of lymphnodes, spleen, liver
- CNS infection is rare
Histoplasmosis – Basal meningitis
Histoplasmosis

Infarct in basal ganglia
Paracoccidioidomycosis
(South American blastomycosis)

- Paracoccidioides brasiliensis
- Organisms found in soil and vegetation
- Frequent in Brazil, Venezuela and Colombia
- Preferential sites: lungs, oral and nasal mucosae, lymphnodes
- CNS involvement is not frequent
Grocott Metenamine Silver
Unusual presentation of fungal infection
50-year-old man with a frontal cerebral tumor
Mycetoma
Etiology

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CEREBRAL TOXOPLASMOSIS

Occurs only in immunodeficient patients

• Acquired
  – Pseudo-tumoral
  – Encephalitic

• Congenital
Patient with AIDS who died in 1986
HIV patient who had Toxoplasmosis and died in 2001
Toxoplasmosis. Chronic, treated, cystic lesions containing macrophages in the periventricular region and cerebellum.
Patient with space occupying lesion operated in 2021
No information about immunodeficiency
Needle biopsy of space occupying lesion
Free forms of T. gondii
“Dirty” necrosis and hemorrhage
Vessel necrosis and thrombosis
Free forms of Toxoplasma in smear and histological section
A cyst in a smear and paraffin section immunostained for Toxoplasma and ultrastructural appearance of Toxoplasma
Toxoplasma encephalitis in immunocompromised old patient

Courtesy of Dr. F Andreiuolo
Congenital Toxoplasmosis
Amebiasis

- Entamoeba histolytica (cerebral abscess)

- Free living amebas
  - Naegleria fowleri (primary amebic meningoencephalitis)
  - Achantamoeba, Balamuthia mandrilaris (granulomatus amebic encephalitis)

- Cerebral involvement may be fatal
Granulomatous amoebic encephalitis. Foci of haemorrhagic softening.
Cerebral Malaria (occurs in the severe form of infection)

- Plasmodium falciparum
- Acquired by the bite of an infected Anopheles mosquito
- Major health care problem in many regions of the tropics and sub-tropics
- Infants and children are particularly affected
- Rapidly progressive encephalopathy with various degrees of consciousness loss and fits.
- Neuropathology helped understanding the pathogenesis
Haemzoin pigment deposition in the lining of the blood vessels (arrows) may obscure the parasites in the trophozoite stage.
Trypanosomiasis

• African (Sleeping sickness)
  – T brucei rhodesiense (east and central Africa) and gambiense (western and sub-Saharan regions)
  – Transmitted by tsetse fly
  – Sub-acute and chronic meningoencephalitis

• American (Chagas’ disease)
  – T cruzi, transmitted by reduviid buds
  – Endemic in South America especially Brazil
  – Autonomic system is particularly affected (megaviscera)
  – CNS involvement uncommon except in reactivated forms
Reactivated disease

• Appeared in endemic areas due to increase in number of immunosuppressed patients
• Extensively necrotic lesions and intense parasitism
Immunostaining for T cruzi
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Neurocysticercosis

- Cysticercus cellulosae, the larval form of Taenia solium.
- Usually found in pork (the intermediate host).
- Humans are intermediate hosts after ingesting the ova of T. solium (usually in vegetables).
- Ova develop into larvae that penetrate intestinal wall, invade lymphatic and veins, disseminate to skeletal muscle and CNS.
- Clinical features depend on number and location of the cysts.
Neurocysticercosis – surgical specimens

scolex

Degenerated

Courtesy of Dr. AC Brito
Cyst walls - various stages
Degeneration of the cysticercus leads to inflammation.
- Neurocysticercosis

Calcification
Racemose Cysticerci
Strongyloidosis

- Strongyloides stercoralis
- Wide geographical distribution, but commonest in the tropics
- Worms live in dump warm soil, deposit eggs, transform in larvae that penetrate skin.
- Larvae pass through lungs, mature in duodenum and jejunum.
- During systemic migration may end up in ectopic sites such as the CNS
- Immunosupression cause massive intestinal growth of worms, colonic ulceration and septicemia.
Strongyloides in the CSF (left) and subarachnoid space (right) of patient who died with AIDS
Schistosomiasis

• Schistosoma *mansoni, japonicum, hematobium* (Latin America, Asia and Africa)

Neuro-schistosomiasis

• CNS involvement is uncommon
• Ova reach the CNS by retrograde passage through the portal mesenteric and pelvic veins and valveless vertebral venous plexus of Batson.
• Anomalous migration of the adult close to CNS and in-situ egg deposition
• Thoracic and lower spinal cord are common locations
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Arboviruses

• Important cause of morbidity and mortality in many tropical regions
• Limited geographical distribution due to the necessity of climatic conditions for the insects to live.
• Dengue virus (Flavivirus): Transmitted by mosquitoes Aedes aegypti
• Causes benign infection but may be haemorrhagic
• Zika virus (ZIKV) - a flavivirus transmitted by the mosquito Aedes aegypti.

• Human infection varies from mild fever, arthralgia, rash, headache, and myalgia, but may be asymptomatic.
Microcephaly in Brazil – 2000 - 2015

2015 – first suspected cases

2016
CP ≤ 31.9 cm
CP ≤ 31.5 cm

Ex vacuo ventriculomegaly and calcifications
Obstructive hydrocephalus
Migration disturbances
Meningeal glioneuronal heterotopia

Cobblestone appearance of this smooth brain of an infant with congenital Zika syndrome
Spinal Cord

Lack of descending motor axons
The corticospinal tract is missing
An abscess in an HIV infected man
CMV (Herpes virus) may cause congenital encephalitis/vetriculitis/microcephaly, but also myeloradiculopathy and (in this case) abscess in immunosuppressed patients.
Progressive multifocal leukoencephalopathy - Polyomavirus – JC virus
Associated with immunosuppression
34-year-old man who coursed with progressive dementia and myoclonus
Clinical hypothesis was prion disease
Diagnosis
SSPE
Post-measles
Retrovirus

HIV

HTLV1

HTLV1

Myelopathy
Tropical Spastic Paraparesis

Affects descending and ascending tracts

Degeneration of descending motor corticospinal tract
Degeneration of ascending sensory tract
Enterovirus - Poliovirus - Poliomyelitis -
Rabies

Cytoplasmic eosinophilic inclusions in Purkinje cells - Negri bodies
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References containing illustrations included in this presentation


References