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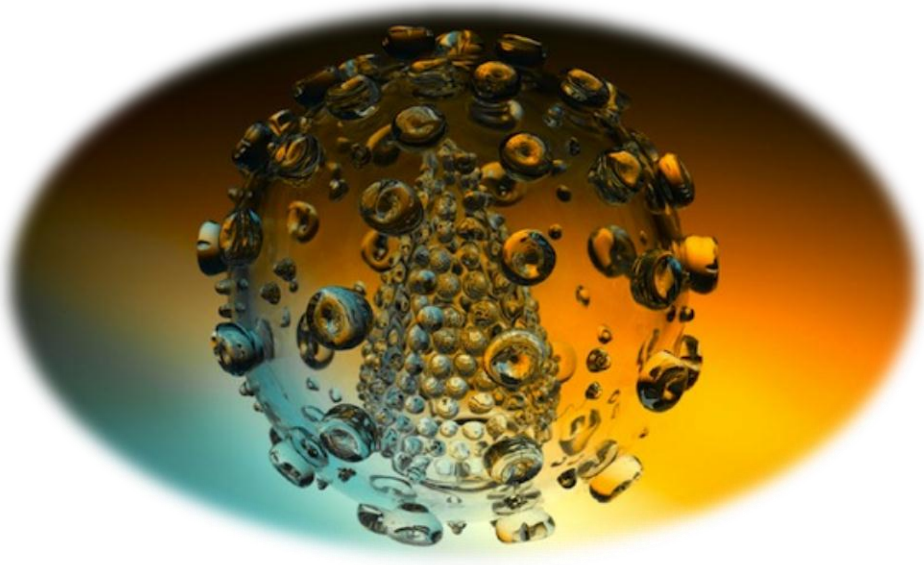
Microbiology Team

CNS BLOCK



Viral Infections of the CNS

Faisal Al Rashed	Eman Al Shahrani
Abdullah Al Turki - Ahmed Saleem	Samiha Al jetaily - Ghaida Alsugair
Tariq Al Jorf - Faisal Al Dawood	Abeer Al Suwailem - Maymonah Alabdely
Al Sulaimani - Abdullah Al Sufiani	Hayfa Alabdulkarim - Nourah Al Swaidan
Yazeed Al Qasim	Noha khalil - sama Al ohali

Done by: Maymonah Alabdely - Abeer Al-Suwailem - Ahmed Saleem

Viral Infections of the CNS

N.B. the doctor pointed at the end of the lecture that what we should focus on is the name of the viruses causing meningitis and encephalitis, and weather it's a DNA or RNA virus, and the vaccines for them if existed, and if it has treatment or no. pathogenesis, geographical distribution are not that important. Clinical manifestation are almost same for viruses causing meningitis and encephalitis and also the diagnosis is almost the same.

- **Acute viral infections of the CNS (specific symptoms appear after 5 days) :**
  1. **Aseptic meningitis & Paralysis (enteroviruses & polioviruses)**
  2. **Encephalitis (herpes simplex virus , rabies virus & arboviruses(West Nile Virus (causes both meningitis and encephalitis))**

     N.B the most important antibodies are IgA, IgG

	Viral meningitis	Bacterial meningitis
Cause	virus	bacteria
Severity	less	Quite severe A)brain damage B)hearing loss c)learning disability
	Resolve without specific treatment in a week or two	It would cause death

Cerebrospinal fluid (CSF) Analysis

	Normal	Aseptic meningitis	Septic meningitis
Color	**clear**	**clear**	**cloudy**
Cells	**<5**	**Increase 100-1000 lymphocytes**	**High/v.high 200-20,000 neutrophils**
Glucose	**45-85**	**normal**	**Low<45**
Protein	**15-45**	**normal/high 50-100**	**High>100**
Causes		**Viruses, others**	**bacteria**

Viral Meningitis (Aseptic meningitis)

1- Enteroviruses ….(Enteroviral infections are asymptomatic infections)

Family: picornaviridae Pico= small	**Structure:** Ss (+) RNA genome,Icosahedral,Nonenveloped =can resist harsh environment e.g.GIT acidity>fecal oral root in contaminated food	**Epidemiology:** **Reservoir**: human **Spread:** fecal- oral mainly (inhalation of infectious aerosols) –crowded poor hygiene & sanitation **Age:** children> adults **Seasons**: summer & fall	**Lab Diagnosis:** **Virus isolation:** stool (best), throat swabs &CSF by inoculation in cultures **CSF analysis:** glucose N or slight↓ and protein levels N or slight↑ & lymphocytosis **PCR** by detecting the EV RNA Serology: limited value	**Management & treatment:** No antiviral Rx **Prevention:** Sanitation & hygienic measures Poliovirus vaccines -IPV -OPV

- **Picornavaridae: includes**
  ---Poliovirus (1, 2, and 3 types)
  ---Coxsackievruses (A&B)
  ---Echoviruses

  ---Enteroviruses(68-71)

Picornavaridae
Pico= small, rna =RNA virus

Other etiological agents for Aseptic meningitis:

- Mumps virus
- Arboviruses
- Herpes viruses
- HIV
- Lymphocytic choriomeningitis virus

2- Poliovirus(replicates in the intestine)

Polio is also from the family of picornaviridae. Poliovirus infections are mostly asymptomatic and 1-2% cause major illness

1-Non paralytic poliomyelitis (aseptic meningitis)

2- Paralytic poliomyelitis (Flaccid Paralysis)

Pathway: Fecal oral root like other enteroviruses>travel to blood or peripheral nerves>Destruction of AHC (motor paralysis) rarely can affect brain stem (bulber poiliomyelitis)

The protection of the polio needs antibodies against all 3 types of polioviruses

Immunity: IgA & IgG= lifelong type specific immunity (in killed vaccine we only give IgG)

***Poliovirus Vaccines:**

A- Inactivated polio vaccine (IPV) (Salk,killed) (S/C or IM) for adults and immunocompramised patients

b- Live-attenuated polio vaccine (OPV) (sabin,oral) for children

OPV induces IgA which interrupts fecal oral transmission and can be found in the stool then spread to contacts and immunize them

In Saudi: First we give IPV then followed by OPV

***Poliovirus Infections:**

1-Nonparalytic poliomyelitis (Aseptic meningitis)

2-**Paralytic poliomyelitis** is characterized by asymmetrical paralysis of the muscles especially the lower limbs without sensory loss

Viral Encephalitis

Etiological agents:

- **Enteroviruses**
- **Herpes viruses (transmitted by direct skin contact or during labour)**
- **Rabies virus**
- **Arbovirus**

1- HSV (Herpes simplex virus) Encephalitis

Caused by: Herpes simplex virus -1(HSV-1)

Ds DNA, enveloped, icosahedral virus

C/F: seizures & altered mental status

High mortality rate

Dx:

MRI

CSF---lymph, glucose-N&protein.. ↑

---detection of HSV-1 DNA by PCR

Rx: **acyclovir (IMPORTANT!)**

2-Rabies Encephalitis (Acute Fatal encephalitis)

Rhabdoviridae	**Structure:** Ss(-)RNA genome Helical, nucleocapsid, Enveloped virus Bullet shaped virus	**Epidemiology:** **Reservoir:** Raccoons,foxes,wolves,and bates, also cats and dogs **Transmission:** **Common:** Bite of a rabid animal **Uncommon:** Inhalation in a bat infested cave Corneal transplant	**Lab diagnosis:** **PCR**: R.RNA in saliva **IF:** rapid virus antigen detection: neck skin, corneal impressions, brain tissue **Histopathology:** Intracytoplasmic inclusions (Negri bodies) Virus cultivation	<u>Management &treatment:</u> Preventable but not treatable Control measures against canine rabies---stray animal's control---vaccination of domestic animals -Pre exposure prophylaxis (vaccine) -post-exposure prophylaxis • Wound treatment • Passive immunization (AB around the wound) +IM. • Active immunization by HDCV (human diploid cell vaccine)

Transmitted by peripheral nerves to skin, cornea, and salivary glands

N.b ss(+) positive polarity RNA: the m-RNA will be translated directly into protein

Zoonotic (from animal carrier) disease.

- **4 phase :**

1-The incubation period: 1-3 m > longer

2-The prodromal phase:

F,H,M,A,N&V.

Abnormal sensation around the wound.

3-Neurological phase ;

1- encephalitis

Nervous , Lacrimation , salivation,Hydrophobia ,Convulsion ,coma & death .

2-Paralytic illness ; Ascending , Death , Bat**.**

4- Recovery; Extremely rare

3-Arthropod-borne viruses (Arboviruses)

Epidemiology:

Reservoir: wild birds and mammals

Vector: Mosquito, ticks and sand fly then transmitted to humans

Transmission: Bite of infected vector

Arboviral encephalitis is preventable worldwide…only <1%will develop CNS disease

- Asymptomatic infections
- Diseases: Fever, Rash & arthralgia ,Hemorrhagic fever ± hepatitis ,and CNS disease

(meningitis & encephalitis

E.g.: West Nile Virus (WNV)

Dx. :

- Isolation(Gold Standards)(Reference Lab) from sample:blood,CSF,viscera then cell culture them identify by IF
- IgM-AB-ElISA,IF :(most used)
- Arbovirus RNA by RT-PCR

Prevention:

Vector Control:

Elimination of vector breading sites using insecticides

Avoidance contact with vectors (repellants, net)

Vaccines:

- Tick-borne encephalitis vaccine
- Japanese encephalitis vaccine

SUMMARY: **The most common type of meningitis is VIRAL**, it's **aseptic** (no organisms detected by routine tests), **milder than bacterial meningitis** and **resolves by its own without treating.**

- **CSF:** **Aseptic** (Clear, mild changes or no changes in Glucose and Protein) **Septic** (Cloudy, ↑Protein ↓Glucose)

Enteroviruses:

- ***Enteroviruses*** are the most common cause of **viral (aseptic) meningitis**.
- The gold standards for diagnosis of **Enteroviruse infections: Isolation by inoculation in cultures except some strains of Cox A viruses.** The gold standard for diagnosing **enteroviruses in aseptic meningitis: PCR by detecting the EV RNA.**
- Vaccinations against enteroviruses are only available for the 3 types of Polioviruses.
- **Adults + Immunocompromised children/patients: use IPV.**
- **Children: use OPV.**
- Non-enveloped (Can resist harsh environments) e.g. GIT. Therefore, transmitted by fecal-oral root through contaminated food.

HSV encephalitis

- Rx: only treatable CNS viral infection is HSV by **Acyclovir**.
- Dx: HSV1-DNA by **PCR**

Rabis encephalitis

- Preventable but not treatable:
  - Pre-exposure: (Vaccine)
  - **Psot-exposure**
    - **Passive immunization by antibodies around the wound + I.M.**
    - **Active immunization by HDCV)**

- **Arthropod –borne Viruses**
  - Arboviruses (mostly asymptomatic), cause diseases like CNS diseases.
  - Vector: Mosquito, ticks
    - **Eg: WNV:**
    - Reservoir: birds. Vector: **mosquitoes** then transmitted to human.
    - Only <1% will develop CNS disease.
    - Dx:
      - Isolation (Gold standard) (Reference Lab) from Samples: blood, CSF, Viscera then Cell culture them Identify by **IF**
      - **IgM -AB - EIISA, IF: (most used)**
    - ***Vaccines: (in Immune compromised patient we don't give life attenuated vaccine)***
    - 1-Tick-borne encephalitis vaccine 2- Japanese encephalitis vaccine

For your knowledge the doctor pointed to **Subacute sclerosing panencephalitis** (**SSPE**) which is a rare chronic, progressive encephalitis that affects primarily children and young adults, caused by a persistent infection measles virus. And that we shouldn't confuse it with acute disseminated encephalomyelitis

Questions

Q1 the most common type of meningitis is?

1- **Viral**
2- **Fungal**
3- **Bacterial**
4- **Parasitic**

Q2 what is the only viral infection of the CNS that can be treated through drugs?

1- **Rabis encephalitis**
2- **HSV encephalitis**
3- **Arboviral encephalitis**
4- **Meningitis caused by Coxsackievruses A**

Right Answers : 1, 2