

Virology

Lecture 2

Today's lecture is about the encephalitis and rabies.

First we'll talk about **encephalitis**:

Definitions:

1. Myelitis: Inflammation of the spinal cord (E.g. Transverse myelitis).
2. Radiculitis: Inflammation of the nerve root.
3. Neuritis: Inflammation of the nerve.

CMV and AIDS can cause all the previous syndromes.

4. Encephalitis: this term includes meningoencephalitis and many of the syndromes we're going to talk about today can be presented as encephalitis alone or as meningoencephalitis, and they're very difficult to be distinguished from each other.

5. Encephalopathy.

What's the difference between "encephalitis" and "encephalopathy"?

We say encephalitis when we have infection (there's an organism) + changes in the brain parenchyma (Inflammation), whereas encephalopathy refers to any various disease of the brain whether it's traumatic, congenital, toxic, alcoholic, vitamin deficiency etc... (There's no organism involved).

Encephalitis:

1. Etiology is found in 40%, which means that in every 100 patients with encephalitis, we'll find a cause to the disease in just 40 patients.
2. There's no effective treatment in most cases, except for HSV encephalitis which can be treated by acyclovir.
3. The mortality rate ranges between (3-15) %, and this is the average because some types of this disease may be fatal and other types may be mild.
4. The disability ranges between (20-40) % and it's represented as (confusion, low IQ, dysarthria, aphasia, seizures, hemiparesis and inability to talk or work)

The disability can be reversible or permanent

Note: Encephalitis can be autoimmune.

Incidence:

1. It's a rare disease affecting 6/100000, in some countries this ratio may reach to 15/100000. In developed countries it is less common.
2. it's more common in children.
3. Encephalitis associated with MMR and VZV has decreased due to vaccination. VZV vaccine is only present in more developed countries.
4. There's a long list of causes, there're hundreds of organisms that may cause encephalitis so it's impossible to mention and memorize all of them. When we want to determine the cause we narrow down the options by looking at the viruses common in that area.
5. Emerging and Re-emerging infections: Enterovirus 71, West Nile Virus, Nipah virus ,Hendra virus, Chandipura virus.

Note: West Nile virus is considered a new virus, it started in Africa then it disseminated worldwide and it's

considered the most common cause of epidemic encephalitis.

6. Parasites, bacteria, fungi, rickettsia as well as viruses can cause encephalitis but in today's lecture we're concerned only with viruses.

Viral etiology:

1. VZV (chicken pox disease) :

- May cause encephalitis whether the infection is primary or secondary or reactivation disease.
- Children: are the targeted group, but it has decreased in children recently due to vaccination. They'll get acute cerebellar ataxia only 1 week after chicken pox rash and its symptoms are: (loss of balance, dysarthria and the patient cannot walk).
- Adults: VZV encephalitis in adults is the second most common cause of encephalitis after HSV encephalitis. It appears with VZV rash and this is how we recognize the VZV encephalitis. The problem is that 44% of adults with VZV encephalitis don't get a VZV rash and they're called (herpes sine zoster) and we need to do VZV PCR for the patient to recognize it and it's rarely done in Jordan.
- Can be treated with high doses of Acyclovir.

2. EBV:

- causes a neuroinvasive disease
- it's a very common virus.
- Syndromes are: (aseptic meningitis, gullain barre syndrome, bell's palsy, transverse myelitis, cerebellitis and encephalitis) and fortunately these syndromes are rare.
- These neuroinvasive syndromes happen during the primary infection, that's why children are mostly affected and that's why the reactivation is not a big deal in such cases.
- Absence of mononucleosis makes the diagnosis more challenging.

3. HHV6 and HHV7

- HHV6 causes Roseola Infantum and febrile seizures in children. roseola infantum starts in children as a fever then the symptoms disappear, and after that they will have skin rash, so they'll get skin rash when they're well with no fever or other symptoms and that's the difference between roseola infantum caused by HHV6 and the one the patients got from measles (In the measles the patient is sick/symptomatic when he has skin rash – has a fever, cough...etc).
- HHV6: encephalitis in children 1-10%.
- HHV7 causes encephalitis in children. (Data is still accumulating).

4. Enterovirus:

- They belong to Picornaviridae (include polio, Coxsackie, and echoviruses)
- Small, non-enveloped, single stranded RNA.
- Very common.
- They cause mostly benign illnesses such as and febrile illness. Also cause gastroenteritis
- They easily reach the CNS. Primarily causes aseptic meningitis and could also cause encephalitis that is mild and most patients recover from it without treatment.
- Encephalitis is a very rare complication in comparison to the number of people who got infected.
- Coxsackievirus A and B and Echovirus 6 and 7 are the most common types of enteroviruses which cause encephalitis.
- It's diagnosed by Enterovirus PCR in addition to the clinical features such as confusion.

- They cause encephalitis in children (10%).
- Most of their syndromes are benign, so the patient recovers quickly, One exception is enterovirus 71 which is characterized by:
 - 1) it causes a Polio-like illness.
 - 2) it causes Encephalitis in children less than 5 years old , syndromes are : (hand-foot-mouth rash, ataxia, nystagmus, monoclonus, oculomotor palsy (inability to move your eyes properly)).
 - 3) Patients die of pulmonary edema due to severe autonomic dysfunction.

5. **Human parechovirus (HPeV):**

- new viruses. (Data is still accumulating).
- Cause encephalitis in children.

6. **Arbovirus :**

- These are arthropods born viruses.
- Most important group is Flaviviruses that includes **West Nile Virus:**
 - 1) It appeared in West Nile village in Uganda and reached New York in 1999
 - 2) Most common cause of epidemic encephalitis (along with Japanese encephalitis).
 - 3) It causes febrile illness
 - 4) usually it causes a mild disease.
 - 5) Less than 1% of people infected with West Nile Virus will develop encephalitis and it will be very severe and this happens especially in patients with underlying causes such as (patients older than 50 years, patients with diabetes mellitus, hypertensive patients and immunosuppressed patients).
- Other flaviviruses:
 - * **Powassan**
 - * **St louis**
 - * **Japanese Encephalitis virus** (a common cause of epidemic encephalitis, especially in Thailand, transmitted through mosquitos).

Now we'll talk about **Rabies:**

Introduction:

- Rabies means madness.
- It's an RNA bullet-shaped virus. It is of the Rhabdoviridae family.
- Most deadly infectious disease.
- One of the oldest documented diseases in the world.

Transmission:

- Mainly: Transmitted by saliva of infected animals (bats, foxes, raccoons, cats and dogs).
- In developing countries -- dogs mostly.
- In developed countries – bats mostly.
- If saliva comes on intact skin then there's no problem, but the problem arises when there are skin abrasions (damaged skin), or if the saliva contacts mucous membranes.
- Problem also arises with: Deep penetrating wounds
- Inhalation in bat caves.
- Aerosols (people who work in labs).
- Ingestion of rabid animals. (Less frequent)

Corneal transplantation (8 cases are recorded).

- Person to person transmission hasn't been recorded but still it's possible.
- Dead donor to recipient transmission has occurred.

Clinical features:

- Two presentations :

1) Encephalitic phase : (2/3) of patients die within 7 days.

2) Paralytic phase: (1/3) of patients will have paralysis which will develop to encephalitis and these patients will die within 2-3 weeks.

Incubation period:

It's variable:

-May be days if the wound was in the head or neck, and it's faster because the distance between the brain and the wound is shorter.

-May be weeks to months if the wound was in the leg, the distance is bigger

- May also reach years (4-6 years).

The average: (1-3) months.

Symptoms:

1) Encephalitic type:

- Fever-malaise-Headache.

- The patient may not remember that he was bitten especially if he was bitten by a bat.

- Tingling and pain at site of injury.

- Weakness of the affected site that might reach paralysis.

- Apprehension (fear with no cause).

- Irritability.

- Dry throat – cough – thirst (but the patient doesn't drink water because of spastic choking causes hydrophobia).

- High fever – rigors – difficulty in swallowing.

- Revulsion to water.

- Bizarre behavior – excitement – agitation – hallucinations – choking – seizure.

- Spasms induced by stimuli (light, sound...etc).

- Then seizures, coma, and finally death.

All of this happens in almost one week.

2) Paralytic type (sometimes referred to dumb type):

- Sometimes: paralysis, then coma, and death.

Management:

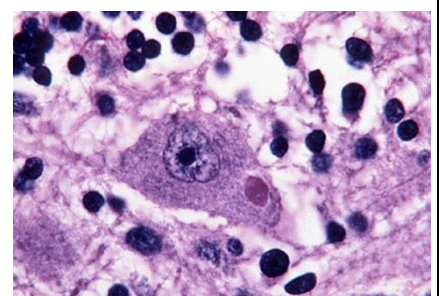
- No specific treatment.

- Supportive care.

- We put the patient in a dark quiet room.

- Sedation – coma induction (we put the patient in a coma for one week).

Note: only 10 people out of 55,000 recorded cases have recovered from Rabies.



Pathology:

- Negri bodies (intracytoplasmic inclusion bodies) and the virus is present around them.
- Post mortem exam to detect disease.
- Mild inflammation.

Epidemiology:

Most common in India.

Prevention:

There is a vaccine and immunoglobulin.

1) Vaccine:

- Rabies is a 100% vaccine-preventable disease.
- The vaccine is given prophylactically (Pre-exposure) or after the bite (Post-exposure).
- 5 doses (0, 3,7,14, and 28) given in the shoulder, but never in the gluteal region because the absorption is minimal.

2) Immunoglobulin

Immunity:

If you take the vaccine on the 1st day -- antibodies will rise by the 7th day.

Note: cats may also transmit rabies.

Thanks to Sally Khateeb for her notes, they were very helpful.

Done by: Mohammad Dmour

Good luck