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Microbiology Unit: 04 – Viral

Diseases

Module Name: Rabies

Module No: 35

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Notes

Outline: Mode of transmission, Pathogenesis, Symptoms, Prophylaxis of Rabies caused by Rabies virus

- Rabies (word is from Latin *rabere* for rage or madness) is a disease caused by highly neutropic viruses.
- Causative agent: Rabies virus - Genus *Lyssavirus* – Family Rhabdoviridae

Rabies virus

- Bullet shaped, with one end rounded or conical and the other planar or concave
- Lipoprotein enveloped virus, Single-stranded RNA genome
- Surface spikes are composed of glycoprotein G, important in pathogenesis – (mediates binding of the virus to acetylcholine receptors in neural tissues) virulence and immunity
- Nucleoprotein is a nucleocapsid protein
- In the nucleocapsid, RNA - dependent RNA polymerase uses the negative strand as a template from which to produce a positive strand. The positive strand serves as mRNA and as a template for synthesis of new viral RNA
- Portal of entry - Skin or parenteral route
- Incubation period 10 days - 1 year

Distribution of Rabies

- Occurs all over the world
- Human rabies dead end

Two epidemiological types of rabies exist:
urban, transmitted by domestic animals like dogs and cats

sylvatic, involving animals in the wild :
Foxes, coyotes, and wolves are the most susceptible;
Intermediates are skunks, racoons, insectivorous bats, and bobcats

Mode of transmission:

- The virus multiplies in the salivary glands of an infected host. It is transmitted to humans or other animals by the bite of an infected animal whose saliva contains the virus
- Aerosols of the virus that can be spread in caves where bats dwell
- Contamination of scratches, abrasions, open wounds, and mucous membranes with saliva from an infected animal

Pathogenesis

- The virus appears to multiply in the muscles, connective tissue or nerves at the site of deposition for 48-72 hours.
- After inoculation, a region of the virions' glycoprotein envelope spike attaches to the plasma membrane of nearby skeletal muscle cells, the virus enters the cells, and multiplication of the virus occurs.
- When the concentration of the virus in the muscle is sufficient, the virus enters the nervous system through unmyelinated sensory and motor terminals; the binding site is the nicotinic acetylcholine receptor.
- It penetrates the nerve endings and travels in the axoplasm towards the spinal cord and brain.
- The movement of the virus in the axons is passive, at a speed of about 3mm per hour.
- The virus spreads by retrograde axonal flow at 8 to 20mm per day until it reaches the spinal cord, when the first specific symptoms of the disease-pain or paresthesia at the wound site may occur.
- A rapidly progressive encephalitis develops as the virus quickly disseminates through the central nervous system.
- The virus then spreads throughout the body along the peripheral nerves, including those in the salivary glands, where it is shed in the saliva.
- Within brain neurons the virus produces characteristic Negri bodies, masses of viruses or unassembled viral subunits that are visible in the light microscope.
- There is a higher attack rate and shorter incubation period in persons bitten on the face or head.
- Hyperemia and nerve cell destruction occur throughout the brain, especially in the cerebral cortex, cerebellum, hippocampus and dorsal spinal ganglia.
- Demyelinization occurs in the white matter, and degeneration of axons and myelin sheaths is common. In the spinal cord, the posterior horns are most severely involved with neuronophagia and cellular infiltrates.
- Rabies virus produces a specific eosinophilic cytoplasmic inclusion, the Negri body, in infected nerve cells. The presence of such inclusions is pathognomonic of rabies but is not observed in at least 20% of cases. Therefore, the absence of Negri bodies does not rule out

rabies as a diagnosis.

- Rabies virus multiplies outside the central nervous system and may produce cellular infiltrates and necrosis in salivary and other glands, in the cornea and elsewhere.

The disease can then take two forms –

I. With paralytic (dumb) rabies (approximately 20% of cases), the patient's muscles slowly become paralyzed (usually starting at the site of the bite). This is the less common form and ends in coma and death.

II. With furious rabies (about 80% of cases), the patient exhibits the classic symptoms of rabies.

Symptoms:

Stages:

1. Prodromal stage (2-10 days):
   - Fever, headache, malaise, fatigue, anorexia
   - Early symptom - neuritic type of pain or paresthesia and fasciculation at the site of virus entry
   - First neurologic signs: Apprehension, anxiety, agitation, irritability, nervousness, insomnia and depression, lasts 2-4 days
   - Excessive libido, priapism, spontaneous ejaculation may occur rarely
2. Acute encephalitic phase: Acute neurologic phase (2-10 days): Progression to delirium, abnormal behavior, hallucinations, insomnia, hydrophobia, aerophobia and photophobia
3. Coma: Some patients may enter into a comatose state (0 – 14 days)
4. Death: within 1-6 days due to respiratory arrest during convulsions

Laboratory diagnosis:

- Virus isolation: Animal inoculation
- Tissue culture
- Antibody demonstration
- Molecular methods: detection of rabies virus RNA by reverse transcription PCR
- Demonstration of inclusion bodies (Negri bodies): are intracytoplasmic, round or oval, purplish pink structures with characteristic basophilic inner granules.
- Direct immunofluorescent antibody of brain tissue

Prophylaxis:

- Pre-exposure: specific prophylaxis – immunization in persons at high risk, such as veterinarians and dog handlers because neural vaccines carry some risk of serious complications – now cell culture vaccines available.
- Post-exposure: called antirabic treatment; consists of local treatment: active immunization with antirabic vaccines and passive immunization with antirabies serum.
- Local treatment: prompt cauterization of the wound helps destroy the virus as animal bites deposit the virus in the wound.

- Wound should be scrubbed well immediately with soap and water as soap destroys the virus effectively.
- After this, the wound is treated with quarternary ammonium compounds, tincture or aqueous solution of iodine, or alcohol (40-70%).
- In severe wounds, antirabic serum may be applied topically and infiltrated around the wound – advisable to postpone suturing the wound.
- Anti-tetanus and antibiotics to prevent sepsis.

CHEMOTHERAPY:

Several types of live attenuated vaccines are available for use in animals, but they are considered to be unsuitable for humans.

The vaccines which are available for humans are inactivated whole virus vaccines.

Antirabies vaccines: 2 main categories:

- neural vaccines (abandoned now) – Semple vaccine; beta propiolactone vaccine and
- non-neural vaccines: duck egg vaccines, live attenuated chick embryo vaccines, tissue culture vaccines, subunit vaccine

Vaccination schedules: antirabic vaccine to be administered:

1. when person has been bitten, scratched or licked.
2. when biting animal can be observed, it should not be destroyed but should be kept for 10 days: observation period is recommended because the virus may be present in the saliva 3-4 days before onset of symptoms and the animal usually dies within 5-6 days of developing the disease.
3. if the animal remains healthy after this period, there is no risk of rabies and vaccination, if already started, may be discontinued.