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Toxoplasmosis: The Pregnancy's Hidden Threat

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Toxoplasma gondii, is an intracellular coccidian parasite responsible for zoonotic infections in humans and all warm-blooded animals. It is one of the major causes of abortion in pregnant women. The organism is an opportunistic pathogen. It infects all animals, including sheep, cattle, birds, rodents, pigs, and also humans as well. Toxoplasmosis is a leading cause of abortion in sheep and goats. It also causes abortion in humans.

Definitive host: Cat (where the mature stage of parasite is present)

Intermediate host: All mammals including man. Cats act as both definitive and intermediate host

Transmission in humans:

1. **Vertical transmission**: Transplacental, (infected mother to child). Women transmit the infection to the unborn child only if primary infection occurs during pregnancy.
2. **Pseudo vertical transmission**: It occurs through consumption of infected milk.
3. **Sexual transmission**: It occurs through semen.
4. **Blood transfusion and organ transplants**: During blood transfusion and organ transplantations.
5. **Transmission through food**: Oocyst contaminated meat, drinking water, fruits, vegetables and hands. Eating undercooked meat like pork, lamb and venison will result in accidental ingestion of asexual stages-tachyzoites (rare) or bradyzoites. Eating food, prepared and cooked using contaminated and unhygienic utensils, knives and cutting board which may have close into contact with raw contaminated meat.

Transmission in cats: By eating infected rodents (either bradyzoites or tachyzoites), and by eating oocyst in the faeces

Forms of toxoplasma gondii: Tachyzoites, Bradyzoites and Oocysts

1. **Tachyzoites**: Rapidly growing stage observed in the early stage of infection (Acute phase). It is present in the body fluid. Arc or Crescent-shaped. One end is more pointed than the other. Sub

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terminally placed nucleus. Asexual form. Multiplies by endodyogeny. It can infect phagocytic and non-phagocytic, cells except RBC.

2. **Bradyzoites**: Also known as tissue cyst/ meront/pseudo cyst/cyst zoites. Cyst size is about 100 µm and contains 60,000 lancets shaped tightly packed bradyzoites. They are slow-growing stage inside the tissue cysts. Bradyzoites mark the chronic phase of infection. Present in the brain and in skeletal and cardiac muscles but can occur in any organ like heart, eyes. This is resistant to low pH and digestive enzymes during passage through stomach. Bradyzoites are released in the intestine and are highly infective if ingested by intermediate host.
3. **Oocyst**: Cat ingests tissue cysts containing bradyzoites. Gametocytes develop in the small intestine. Sexual cycle produces the oocyst which is excreted in the faeces. Oocysts appear in the cat's faeces 3-5 days after infection by cysts. Oocysts require oxygen and they sporulate in 1- 5 days.

Life Cycle:

- Infected cats (definitive hosts) shed unsporulated oocysts in their feces into the environment.
- In the environment (soil, water, etc.), oocysts sporulate within 1–5 days, becoming infectious.
- Other animals (birds, rodents, livestock, humans) ingest sporulated oocysts through contaminated food, water, or soil.
- In the intermediate host's body, oocysts release sporozoites, which invade cells and rapidly multiply as tachyzoites.
- Tachyzoites spread throughout the body via blood and lymph, infecting various tissues (muscle, brain, eyes).
- The immune response forces tachyzoites to transform into slow-growing bradyzoites, forming tissue cysts.
- Cats become infected by eating intermediate hosts (e.g., rodents, birds) that contain tissue cysts.
- In the cat's intestine, bradyzoites are released, undergo sexual reproduction, and form new oocysts.
- These oocysts are again shed in cat faeces, contaminating the environment and starting the cycle anew.
- Humans can also get infected through undercooked meat (containing tissue cysts) or trans placentally (mother to foetus).

Pathogenesis:

In acute infections, when sporozoites are released in the intestine, they enter the blood/lymph stream and multiply as tachyzoites and actively invade various tissues/organs. Multiplication occurs,

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causing necrosis of the cells and death in high parasitaemia. Tachyzoites are excreted in urine, faeces, milk, conjunctival fluid and even saliva (rare) in this phase. The tachyzoites, however, cannot survive long outside and hence, there is no risk of spread of infection during the acute stage. In sub-acute cases, antibodies formed clear the tachyzoites while in chronic conditions there are persistent bradyzoites.

In Man: Two forms are present: Congenital and acquired forms.

1. **Congenital form**: Occurs in children who pick up the infection from their mother. Three signs of infection include chorioretinitis, intracranial calcification and hydrocephalus.
2. **Acquired form**: Lymphadenopathy (Enlarged lymph nodes persist for months, along with malaise, fever, sore throat, fatigue), typhus (exanthema, myocarditis, pneumonia, meningoencephalitis), cerebrospinal form (fever, encephalitis, convulsions, delirium, lymphadenopathy, pleocytosis), ophthalmic form (chronic chorioretinitis).

In Dogs: Respiratory distress seen. Organisms are present in alveoli/trachea/bronchi. Alimentary disturbances involve haemorrhagic diarrhoea, ulceration of digestive tract-duodenum/rectum. Neurologic disturbances occur when brain harbours cysts.

In Cats: Rarely show symptoms

In Cattle: There is increased temperature, dyspnoea, coughing, sneezing, nasal discharge, trembling and shaking of head due to the presence of organism in the brain, lungs, and lymph nodes. Presence in brain/CNS can result in neurological signs and sudden death.

In Sheep: Abortion storm occurs in sheep. Neonatal death and still birth can occur. Abortion and prenatal mortality occur in lambs, and infection at 45-55 days of early gestation causes death and expulsion of foetus. This generally goes unnoticed. In twinning, only one lamb may be affected. Infection at 90 days of gestation results in presence of organism in foetal tissues. Infection at 120 days of gestation results in infection of foetus but there may be no death. Lambs survive but are weak and may not be able to suckle. Post mortem lesions include cotyledons with white, 2 mm diameter necrotic lesions. Acute focal necrosis in brain results in nervous signs causing circling disease in 75% of cases in lambs. Glial nodules in cerebellum of sheep are seen in chronic conditions.

In Birds: In fowls, there is anorexia, emaciation, diarrhoea and blindness. In most birds, however, the condition is asymptomatic.

Diagnosis

Mice inoculation: Inoculation of suspected material in mice subcutaneously, is useful in diagnosis. In 1-14 days, pneumonia develops and lung impression shows organism. Peritoneal/pleural fluid also shows organism; Pseudo cyst can be seen in brain after a month

Serological tests: Serological tests include CFT, IFAT (preferred), HAT and ELISA. High levels of IgM in adult indicate recent infection and the titre of less than 1:64 is considered to be normal. In

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neonates, there is no titre. If high levels of IgG are seen, then it means the infection has occurred recently. Low titres of IgG mean infection occurred in the past. Once infected, the animal usually remains infected for life and there is no possibility of reinfection with other strains.

Dye test: Sabin Feldman Dye test is used in diagnosis. Antibodies, in the presence of accessory factors modify living Toxoplasma tachyzoites. The modified tachyzoites fail to stain with methylene blue at pH 11. In addition, organism exposed to antibody containing serum appears thin and distorted. This is because the membrane is disrupted and organism is lysed due to activation of the complement system. Normal serum with methylene blue and tachyzoites results in the deep blue staining of cytoplasm and nucleus of the intact organism after incubation. Sabin Feldman Dye test is not safe since it involves handling of live tachyzoites.

Ring enhancing lesions in CT/MRI scans: In AIDS patients (70-80%) who have toxoplasma encephalitis, head CT scans reveal multiple ring enhancing lesions. However, these ring-enhancing lesions also occur in AIDS patients with CNS lymphoma and CT imaging helps in differential diagnosis.

IN Pregnant woman, TORCH test is done.

Treatment

Clindamycin (10 – 12.5 mg/kg, PO/IM, q12h, for 2 – 4 weeks) – decrease oocyst shedding

Pyrimethamine (0.25 – 1mg/kg, PO, q24h, for 2 weeks), is given in combination with folinic acid (2 – 5 mg total dose, PO, q24h, for 2 weeks) to decrease toxicity of pyrimethamine

Sulphadiazine (20 – 50 mg/kg, PO, q12h, for 2 weeks) and folinic acid (Leucovorin)

Spiramycin (75000 IU/kg, PO, q12-24h, for 3 weeks)- women during 1st term of pregnancy.

Control

Food hygiene: Meat frozen to sub-zero temperature for 3 days reduces the chances of infection. Vegetables should be thoroughly peeled/washed before eating. Drinking of unpasteurized goat milk should be avoided. Children should be taught the importance of washing their hands.

Use of gloves: Wearing gloves while gardening and handling the litter of pet cats help in disease prevention

Vaccination: The S48 strain live vaccine Toxovax, is the only commercial vaccine available worldwide to protect against congenital toxoplasmosis in sheep. The main drawback of this vaccine is that it is live which may give rise to safety concerns.

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