TOXOPLASMOSIS

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OBJECTIVES

At the end of this session each student will be able to:

1. Define toxoplasmosis.
2. Describe the epidemiology of toxoplasmosis.
3. Describe the cause of toxoplasmosis.
4. Describe the pathophysiology of toxoplasmosis.
5. Describe the clinical features of toxoplasmosis.
6. Describe the complications of toxoplasmosis.
7. Describe the differential diagnoses of toxoplasmosis.
8. Investigate patients with toxoplasmosis.
9. Treat patients with toxoplasmosis.
10. Describe the prognosis of patients with toxoplasmosis.
11. Describe the preventive measures to toxoplasmosis.

Definition

- Toxoplasmosis is an infestation caused by an obligate intracellular protozoon, *Toxoplasma gondii*.

Epidemiology

Individuals at high risk of toxoplasmosis:

- Slaughterhouse workers.
- Immunodeficient patients i.e. those with defective T-cell mediated immunity:

a. Haematological malignancies.
b. Bone marrow and solid organ transplants.
c. AIDS.

Mode of transmission to human

1. **Oocysts:**

a. Ingestion oocysts of following the handling of contaminated soil or cat's faeces.

b. Oocysts can be transported to food by flies and cockroaches.

c. Consumption of contaminated water or food sources e.g. unwashed garden vegetables.

2. **Tachyzoites:** (rare)

a. Ingestion of unpasteurized milk.

b. Direct entry into the blood stream through a blood transfusion or laboratory accidents.

Mode of transmission to human

3. **Tissue cysts:** (bradyzoites)

a. Ingestion of uncooked meat (pork, lamb, beef containing *Toxoplasma gondii*).

b. Transplantation of an organ containing tissue cysts.

4. **Transplacental and perinatal:**

- The infection may be transmitted to the foetus transplacentally or during vaginal delivery.
- The risk of transplacental transmission is greatest during the third trimester of pregnancy.

Epidemiology....

- **Race:**

  The highest incidence among AIDS patients in the USA occurs in emigrants from Haiti (11.2%).

- **Sex:**

  The incidence does not vary significantly between sexes.

- **Age:**

- The occurrence of toxoplasmic antibodies increases with age.
- The seroconvertion rate for women of child-bearing age is 0.8 per year.

Epidemiology….

Toxoplasmic seropositive prevalence rates:

- El-Salvador and France: 75% by the 4th decade of life.
- France: 90% of adults.
- Germany: 50% of adults.
- Women of child-bearing age in western Europe, Africa and south and central America: > 50% of adults.
- HIV-infected individuals in certain areas of western Europe and Africa: 50-70% of adults.

Cause

- It is caused by *Toxoplasma gondii*, an obligate intracellular protozoon.

Pathophysiology

***Toxoplasma gondii* exists in 2 forms:**

- Tachyzoites i.e. the rapidly dividing form observed in the acute phase of infection.
- Bradyzoites i.e. the slowly growing tissue cysts.

Life cycles

The *Toxoplasma gondii* has 2 distinct life cycles:

- **Sexual cycle:**

  It occurs only in cats, the definitive host.

- **Asexual cycle:**

  It involves other mammals e.g. humans and various strains of birds, pigs, lamb and cattle.

Sexual phase

- It begins in the gastrointestinal tract of the cat.
- The macrogametocytes and microgametocytes develop from ingested bradyzoites and fuse to form zygotes.
- The zygotes then become encapsulated within a rigid wall and are shed as oocysts.
- Within the oocyst, the zygotes sporulate and divide to form sporozoites.

Sexual phase

- Sporozoites become infectious 24 hours or more after the cat sheds the oocysts.
- During the primary infection, the cat can excrete millions of oocysts daily for 1-3 weeks.
- The oocysts are very hardy and may remain infectious for more than one year in warm and humid environments.

Asexual phase

- Bradyzoites are released when the tissue cysts are ingested and sporozoites when oocysts are ingested.
- The parasite rapidly enters the host cells in the process that is significantly faster than phagocytosis.

Asexual phase

- The vacuole is then formed primarily by invagination of the host cells plasma membrane, which is pulled over the parasite through the determined action of the actin-myosin cytoskeleton of the parasite.
- Inside the vacuole, the *Toxoplasma gondii* multiply, rupture cells and infect nearby cells.

Asexual phase

- They are transported via lymphatics and disseminated haematogenously throughout the tissues.
- Tachyzoites proliferate, producing necrotic foci in tissues surrounded by a cellular reaction.
- With development of the normal immune responses, tachyzoites disappear from tissues.

In immunodeficient individuals and some immunologically healthy patients

- The acute infection progresses and may cause potentially lethal consequences e.g. pneumonitis, myocarditis or necrotizing encephalitis.
- Cysts form as early as 7 days after infection and remain for the life span of the host producing little or no inflammatory responses but cause recrudescent disease in immunocompromised patients or chorioretinitis in congenitally infected older children.

Clinical features

A. History:

I. Acute toxoplasmosis in immunocompetent hosts:

- Approximately 80-90% of patients are asymptomatic.
- Lymphadenopathy:

a. Cervical lymphadenopathy with discrete, non-tender nodes, < 3 cm in diameter.

b. Retroperitoneal and mesenteric lymphadenopathy.

I. Acute toxoplasmosis in immunocompetent hosts

- Abdominal pain.
- Fever.
- Malaise.
- Night sweats.
- Myalgia.
- Sore throat.
- Chorioretinitis.

II. Acute toxoplasmosis in hosts who do not have AIDS but are immunodeficient

- The disease may be newly acquired or may be a reactivation.
- CNS disease occurs in nearly 50% of patients as:
  - Encephalitis.
  - Meningoencephalitis.
  - Mass lesion.
- **Manifesting with:**
  - Hemiparesis.
  - Seizures.
  - Mental status changes.
  - Visual changes.
  - Myocarditis.
  - Pneumonitis.

III. Toxoplasmosis in AIDS patients

A. Toxoplasmic encephalitis:

- Subacute onset with focal neurological abnormalities e.g. hemiparesis.
- Abrupt onset with seizures or cerebral haemorrhage.
- Speech abnormalities.
- Brainstem involvement:
  - Cranial nerve palsies.
  - Cerebral dysfunction with disorientation.
  - Altered mental state.
  - Lethargy.
  - Coma.

A. Toxoplasmic encephalitis

❑ **Neuropsychiatric manifestation:**

- Paranoid psychosis.
- Dementia.
- Anxiety.
- Agitation.

❑ **Spinal cord involvement:**

- Motor weakness of a single or multiple limbs.
- Sensory disturbances of a single or multiple limbs.
- Bladder or bowel dysfunction or both.
- Local pain.

A. Toxoplasmic encephalitis

- Cerebellar signs.
- Meningismus.
- Movement disorders.

❑ **Less common manifestations:**

- Syndrome of inappropriate secretion of anti-diuretic hormone (SIADH).
- Hemichorea-hemiballismus.
- Parkinsonism.
- Focal dystonia.
- Panhypopituitarism.
- Diabetes inspidus.

B. Pulmonary toxoplasmosis (Pneumonitis)

- The diagnosis can be confirmed by demonstrating the parasite in bronchoalveolar lavage (BAL) fluid.
- It mainly occurs in patients with advanced AIDS (mean CD4 count of 40 cells/ml ± 75 SD) not receiving appropriate anti-HIV drugs or primary prophylaxis for toxoplasmosis.
- Prolonged febrile illness.
- Cough.
- Dyspnoeia.
- Extrapulmonary toxoplasmosis (50% of patients).

C. Toxoplasmic chorioretinitis

- Blurring of vision.
- Ocular pain.
- Loss of visual acuity.
- Funduscopy reveals necrotizing lesions that may be multifocal or bilateral.
- The overlying vitreal inflammation is often present and may be extensive.
- Optic nerve involvement occurs in 10% of patients.

D. Uncommon manifestations

- Syndrome of inappropriate secretion of anti-diuretic hormone (SIADH).
- Multiple organ involvement:
  - Acute respiratory failure.
  - Haemodynamic abnormalities similar to septic shock.
- Panhypothyroidism.
- Diabetes inspidus.
- Orchitis.

D. Uncommon manifestations

❑GIT:

- Abdominal pain and ascites due to involvement of the stomach, peritoneum or pancreas.
- Diarrhoea.
- Acute hepatic failure.

IV. Congenital toxoplasmosis

- It is most severe when maternal infection occurs early in pregnancy.
- Approximately 67% of patients are asymptomatic.
- Chorioretinitis.
- Intracranial calcification.
- CSF Pleocytosis and elevated protein levels.
- Anaemia, thrombocytopenia and jaundice at birth.
- Microcephaly.

IV. Congenital toxoplasmosis

The affected survivors get:

- Mental retardation.
- Seizures.
- Visual defects.
- Spasticity.
- Other severe neurological sequelae.

V. Ocular toxoplasmosis

(Chorioretinitis/focal necrotizing retinitis)

- A congenital disease is usually bilateral while acquired disease is unilateral.

Lesions:

- Yellowish white elevated, cotton-like patches with indistinct margins which may occur in small clusters.

Symptoms:

- Blurred vision.
- Photophobia.
- Scotoma.
- Ocular pain.

Physical examination

CNS examination findings:

- Alternation of mental status.
- Seizures.
- Motor weakness.
- Cranial nerve disorders.
- Sensory abnormalities.
- Cerebellar signs.
- Meningismus.
- Movement disorders.
- Neuropsychiatric manifestations in immunocompromised patients.

Physical examination

- Rash.
- Low-grade fever.
- Hepatosplenomegally.
- Lymphadenopathy.
- Funduscopy reveals multiple yellowish white, cotton-like patches with indistinct margins located in small cluster in the posterior pole.

Complications

A. CNS lesion:

- Seizure disorders.
- Focal neurological deficit.

B. Ocular toxoplasmosis:

- Partial or complete blindness.

C. Congenital toxoplasmosis:

- Mental retardation.
- Seizure disorders.
- Deafness.
- Blindness.

Differential diagnoses

I. Toxoplasmic encephalitis

A. Space occupying lesion:

- Brain abscess.
- Lymphoma.
- Brain tumour.
- Cysticercosis.
- Tuberculoma.

I. Toxoplasmic encephalitis

B. CNS-Infections:

- Cytomegalovirus infection.
- Herpes simplex infection.
- Neurosyphilis.
- Progressive multifocal leucoencephalopathy (PML).
- Histoplasmosis.
- Meningitis.

I. Toxoplasmic encephalitis

C. Others:

- Metastatic cancer of unknown site.
- Infectious mononucleosis.

Differential diagnoses

II. Pulmonary toxoplasmosis:

- Pneumocystis Jirovecii Pneumonia.

III. Congenital toxoplasmosis:

- Rubella.
- Encephalopathies.
- Erythroblastosis fetalis.

Investigations

Laboratory:

Evidence of infection is by the demonstration of the Toxoplasma gondii organisms in blood, body fluids or tissues.

1. Mouse inoculation of infected amniotic fluid.
2. Polymerase chain reaction on body fluid.
3. Serological tests:

a. ELISA.
b. Indirect fluorescent antibody test.
c. The IgM fluorescent antibody test.
d. The indirect haemaglutination test.

Investigations

Radiology:

- Computed tomography scans of the brain.
- Magnetic resonance imaging.
- Obstetric ultrasound scans.

Treatment

A. Outpatient treatment:

- Acquired disease in hosts who are immunocompetent.
- Ocular toxoplasmosis.

B. Inpatient treatment:

- CNS toxoplasmosis.
- Acute disease in hosts who are immunocompromised.

Treatment

Most effective regimens are:

1. Sulphadiazine combined with pyrimethamine.
2. Trisulphapyrimidine:

- Sulphamerazine.
- Sulphamethazine.
- Sulphapyrazine.

Others:

- Clindamycin plus pyrimethamine.
- Spiramycin.

Follow-up visits

- Every 2 weeks until stable, then monthly during therapy.
- Full blood picture weekly for the first month, then every 2 weeks.
- Renal and liver function tests monthly.

NB:

- The efficacy of azithromycin, clarithromycin, co-trimoxazole and dapsone in treatment of toxoplasmosis are unclear.

Prognosis

- Immunodefiecient patients often relapse if treatment is stopped.
- Treatment may prevent the development of untoward sequelae in both symptomatic and asymptomatic infant with congenital toxoplasmosis.
- Mortality:

- Pulmonary toxoplasmosis: As high as 35%.
- Congenital toxoplasmosis: Children often die in the first month of life.

Prevention

- Avid eating raw meat, unpasteurized milk and uncooked eggs.
- Wash hands after touching raw meat and after gardening or other contact with soil.
- Use gloves while working in gardens.
- Wash fruits and vegetables before eating.
- Avoid contact with cat faeces.
- Keep house cats inside - avoid wandering cats!
- Routine serological screening for congenital toxoplasmosis among pregnant women.
- Avoid transfusion of blood products from infected donor.
- Avoid organ donated by infected individuals.

Thank you for your attention

Reference

- Hökelek M and Safdar A. Toxoplasmosis; www.emedicine.com/med/topic2294.htm Last updated: May 16, 2006.