Viral Glandular Fever Lecture

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Viral Glandular Fever

- There are generalized infection by viruses with a predilection for glandular tissue.
- There are many viruses causing glandular fever but the most important once are:
  - Mumps virus
  1. Epstein-Barr virus
  2. Cytomegalovirus
Mumps (Parotitis)

- Acute enlargement of the Salivary glands is mostly due to infection with mumps virus.

- There are 3-pairs of salivary glands:
  - 2 partoid glands (largest, mainly infected)
  - 2 submandibular glands
  - 2 sublingual glands

- Is a disease of children (**5-15 years**), but also can be seen in young adult with more complicated feature

- Seasonal variation peak mainly in winter.
**Virology Aspect:**

- One of paramyxoviridae family
- Enveloped virus with ssRNA with negative sense
- Two glycoprotein spikes,
  - The HN has both hemagglutinine and neuraminidase activity.
  - The F, enables the virus to fuse infected cells to form syncytia (*multinucleated giant cell*)
Pathogenesis and Epidemiology

- Mumps virus infect only human
- Transmitted by inhalation of respiratory droplets, during sneezing and coughing
- Long incubation period 18-21 days.
- Infection started in the epithelial cells of upper respiratory tract, then virus spread by viremia to salivary glands (mainly parotid), CSF, Testes, Ovary and pancreas.
Mumps
Mumps
Clinical Feature:

- Moderate fever, Malaise
- Pain on chewing or swallowing, followed by Painful swelling of the salivary glands, particularly the parotid glands.

- Period of communicability is from few days before to one week after clinical onset.
**Complications:**

- Aseptic meningitis
- Encephalitis
- Orchitis - risk factor for infertility
- Pancreatitis
- Oophoritis
- Thyroiditis

**Prognosis:**

- Self-limiting disease
- Recovery is usual, but complication can be seen in adult patients.
Orchitis usually unilateral
Lab. Diagnosis:

**Serology**
- By detection of IgM-Ab to mumps virus

**Viral Culture:**
- Mumps virus can be isolated from saliva during first week of infection or from urine for another 1-2 weeks.
- Virus can be isolated from CSF if meningitis occur.
- Mumps virus replicate well on Monkey Kidney multi-nucleated giant cells.
Prevention and Treatment:

- A live attenuated vaccine is available (MMR)
- Contains mumps, measles and rubella given to all children intramuscular or subcutaneous at 15 month and booster does at school age with excellent long last protection.
- There is no specific anti-viral drug therapy
- The child must rest in bed until the fever goes away.
- Isolate the child, to prevent spreading the disease to other.
- Use analgesics and anti-pyretic to relive symptoms.
**Epstein Barr Virus (EBV)**

**Virology Aspect:**

- One of Herpesviridae family
- Enveloped, icosahedral nucleocapsid, ds-DNA
- Replicate in the nucleus Intra-nuclear inclusion body.
- Remains latent in **B-lymphocyte cells**
- Has the oncogenic potential

**EBV** ➔ **Burkittis lymphoma**

**A plastic Nasopharyngeal carcinoma**

**B-cell lymphoma in immunocompromised**
Electron Microscopy of Herpes Virus
Clinical Syndromes Associated with EBV Infection

- Infectious mononucleosis (IM)
- Chronic EBV-infection → Chronic fatigue syndrome
- X-linked lymphoproliferative syndrome.
- Lymphoproliferative disorders in immunocompromised patients
- Burkett's lymphoma
- Nasopharyngeal carcinoma
Infectious Mononucleosis

- The primary infection is usually asymptomatic in children, however in young adult and adolescents the typical primary acute presentation is Infectious mononucleous (glandular fever)

- EBV transmitted by close contact, the virus is secreted in saliva, mainly kissing and sharing contaminated drinking glasses with long incubation period 30-50 days.
Symptoms of Infectious mononucleosis:

- Started as:
  - Fever, Sore throat, greatly enlarged Tonsil with membrane and necrotic ulcer → airway obstruction
  - Generalized lymphadenopathy especially submandibular and axillary.
  - Malaise, fatigue
  - Splenomegaly IN 50% of patient → splenic rupture
  - Hepatomegaly and hepatitis → liver enzyme
  - Maculapapular rash in 5% of patient
Infectious Mononucleosis
Infectious Mononucleosis
Symptoms of Infectious mononucleosis (Continued):

**Prognosis:**

- Self-limiting disease *(last 1-4 weeks)*, but the virus remains latent in B-cells for life.

- If the disease lasts for more than 6-months, it is frequently called chronic EBV- infection *(chronic fatigue syndrome)*

- No effective treatment or vaccine available for EBV
Complications of I.M.

- Severe airway obstruction
- Splenic rupture
- Encephalitis, Meningoencephalitis
- Thrombocytopenia
- Haemolytic anaemia
- Carditis, Cardiac arrest
**Lab. Diagnosis:**

- EBV infection is diagnosed by detection of IgM-Ab to the viral capsid antigen (VCA)

- Lymphocytosis with Atypical lymphocytes in peripheral blood

- Development of *Hetrophil Ab* that agglutinate sheep RBCs by Paul Bunnell test
**Chronic Fatigue Syndrome**

- Consider as reactivation of latent virus in β-lymphocyte or as complication of acute I.M.

- Extreme fatigue, muscle weakness, decreased memory associated with sore throat, low grade fever and painful lymph nodes.

- Self limiting last 1-6 months diagnosed by:
  - **EBV Abs**
  - +ve heterophil Ab
  - Atypical lymphocytosis in peripheral blood.
**X-Linked Lymphoproliferative Syndrome**

- Approximately half of individuals with this syndrome develop severe life-threatening *Infectious mononucleosis* and *Malignant lymphoma* when they expose to primary EBV-infection.
  - Generalised lymphadenopathy
  - Hepato & Splenomegalgy
  - Thrombocytopenia
  - Aplastic anemia
- This disorder is usually fully expressed in *males* only.
Burkitt Lymphoma (BL):

- A highly malignant tumor of the lymphoid tissue of the neck or below the jaw.
- Among children from 5-10 years of age and especially in regions endemic with *malaria* in East Africa.
- The swollen lymph nodes are often painless and can grow very rapidly.
- **EBV DNA** copies are found in high numbers in Burkitt Lymphoma Tumour cells.
Burkitt lymphoma (EBV)
Nasopharyngeal carcinoma (NPC)

- NPC is a malignant tumor of the squamous epithelium of the nasopharynx.
- It is prevalent in South China, Hong Kong, Malaysia.

Lymphoproliferative disorder of immunocompromised

- Severe lymphoproliferative disease which may be fatal and characterized by infiltration of organs and tissue by atypical B-lymphocyte.
Cytomegalovirus (CMV)

- One of Herpesviridae family
- Enveloped, icosahedral nucleocapsid, ds-DNA virus
- Replicate in the nucleus → intra-nuclear inclusion body.
- Remain latent in lymphocyte and macrophage
Schematic structure of herpes group viruses

- Viral glycoproteins
- Envelope
- Capsid
- Capsid (protein subunit)
- DNA core
Electron Microscopy of Herpes Virus
Transmission:

- This virus is excreted in urine, blood, saliva, semen, cervical secretion, and breast milk.
- CMV can be transmitted by close contact, kissing, sexual contact, vertical from mother to fetus, blood transfusion and organ transplant.
Disease associated with CMV Infection

- CMV rarely causes diseases in healthy people, particularly when infection occurs in childhood about 70-90% of adults have Ab to CMV without previous symptoms.

- However CMV can cause:
  - Infectious mononucleosis like syndrome
  - Severe disease in the immunocompromized patients.
  - Congenital infection
Infectious Mononucleosis like syndrome
Infectious Mononucleosis like syndrome

- Asymptomatic infection is very common in young children.
- However, infectious mononucleosis like syndrome may develop in young adults.
- Same picture as EBV but without heterophil Ab.
- Self limiting disease last 2-4 weeks.
- Diagnosed by detection of IgM – Ab to CMV.
Treatment and Prevention

- Infectious mononucleosis like syndrome is fairly mild illness, requires no anti-viral drug treatment

- There is no vaccine available
However, severe CMV infection can occur in people with impaired immunity (immunocompromised), such as transplant patients, patients with AIDS and people receiving chemotherapy or other immunosuppressive therapy.

- Disease can be primary or even reactivation of latent virus.
- The most common sites of involvement are adrenals, lung, Gastrointestinal tract, CNS and eyes (Retinitis).
Prevention

- Ganciclovir or foscarnet may be used to decrease the incidence of new infection or reactivation in patients with AIDS or those who have received organ or bone marrow transplants.

- CMV immunoglobulin to transplant patient.

- Screening of donor and recipient in organ transplantation.

- Vaccine still not available.
Congenital CMV – Infection (Intra-uterine or Transplacental)

- Congenital CMV occurs mainly when non-immune pregnant woman acquires the virus (*primary infection*) at any gestational stage, however recurrent CMV-infection during pregnancy can produce fetal damage but in less ratio.

- Most infected infants appear *normal at birth*, will subsequently develop deafness or mental retardation.
Congenital CMV – Infection (Intra-uterine or Transplacental) Continued

- Generalized cytomegalic inclusion disease of the new born results mostly from primary maternal infection. This condition is associated with:
  - Jaundice
  - Hepato-splenomegaly
  - Thrombocytopenia
  - Hemolytic anemia
  - *Microcephaly*
  - *Chorioretinitis*
  - *Deafness*
Severe generalized cytomegalic inclusion disease
(Microcephaly hepatosplenomegaly)
Diagnosis of congenital CMV:

- Isolation of the virus in tissue culture, followed by identification of the isolated virus
  - Specimens, urine, saliva, must be obtained during the first 3-weeks of life
- Detection of CMV-DNA in urine using PCR

Treatment of congenital CMV:

- Ganciclovir
- Foscarnet