Herpes simplex and genital warts

Editing File
Summary

MED439
KING SAUD UNIVERSITY

MICROBIOLOGY
Team 439

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- Girls' slides
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Objectives:

- The main structural components of HSV-2 and HPV
- Mode of transmission in HSV-2 and HPV infections
- Main clinical features of HSV-2 and HPV infections
- Diagnosis, Treatment and prevention

Herpes

Introduction

- Genital herpes and genital warts are recognized as the main sexual transmitted viral infections[1] that might be acquired by any types of sexual contact.

Risk groups[2]

- Adults who have multiple sexual partners.
- Immunocompromised individuals.
- Infants of infected mothers.
- Sexual child abuse
- Homosexual

Etiology of genital Herpes

- There are two species of herpes virus capable of causing genital herpes:
  - Herpes simplex virus type 1 (HSV-1).
  -Herpes simplex virus type 2 (HSV-2).
- 90% of genital herpes cases are due to HSV-2 infection, whereas 10% are due to HSV-1[3]
- Both (HSV-1 & HSV-2) are structurally very similar and share about 70% sequence homology

Characteristics of Herpes virus

- Family of herpesviridae
- Virion consist of:
  - -Glycoprotein envelope
  - -Icosahedral capsid -Linear ds-DNA

- ★ **The Herpes viruses has the ability to induce latent infection:**
  - -HSV (1&2) → Nerve cells
  - -HSV-1 → Trigeminal ganglia[4]
  - -HSV-2 → Sacral ganglia[5]

Transmission of Genital HSV

Sexual Transmission :

- The number of different sexual partners correlates directly with acquisition of HSV-2 in both male & female.
- **Homosexual men** are more susceptible to HSV-2 infection.
- Genital infection can be acquired by auto-inoculation from lesions elsewhere on the body by touching vesicular fluids from any herpetic lesions (HSV-1&2).
- HSV-1 can cause genital herpes infection after oral sex, also can be seen in cases of child abuse

Perinatal Transmission (During Delivery):

- The majority of maternal infection (85%) occurs **during delivery**, due to direct contact between the baby and infected maternal birth canal.
- The risk of perinatal transmission is about **50%** if the mother has primary genital herpes, while the risk is **8% i**f mother has recurrent infection.
- In the baby: this infection can lead to either massive herpetic skin lesions or generalized infection affecting skin and internal organs e.g. lungs (inhale the/drink secretions during delivery), liver or brain (neonatal herpes infections)
- **To avoid perinatal infection we do caesarean section.**

Intrauterine (Vertical Transmission) (10%):

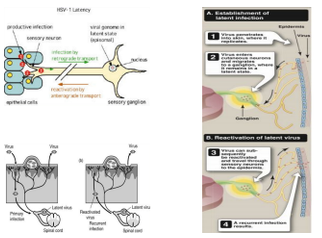
- Maternal primary genital HSV (HSV-2) infection of the mother during first trimester can leads to spontaneous abortion.
- Maternal primary genital HSV (HSV-2) infection which develops after 20 weeks of gestations may induce malformation such as **microcephaly, jaundice, hepatosplenomegaly, chorioretinitis and herpetic vesicles on the skin.**

1. Along with HIV
2. The same risk groups for all sexually transmitted disease (bacterial or viral)
3. HSV-1 infections generally occur above the waist and HSV-2 infections generally occur below the waist
4. Because it mainly causes orofacial infection (virus enters local sensory nerve endings → axonal transport proximally to sensory ganglion cell bodies → latent infection of trigeminal ganglion)
5. Because it mainly causes genital herpes

Genital herpes

Pathogenesis of HSV-2 (Genital herpes infection)

- Primary infection occurs when HSV-2 infects **(1) epithelial cells** covering the mucosa → Then the virus **(2)** replicates and migrates to the nearest **ganglion** (sacral ganglia) via neurons where it establishes latency for life → Once its reactivated (due to immunosuppression) it **(3)** travels back through neurons to the site of the primary infection and causes recurrent infection.
- Once the virus enters the human body, it remains for life (latency).



Clinical features of HSV-2 infection

Primary genital herpes

- Vary from asymptomatic to mild or severe painful episode.

If symptoms are present (Incubation period: 2-12 days) they may include:

- Fever, Malaise, dysuria
- **Inguinal lymphadenopathy**[1]
- **Vesicular herpetic lesion or ulcer** localized to the cervix, vagina, vulva or perineum of the female or the shaft of the penis in the male, Herpetic proctitis can be seen in homosexual.
- Aseptic meningitis have been observed in about 10% of cases as extra genital presentation

Recurrent genital herpes

- Occurs after reactivation by environmental or physiological factors such as stress, exposure to U.V. light, menstruation, **pregnancy** or any condition that decreased the immunity.
- This can be as frequent as six or more episode a year, the attacks are **milder and shorter than primary episode.**
- Accompanied with the appearance of herpetic vesicles on the external genitalia.
- Symptoms may include pain and itching.

Neonatal herpes infection

- Is not a common condition, but the **mortality is >70%** when it happens.
- It occurs **during labor and delivery through the vaginal canal** when a mother is having a **primary active herpetic lesion**[2] and shedding the virus, also in small % as vertical transmission during pregnancy.
- It may spread to other organs such as lungs, liver, brain.

1. Remember in HIV lecture there was lymphadenopathy but it was NOT in the inguinal area
2. the risk is higher if the mother is having a primary infection than if she is having a recurrent infection

Genital herpes

Neonatal herpes infection (has three forms)

Localized skin infection
limited to massive skin vesicular lesions **mild infection.**

Localized brain infection
limited to CNS invasion causing encephalitis. **mortality is high**

Generalized neonatal herpes infection
- severe massive infection of the skin (massive skin herpetic lesions) accompanied with internal organs infection including lungs (pneumonia) , liver (hepatosplenomegaly) , and brain (encephalitis).
- usually fatal.

LAB DIAGNOSIS

★**ELISA**[1] main test for diagnosis	**Serum sample** is analyzed for detection the **IgM Ab**
IF (Direct immunofluorescence)	Scraping of the base of the **lesion sample** or vesicle fluid sample is analyzed for detection the **viral Ag**.
★ **PCR** [2]	CSF sample in case of neonatal herpes.
Tissue culture[3]	vesicle fluid sample is cultured in cell line **(Vero or Hep-2 cells)** and then identified by the following: ○ Observe the viral CPE (cytopathic effect) ○ **Direct immunofluorescence (IF)**
Tzanck smear	A rapid diagnosis can be made from skin lesion by using Tzanck smear ,in which: ○ Cells from the base of the vesicle are stained with Giemsa stain ○ The presence of multinucleated giant cells and cowdry type A intranuclear inclusions suggests herpes virus infection.

Management

- **No vaccine is available** to prevent HSV-2 infection, and thus the best way to control the HSV infection is by:
- Avoid sexual contact with infected individuals.
- Abstain from making prohibited relations.
- Note: Condoms are not 100% protective against genital herpes infection
- Cesarean section is recommended for women who are having genital herpetic lesion.

Treatment

- **Acyclovir: The 1st choice therapy, and suitable for pregnant women.**
- Famciclovir
- Valacyclovir

1. important to determine the type of HSV that the patient is suffering (HSV-1 or HSV-2) by looking for the IgM of each.
2. Mostly used for conformation + in case of neonates.
   If the patient has meningitis or encephalitis, do PCR first.
3. Mostly used for research not diagnosis (because it needs 3-4 days to grow)

Human Papillomavirus

Family

- Family of Papillomavirida

Characteristics

- Virion is small non-enveloped and consist of:
  - Icosahedral capsid
  - Circular ds-DNA
- They cause disease only in skin and mucous membrane[1]
- ★ **Does not grow in tissue culture (MCQ)**
- **Resists detergent, heat, and can remain infectious in the environment for long time**

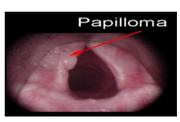
Type of wart and HPV genotypes

- 1- Cutaneous warts
- 2- Genital/Anogenital and Mucosal warts

1. Cutaneous

Transmission	The virus is transmitted from infected skin, either by direct contact hand to hand (common warts) or through fomites and enter its new host through abrasions especially in swimming pools (plantar warts) and changing rooms are fertile sources of the infection, skin warts are most liable to affect young children.		
Types Numbers here are not important	Common Warts[2]	**(HPV genotype 2,4)**	 
	Plantar Warts[3]	**(HPV1,)**	
	Flat Warts[4]	**(HPV 3,10)**	

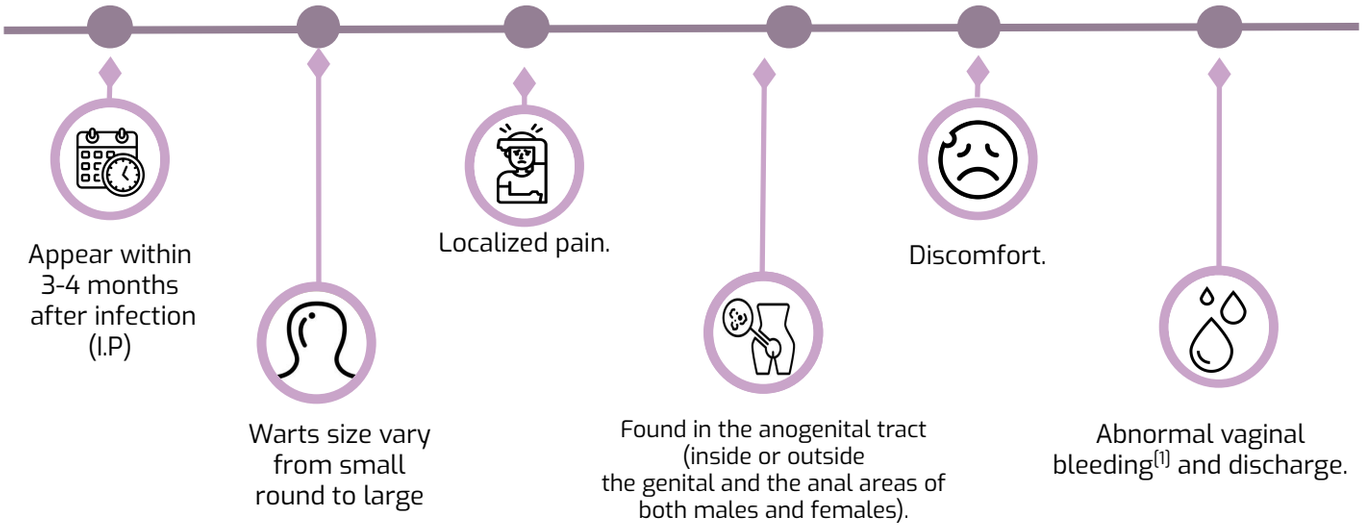
2. Anogenital or mucosal Warts

Transmission	○ Transmission of genital warts mainly occurs during **sexual activity** ○ There is strong association between increasing numbers of sexual partners and prevalence of genital HPV infections. ○ often occur in association with other sexual diseases as **gonorrhea or chlamydial infection.** ○ **Vertical transmission**; from mother to infant or prenatal transmission lesions appear within the first 6 weeks of life have been demonstrated as laryngeal papilloma		
Types	Condyloma acuminata (benign)	(HPV 6,11)	  
	Cervical carcinoma (malignant)	**(HPV 16, 18, 31,45)**	
	Penile and anal carcinoma in men (malignant)	**(HPV 16,18)**	
	Laryngeal Warts (benign)	(HPV 6,11)	

1. HPVs exhibit great tissue and cell specificity, infecting only surface **epithelia** of skin and mucous membranes.
2. On hand
3. On sole of the foot
4. On the face

Human Papillomavirus

Clinical symptoms



HPV and cervical cancer

- Persistent HPV infection is considered the **main cause of cervical cancer**.
- HPV DNA can be detected in most grades of premalignant lesions of the female and male genital tract.
- Dr mona: type 6 and 11 are benign but if it was left untreated for a long time it might become malignant.
- **HPV type 6 and 11** (Condylomata acuminata) are mostly found in **low-grade disease,** is unusually to become malignant, but they occasionally progress to squamous cell carcinoma.
- **HPV 16 and 18** are more commonly associated with lesions of greater severity and great dysplasia which involve all layers of stratified epithelium, and has high chance of progression to metastasizing carcinoma and invasive cancer.
- **> 90% of positive Pap-smear is due to HPV infection.**
  - **Pap-smear:** is a screening test for detection abnormal epithelial cells of the cervix.[2]

Diagnosis

- **External genital warts** can be easily diagnosed by **medical examination**.
- **Internal genital warts** can be visualized by **colposcopy**.
- Lab diagnosis:
  - **Polymerase chain reaction (PCR)** (main test for diagnosis) is used to detect HPV DNA.
  - In-situ DNA hybridization is used for HPV genotyping.
  - **Pap-smear** test is used to identify abnormal epithelial cells of the cervix (cervical dysplasia). **Dr mona:** Pap smear is NOT diagnostic for HPV itself! It only tells us if the epithelium was abnormal. **(make sure u don't mix in the exam)**

Prevention

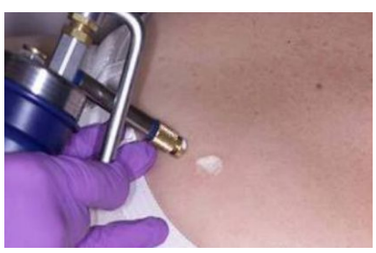
- There are two vaccines available **Gardasil** and **Cervarix** and both are:
  - Recombinant viral-like particles with **no DNA**.(only viral capsid)
  - Given in 3 doses at 0[3], 2, 6 months.
  - **Recommended** for young individuals ages 9-26 yrs old.
  - Not given to pregnant women.
- **Gardasil**: a quadrivalent vaccine, provides **protection against HPV genotypes 6,11,16,18** which causes genital warts and cervical cancer. **(BETTER)**
- **Cervarix**: a divalent vaccine, provides **protection against HPV genotypes 16 and 18** which causes cervical cancer.

1. Usually after sexual intercourse
2. Doesn't detect HPV directly, it detects the epithelial abnormality.
3. 0 doesn't mean at birth, it's just the beginning of the baseline provided for the vaccine. (first shot)

Human Papillomavirus

Dr: not important

Treatment
Topical treatment Applied directly on external warts and Used for several weeks. Examples: ○ Imiquimod, Podofilox. ○ Podophyllin is applied by a doctor and contraindicated in pregnancy. ○ Trichloroacitic acid (T.C.A) safe in pregnancy
Injection: ○ Interferon alpha, 5-flurouracil epinephrine gel. ○ Could be taken for several weeks (8-12).
Cryotherapy: ○ freezing warts by liquid nitrogen
Electrocautery treatment: ○ destroying warts by an electric current
Laser therapy: ○ destroying warts by a focused light beam
Surgical excision: ○ removing warts by surgical tools



Summary

Herpes

Sexually transmitted causes genital warts due to any type of sexual contact

it has 2 types :

HSV-1 , **HSV-2** (more common)

characteristics of the virus :

- **structure :** Ds-DNA with capsid & glycoprotein envelope
- **Ability to induce latent infection**

Pathogenesis :

- **Primary**
  - HSV infect epithelial covering mucosa → replicate → migrate to nearest ganglion to hide
- **Recurrent**
  - When immune system is suppressed it gets reactivated & travel back to primary site causing recurrent infection

Transmission :

- **Sexual transmission**
  - **different sexual partners** correlates directly with acquisition of HSV-2
  - **Homosexual men** are more susceptible to HSV-2 infection.
  - **auto-inoculation**
- **Perinatal transmission during delivery**
  - **50% if the mother has primary genital herpes, while the risk is 8% if mother has recurrent infection.**
  - **To avoid perinatal infection we do caesarean section.**
- **Intrauterine transmission**
  - if maternal primary genital infection developed in 1st trimester → abortion , but if after 20 weeks → induce malformation in baby , 3 forms :
    - Localized skin infection
    - Localized brain infection
    - generalized neonatal herpes infection

Lab diagnosis :

1. **ELIZA** (main) : detect IgM Ab
2. direct IF
3. PCR : in case of neonatal herpes.
4. Tissue culture
5. Tzanck smear

Treatment :

acyclovir

HPV

Characteristics :

- Ds-DNA with capsid
- **Does NOT grow in tissue culture & is very resistant & can remain in environment for long period**

Types :

1. **Cutaneous** : transmitted by **hand touch** , causing common , planter or flat wart
2. **Anogenital** : transmitted **during sexual activity**
   a. Condyloma acuminata & laryngeal wart **(HBV 6,11)**
   b. Cervical carcinoma **(HBV 16,18,31,45)**
   c. Penile/anal carcinoma **(HBV 16,18)**

Lab Diagnosis :

1. **PCR** (main) : detect HBV DNA
2. In situ hybridization
3. Pap smear of cervix epithelium

Vaccines :

- **gardasil : protect against HBV 6,11,16,18**
- **Cervarix : protect against HBV 16,18**

Quiz

MCQ

Q1: in primary genital HSV-2 infection the the virus replicates and migrates to the nearest ganglion which is?

A- Dorsal root ganglia
B- Trigeminal ganglia
C- Sacral ganglia
D- Paravertebral ganglia

Q2: Which of the following antiviral drugs is the first choice in the treatment of HSV-2?

A- Famciclovir.
B- Spiramycin.
C- Acyclovir.
D-sulfadiazine.

Q3: a 32 years old pregnant woman came with inguinal lymphadenopathy and vesicular lesion on the vulva and perineum.
What is the best treatment plan in this conditions?

A- Acyclovir
B- Ganciclovir
C- Zidovudine
D- All the drugs are contraindicated because she is pregnant

Q4: Herpes virus genome consist of?

A- ss-DNA
B- ds-DNA
C- ss-RNA
D- ds-RNA

Q5:Which one of the following HPV genotype commonly cause flat warts?

A- HPV-3
B- HPV-2
C- HPV-1
D- HPV-4

Q6: Which one of the following HPV genotype commonly cause laryngeal warts ?

A- HPV 13
B- HPV 31
C- HPV 11
D- HPV 16

Answers: Q1:C | Q2:C | Q3:A | Q4:B | Q5: A | Q6:C

SAQ

CASE: A woman came to the clinic suffering from itching, pain and herpetic vesicles on the external genitalia. The symptoms appeared after menstruation and she mentioned that she had multiple sexual partners:

Q1: What is the most likely diagnosis?
A: Recurrent genital herpes infection

Q2: What is the most likely causative agent?
A: HSV-2 , HSV-1

Q4: What are the lab methods used for her diagnosis?
A: ELISA, IF, PCR, Tissue culture, Tzanck smear

Q5: What is the appropriate treatment for this patient?
A: Acyclovir, the 1st choice therapy

ALL DONE !

Since it's the last microbiology lecture for the basic years, we hope that we were able to simplify as much information as possible and made studying microbiology more easy and fun!

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This amazing lecture was originally done by 438's team

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