Lecture outline:

PAPILLOMA VIRUSES AND ONCOVIRUSES - *2016*

Prof. N.P. Sunil-Chandra, Senior Professor of Microbiology, Faculty of Medicine, University of Kelaniya

PAPILLOMA VIRUSES

Classification:

Family Papovaviridae (3 distinct genera)
- Papilloma
- Polyoma
- Simian vacuolating virus

ds DNA circular genome.
Icosohedral nucleocapsid.
Naked (Non enveloped.)
EM 52-55nm.

Papilloma viruses further classified into types based on the degree of DNA sequence homology of virus genome -over 60 that infect humans

Papilloma (wart) viruses

Infect and replicate in squamous epithelium on both keratinsed and mucousal surfaces
Causes proliferation of sq epithelium leading to WARTS.
Virus NA is found in basal epithelial cells (basal epithelial layer).
Capsid protein is detected in upper most layer of keratocytes (differentiated cells.)

Anatomical sites of HPV infection:

Infections are extremely common. Clinical presentations may be;
- Cutaneous /Skin Warts (Skin region).
- Mucosal
- Anogenital

Cutaneous warts (HPV types 1-4)

Most frequent in childhood and early adolescence
- Hands (verruca vulgaris)
- Feet (verruca plantaris or plantar wats)
- May occur elsewhere, i.e. face

Mucosal warts

1. Single papillomas may occur in mouth, at any age, and rarely recur after surgical excision
2. Multiple papillomas associated with HPV types 6 & 11 (STD);
   - Commonest benign epithelial tumors of the larynx (laryngeal papilloma) -in children infected via birth canal.
   - More frequent in children than adults
   - Frequently recur after surgical incision

Anogenital warts

An increasingly common STD
Benign warts (condylomata accuminata); may occur on the penis, vulva, cervix, perianal areas due to HPV 6 or 11
Malignant transformation in the cervix associated with **HPV types 16** & **18**

Epidermodysplasia verruciformis:

Rare autosomal recessive disease characterized by multiple warts by
Many wart viruses -types 5 & 8.
May undergo malignant changes. Rare. (e.g ; skin warts ⟶ cancer).
But no evidence for regular skin warts to cause cancer.

Butcher's warts

Associated with type 7.
- Occupational hazard.

Transmission ;

Direct (from skin to skin) & Indirect contact
because they are stable, so can infect indirectly.
i.e.
Acquire plantar warts from contaminated floor, non slip surfaces of swimming pools.

One site to another site - in an individual by shaving.
Between mucosae by sexual intercourse.
Via birth canal laryngeal warts in children.

CLINICAL FEATURES & PATHOGENESIS

Incubation period 1-6 months after the initial infection.
Virus enter via surface abrasion & infect basal cells of skin & mucosa.
Virus replication depends on differentiation stages of host cells.
Virus DNA present in basal cells.
Antigens & infectious virus present in sq keretinised cells.

Skin warts;
- marked proliferation of superficial cells.
-finger like projections.
-flat topped.

Genital warts;
-cauliflower like.

Cervix;
-flat area of dysplasia.

Immunity;

Eventually virus replication is controlled in several months after infection & then warts regresses.
Antibodies are demonstrable.
CMI is more important to recover.
Viral DNA latent in basal layer;

1. May infect occasional stem cells cell Differentiation → shed from surface.

2. In immunocompromised persons crops of warts due to reactivation of latent virus in skin.

Complications;

Association between genital warts & CA of cervix, vulva, penis & rectum.(type 16 & 18).

Epidermo verruciform dysplasia may turn into malignancy.

Cervical cancer risk factors are;

- early age at 1st intercourse.
- multiple sexual partners.
-high parity.
-promiscuity.

Pre malignant lesion ,

- cervical intraepithelial neoplasia (CIN).
("carcinoma in situ")
Type 6 & 11.
-type 16 & 18 in invasive CA.

Treatment;

Variety of treatment. Some of them are doubtful, because warts eventually disappear without treatment.
Current treatment;

1. Application of karyolytic agents.
E.g. Salicylic acid.
2. Destruction of wart tissue by freezing
with dry ice (solid CO2) or with liquid
Nitrogen.
Most commonly used & effective method.

Diagnosis;

is clinical.
Viruses cannot be cultivated.
Serological test not useful.
EM demonstrates particle in skin wart.
Viral Ag by Immuno Fluorescence test , ImmunoPeroxidase test.
Viral DNA In situ hybridization & PCR.

Diagnosis HPV lesions

Laboratory diagnosis:

Evaluation of women with HPV lesions of the cervix detection of cytologic abnormalities in

- Cervical smears
- Colposcopic examination
- Biopsy of suspicious lesions

Biopsy: Screening women for the presence of HPV DNA in premalignant and malignant lesions by PCR is more sensitive than cytology.

Women with genital warts and female partners of males with genital warts should be advised to give regular cervical smears

ONCOGENIC VIRUSES

ONCOGENIC VIRUSES

- Viruses which have the ability to transform host cell to malignant form.
- Result in ; changes in morphology, contact inhibition & biochemical & physical properties.
- Change is brought about by viral nucleic acid (which carries an oncogene) been incorporated to host cell chromosome.

Viruses & Human Cancers

Virus	**Cancer/malignancy**	**Strength of association**	**Co-factor**
1. EBV	Burkitt's lymphoma	++	Malaria Nitrosamine
	Nasophrangeal carcinoma	++	Immunosuppression
	Hodgkin disease	+	Immunosuppression
2. HHV-8	*Kaposi's Sarcoma*	++	?
3. HPV	CA cervix	++	-
	Skin cancer	+/-	-
4. HBV & HCV	Liver cancer/ hepatocellular carcinoma	++	-
5. HTLV 1&2	T cell leukaemia	++	-