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Original Research Paper

Oral Pathology

VIRAL INFECTIONS OF ORAL CAVITY – A REVIEW

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ABSTRACT Examination of oral cavity is an integral part of general dentistry. It is common to come across various viral diseases in the oral cavity. The clinical diagnosis of viral lesions sometimes become confusing due to similar clinical presentations, confusion leads to misdiagnosis and eventually the treatment 1. Infections of the oral cavity manifest as either ulceration or blistering presentation of oral tissues. Different viral agents, such as oral herpesviruses, human papillomavirus, and Coxsackie virus, are responsible for primary oral lesions, while other viruses, such as human immunodeficiency virus, affect the oral cavity due to immune system weakness 3. The clinical presentation, diagnosis and management of common viral infections of the oral mucosa are discussed2

KEYWORDS : Viral infections, Herpes virus, Human papilloma virus

INTRODUCTION:

A viral disease of the oral cavity is the infectious type of pathology affecting the oral tissues. Viral diseases may occur either due to cellular destruction or consequence of immune reaction following viral proteins. Viral infections typically present with sudden onset and association of solitary or multiple blister or ulcerations[4]. Some viral infections are associated with tumor formation hence, early reporting and referral to oral disease management are essential in dental practice[4]. Dentists play a crucial role in examining, diagnosing, and managing such lesions, particularly considering the impacts of oral diseases on overall health and quality of life.

Commonly Occuring Viral Infections Of Oral Cavity:

1) HERPES SIMPLEX INFECTION
2) VARICELLA ZOSTER
3) COXSACKIE VIRUS
4) HUMAN PAPILLOMA VIRUS
5) MEASLES OR RUBELLA
6) EPSTEIN BAR VIRUS
7) HUMAN IMMUNODEFICIENCY VIRUS (HIV)

Herpes Simplex Infection:

Herpes SimplexVirus belongs to herpes viridae group and is a significant pathogenic virus that cause mucocutaneous conditions in the oral cavity and genital region[4].

Two immunologically different types of HSV are seen: Type 1 & Type 2.

HSV Type 1 can be isolated from two lesions of the Oral cavity–

1. ACUTE HERPETIC GINGIVOSTOMATITIS
2. HERPES LABIALIS[1]

1. Acute Herpetic Gingivostomatitis:

Etiology:

Herpes simplex virus-1 causes primary herpetic gingivostomatitis. Herpes virus is a DNA virus which will replicate in the nucleus of host cell[9].

Pathophysiology:

Both HSV-1 and HSV-2 have three major biological properties that plays an important role in disease pathogenesis. These properties include neurovirulence, latency, and reactivation. Neurovirulence is the ability of the virus to invade and replicate in the nervous system, and latency is the ability to maintain the latent infection in the nerve cell. Reactivation is the ability of the virus to replicate and cause the disease process again, once induced by specific stimuli[11]

The vesicles formed by lysis of epithelial cells rupture to formulcers which heal without scar formation. Spreads through the infected saliva or droplets. Infection exists even in the absence of visible lesions. The virus remains latent in the regional ganglion after the primary infection and then reappears whenever there is a trigger[9]

Clinical Features:

HSV-1 infection of oral cavity includes vesicles as well as ulcerations that appear on the oral mucosa and generalized acute marginal gingivitis, often follows prodromal symptoms[6,7]

The initial sign of herpetic gingivostomatitis is hyperemia of oral and perioral mucosa, followed by rapidly spreading vesicular lesions on the gingiva, palate, buccal, and labial mucosa. The lesions may ulcerate and then rupture. On physical examination, these may appear as flat, yellow color, and approximately 2 to 5 mm in size. The ulcers are rapid to bleed and typically heal without scarring in 2 to 3 weeks[11]

Histopathological Features:

Histopath features suggests characteristic ballooning degeneration which are actually the swollen infected cells with pale eosinophilic cytoplasm and large vesicular nuclei. In other cases Lipschutz bodies I.e eosinophilic, ovoid, homogenous structures within the nucleus that displace the nucleus and nuclear chromatin peripherally can be seen[1]

Histological appearance of a mucosal herpetic infection includes degeneration of stratified squamous epithelial cells, acantholysis, and formation of an inflammatory infiltrate surrounding the capillaries of the dermis. The characteristic

feature of intranuclear inclusion bodies known as Cowdry type A are found on light microscopy showing arrays of viral capsids and electron-dense glycoproteins[11]

Management:
Primary HSV infections are treated with palliative care. Symptomatic and milder patients are managed by supportive care that includes maintenance of fluids, acetaminophen that reduces fever, and use of topical anesthetics such as lidocaine, liquid Benadryl, to relieve oral burning sensation and pain.[4]

The important component in the management of herpetic gingivostomatitis is hydration. Adequate hydration is achieved with pain control; thus, analgesics such as oral acetaminophen and oral rinses are encouraged to make the patient more comfortable and promote fluid intake [11]

Systemic acyclovir can be used for immunocompromised individuals.

Differential Diagnosis:
- Herpes zoster
- Primary chickenpox
- Herpetiform aphthae
- Erythema multiforme
- Acute necrotizing gingivostomatitis
- Cytomegalovirus ulceration
- Traumatic ulcers
- Burns and chemicals

2. Herpes Labialis
Etiology And Pathogenesis:
Common colds, influenza, fever, UV exposure, menstruation, emotional stress and anxiety predispose the patient to recurrent infection, as these cause reactivation of the virus, which subsequently migrates along one of the sensory divisions of the trigeminal nerve[2]

Clinical Features:
The lesions are most commonly seen at the mucocutaneous junction of the lip or peri-oral skin. A burning sensation usually initiates the development of a small cluster of vesicles[1]

Classic manifestation of this form of recurrent herpes is localized cluster of small vesicles along the vermilion border of the lip or peri-oral skin. The vesicles turn to ulcers, and crust within 24 to 48 hours. The crust falls off and uneventful healing occurs within 7 to 10 days. It is highly contagious and spreads even when the sores are not visible[9]

Histopathological Feature:-
It is Characterized by Ballooning degeneration, chromatin margination and Lipschutz bodies, and multinucleated giant cells.

Treatment:
Acyclovir is a potent drug of choice and may be life saving for herpetic encephalitis and disseminated infection, especially in those individuals who are immuno-compromised. It will accelerate healing if used sufficiently in the early disease stage[2]

Varicella Zoster:
The Varicella-zoster virus (VZV) or human herpes virus 3 is the causative virus for both chickenpox/varicella and shingles/ Herpes zoster (HZ)[8]

This pathogenic virus that is known to cause mucocutaneous conditions in oropharyngeal mucosa and skin[7]

Chickenpox (varicella) results from primary infection, while reactivation of the infectious virus is known as herpes zoster (shingles)[1] Conditions leading to herpes zoster are those that cause immunosuppression, such as cytotoxic drugs, radiation, internal malignancies, malnutrition, old age, and alcohol and substance abuse[1]

Clinical Features:
Intra-oral vesicles , are seen on the tongue, buccal mucosa, gingival, palate and oropharynx. They generally are not very painful. Following the primary infection, the virus is transported through the sensory nerves to the dorsal spinal ganglia or trigeminal ganglion, where it remains latent[2]These unilateral vesicles forms clusters with areas surrounding erythema, ending abruptly in the midline. These vesicles ulcerate and form pustules within three to four days. A crust lesion is then formed, and healing takes place within seven to ten days[1]

Vesicular change occurs which rupture later leaves behind shallow ulceration surrounded by erythematous halos which can be painful. Soft palate is the common site of involvement usually between the tonsils and the uvula. Lesions heals spontaneously after few days[10]

Histopathological Features:
Edema is seen both intracellular and intercellular with an intraepithelial vesicle. Reticular degeneration, and ulceration surrounded by mixed inflammatory cell infiltrate is often observed[9]

Treatment:
Antiviral medication is prescribed in patients with frequent episodes. Hot or cold compresses can be used to reduce discomfort. Hydration of the child should be maintained. Medications for fever and pain reduce the discomfort and antibiotics prevent secondary bacterial infection[9]

Coxsackie Virus:
Herpangina:
Herpangina affects children, mainly during summer, and is characterised by a sudden onset of malaise, fever and sore throat[2]

It is Caused mainly by Coxsackie Virus group A. Herpangina affects children, during summer, and is characterised by a sudden onset of malaise, low grade fever, sometimes vomiting, prostration abdominal pain and sore throat[1]

Clinical Features:
Manifestation in oral mucosa as vesicles, ulcerations and diffuse erythema on the soft palate, fauces and tonsillar areas.The ulcers grow in a crop like fashion and with an grey base with inflamed periphery on the anterior faucial pillars and sometimes on hard and soft palate[1].Patients present with vesicles, ulcerations and diffuse erythema on the soft palate, fauces and tonsillar areas[2].The systemic symptoms reduces in two to three days and the ulcers heal in seven to ten days[2]

Hand, Foot And Mouth Disease:
Hand, foot, and mouth disease (HFMD) is a common viral infection usually affecting infants and children but can affect adults[12].An epidemic infection which is Caused by the enterovirus Coxsackie A16[1]

Pathophysiology:
The spread of the human enterovirus is initiated by oral ingestion of the shed virus from the gastrointestinal or upper respiratory tract of infected hosts or through vesicle fluid or oral secretions[12].After ingestion, the virus multiplies in the lymphoid tissue of the lower intestine and the pharynx and spreads to the regional lymph nodes[13]

Clinical Features:

The most common symptom of hand, foot, and mouth disease is usually mouth or throat pain secondary to the enanthem. The presence of vesicles is surrounded by a thin halo of erythema, rupturing and forming superficial ulcers with a grey-yellow base and erythematous rim[12].Dysphagia is one of the most common findings, which can be a differential diagnosis with other oral ulcerations and vesicular lesions like Herpangina [1]

Treatment:
Hand, foot, and mouth disease is a clinical syndrome and will resolve within 7 to 10 days. Treatment is primarily supportive. Pain and fever can be treated with NSAIDs and acetaminophen[12]

Human Papilloma Virus:
Focal Epithelial Hyperplasia (heck's Disease):
Etiology And Pathogenesis:
Papillomaviruses are one of the oldest existing viruses. Human papillomaviruses have tropism for the squamous epithelium (10). Viral particles attaks the basal cells of the epithelium, which are exposed through micro-abrasions or epithelial wounding[13]

Clinical Features:
Presents with multiple asymptomatic, slightly elevated, mucosa-coloured, smooth-surfaced nodules that occurs on the labial or buccal mucosa gingivae or tongue of children[1].Individual lesions tend to be small (0.3 to 1 cm), and they frequently cluster and coalesce, giving the mucosa a cobblestone or fissured surface[1]

B. Squamous Cell Papilloma:
Caused by HumanPapillomaVirus type 6 and 11. It may occur at any age, but is most commonly diagnosed in the age group 30 to 50 years. It is clinically and microscopically indistinguishable from verruca vulgaris which is a virally induced focal hyperplasia of epidermis[1].Exophytic growth made up of numerous small finger like projections which result in lesions with a roughened verrucous and cauliflower like surface. Nearly a well circumscribed pedunculated tumor, occasionally sessile. It initially grow rapidly, but seldom grows beyond 5 mm in diameter Generally painless usually white but sometimes pink in colour[1]

Verruca Vulgaris:
Also called as Common Wart. Frequent tumor to skin analogous to oral papilloma. Verruca vulgaris is a very common in childhood.

C. Condyloma Acuminatum:
Condyloma accuminatum is usually seen on the genitals, although it may be found in the oral cavity. Oral lesions are predominantly transmitted through oral-genital contact. It consists of several cauliflower-like lesions, some of which are larger than 0.5 cm. They may enlarge and become as large as 3 cm in size. The most common intra-oral sites are labial mucosa and the lingual frenum and soft palate[2]

Treatment:
No treatment is usually required for focal epithelial hyperplasia, as these nodules undergo spontaneous regression during puberty[2].Human papillomavirus antibodies can be detected in the saliva, and their concentrations are increased after Human PapillomaVirus vaccination. This supports the view that HPV vaccines can be protective in the head and neck region, if given before the first exposure to HPV[13]

Measles:
Measles, a paramyxovirus infection, is most commonly seen in children as an acute febrile illness and as anerythematous maculopapular skin rash[2].Acute, contagious, dermatotrophic and endemic viral infection, primary affecting children and occurring many times in endemic form[1]

Clinical Features:
It is Characterized by acute febrile illness and erythematous maculopapular skin rash. Fever, malaise, conjunctivitis, cough and coryza are mainly seen as prodromal symptoms which is followed by a generalized exanthematous skin rash[1]

Oral Manifestation:
The common oral manifestation of measles is known as Koplik's spots. Occurs early in the course of the infection and often precede the skin rash by 1 to 2 days. These are white-red macules that appear on the buccal and labial mucosa. These macules represent foci of epithelial necrosis [14]

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Rubella:
Rubella is also known as German measles. Its clinical appearance is very similar to rubeola/measles. Like measles it is seen in children and adults and sometimes can even result in any congenital abnormality if mother of the fetus is infected. The causative agent is rubella, which is an RNA virus. The virus is shed from the throat and is spread through respiratory tract droplets[9]

Symptoms includes exanthematous rashes, fever, malaise and lymphadenopathy. Intra-orally palatal petechiae are seen on the soft palate, which is known as the Forchheimer sign. Conjunctivitis, orchitis, and arthritis are the other complications of rubella infection[9]

Characterised by erythematous or violaceous plaque that develop into tumorous growths over time.These larger lesions may become ulcerated and painful and interfere with function[1]

Treatment:
Supportive therapy including bed rest, fluids, adequate diet and non-aspirin antipyretics are recommended for relief[2]

Epstein Barr Virus:
Epstein–Barr virus (EBV), a B-lymphotropic gamma-herpesvirus, causes infectious mononucleosis and oral hairy leukoplakia, and it is associated with various types of lymphoid and epithelial malignancies[15]

Cell entry is a fundamental part of the infection process for any virus, and cell surface receptors are the critical molecules for target cell recognition determining cell tropism and species specificity [17,18,19]

The transmission of EpsteinBarrVirus infection occurs following contact with the oral secretions, saliva on fingers, toys or other objects. It replicates in epithelial cells of the oropharynx and viruses are usually shed in the saliva.4.EBV is responsible for infectious mononucleosis. EBV is reported to be associated with several lymphoproliferative disorders, lymphomas (African Burkitt's lymphoma), and nasopharyngeal carcinoma[4]

Clinical Features:
The classical triad of EBV are fever, lymphadenopathy, and pharyngitis. Other symptoms of Epstein BarrVirus infection are fever, lymphadenopathy, pharyngitis, hepato splenomegaly, oral ulcerations, rhinitis and cough. Hepatomegaly, rhinitis, and cough are frequently observed in children less than 4 years of age [4]

EBV infection with damage of the periodontal pocket epithelium may contribute to gingival bleeding, as suggested by a high prevalence of EBV[15]

Management:

Supportive therapy is given in the management of EBV infection. Corticosteroid and antiviral medication are usually employed for immunocompetent patients[4]

Human Immunodeficiency Virus:

Oral lesions are among the earliest clinical manifestations of human immunodeficiency (HIV) virus infection and are important in early diagnosis and for monitoring the progression to acquired immunodeficiency syndrome (AIDS)[25] Routes of HIV transmission includes transfusion of blood and its products [9]

Oral manifestations of HIV infection

1. Infections: bacterial, fungal, viral
2. Neoplasms: Kaposi's sarcoma, non-Hodgkin's lymphoma
3. Immune mediated: major aphthous, necrotizing stomatitis
4. Others: parotid diseases, nutritional, xerostomia
5. Oral manifestations as adverse effects of antiretroviral therapy[20]

Fungal:

Candidiasis:

Oral or pharyngeal candidiasis are the commonest fungal infections observed as the initial manifestation of HIV infection[4].The commonest species of candida involved is Candida albicans although nonalbicans species have also been reported.

There are four forms of oral candidiasis:

Erythematous candidiasis, pseudomembranous candidiasis, angular cheilitis, and hyperplastic or chronic candidiasis.[2] candidiasis appear as creamy white curd-like plaques on the buccal mucosa, tongue, and otheroral mucosal surfaces that can be wiped away, leaving a red or bleeding surface Treatment of oral candidiasis depends on the type, distribution, and severity of infection. Topical treatment is effective for limited lesions. Clotrimazole troches and nystatin oral suspension are effective for mild-to-moderate erythematous and pseudomembranous candidiasis.[20]

Viral Infections:

Oral hairy leukoplakia:

Characterized by white, corrugated, non-removable lesion on the lateral margin or ventral margin of the tongue. Surface may or may not be corrugated but corrugation can be seen on inferior surface of the tongue or in the buccal mucosa[1].It could be differentiated from chronic hyperplastic candidiasis or leukoplakia (a potentially malignant lesion)[2]

Lesions may be variably sized and may appear as white striations, corrugations, or as flat plaques, or raised, shaggy plaques with hair-like keratin projections. In most cases, hairy leukoplakia is bilateral and asymptomatic. When it leads to discomfort it is usually associated with superimposed candidal infection[20].This condition usually does not require treatment but use of oral acyclovir, topical podophyllum resin, retinoids, and surgical removal is recommended.[20]

Bacterial Infections:

Linear erythematous gingivitis

Necrotizing ulcerative periodontitis (NUP)

NEOPLASMS:

Kaposi's sarcoma:

Kaposi's sarcoma is characterised by erythematous or violaceous plaque like lesion that develop into tumorous growths over time. These larger lesions may become ulcerated and painful and may interfere with function[2] Characterised by erythematous or violaceous plaque like lesions that develop into tumorous growths over time.These larger lesions may become ulcerated and painful and may interfere with function. ORAL SITES: Predominantly seen in the palate or on the attached gingivae, but can appear on other mucosal sites [1]

A variety of treatment options are available varying from intralesional injection of chemotherapeutic or sclerosing agents to surgery and radiation[2]

CONCLUSION:

The most common reason for oral ulcerations and blisters are viral infections[4]Since oral cavity harbours many infectious diseases thorough examination. Routine check up is needed[1].The conditions of the immune system highly influence the risk of developing these infections. Additionally, immunosuppression, malnutrition, and immunoflourescence are the most frequent disorders involved in the reactivation of herpesviruses. The differential diagnosis of other infections is very important to ensure the proper treatment of patients[26].Examination of the oral cavity should be routinely performed as the oral mucosa and is often the first site affected by viral infections[2].

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