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Viral Pathology in Pediatric Patients.

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Abstract

This review aims to summaries common pediatric viral oral and maxillofacial pathologies. It will focus on lesions that have a particular predeliction for children. Recognition and appreciation of the clinicopathological features should facilitate an appreciation because certain oral and maxillofacial lesions are more common in this age group.[1]

Keywords: Oral, Pathology, Clinical

Introduction

Viral infections of the oral mucosa are frequently encountered in paediatric patients. The clinical diagnosis of these lesions can sometimes be confusing due to similar clinical presentations. The clinical presentation, diagnosis and appropriate management of common viral infections of the oral mucosa are discussed. [2]

Herpetic Infections

Primary Herpetic Gingivostomatitis

The infection that accompanies primary herpetic gingivostomatitis is usually subclinical in early childhood and only a small percentage of patients develop an acute primary infection. This usually occurs in older children and consists of fever, malaise, headache, cervical lymphadenopathy and a vesiculo-ulcerative eruption on the perioral skin, vermilion or any intra-oral mucosal surface.[3] The vesicles, which are 2 to 3 mm in diameter, rupture, leaving painful ulcers that heal without scarring after seven to ten days. The gingivae are swollen and reddish due to a general inflammation. The virus then migrates to the trigeminal ganglion, where it remains latent. In more affluent countries with better living conditions and less overcrowding, many young adults do not acquire the infection during childhood. They are at risk of developing a

symptomatic infection as an adult, usually presenting as a pharyngotonsillitis, with constitutional symptoms of fever, malaise and headaches. In the case of cervical lymphadenopathy, the vesicles and ulcers on the tonsils and posterior pharynx can resemble infectious mononucleosis or a streptococcal sore throat infection. Primary infection in an immunocompromised adult can be life threatening, with disseminated disease, or it may present with extensive non-healing oral ulceration.[4]

Secondary Herpes Labialis

Around 15 to 30% of the community is affected by episodes of secondary herpes simplex lesions (herpes labialis). Common colds, influenza, fever, UV exposure, menstruation, emotional upset, 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. The lesions are most often seen at the mucocutaneous junction of the lip or perioral skin. A burning sensation usually precedes the development of a small cluster of vesicles. These vesicles enlarge, coalesce, ulcerate and become crusted before healing within 10 days.

Diagnosis and management

The clinical features are usually sufficient to diagnose these conditions. The differential diagnosis of primary herpetic gingiva-stomatitis includes recurrent aphthous ulceration, which forms ulcers on non-keratinised oral mucosa without a vesicle phase.

There currently is no drug available to prevent the migration of the herpes virus to the trigeminal ganglion after primary infection. Acyclovir is a potent drug 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 early in the disease stage. Bed rest, fluids and a soft diet, with antipyretics for fever, are recommended for primary herpetic gingivostomatitis. Preventative therapy, such as using sun block, is the management of choice for herpes labialis, while antiviral drugs such as acyclovir are only useful if applied at the prodromal stage before the development of vesicles.[5] Patients must be discouraged from touching the lesions in order to reduce the risk of spreading the infection to other sites. Systemic acyclovir may be used for immuno-compromised individuals.[3]

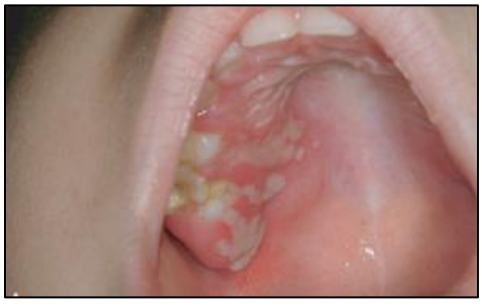

Fig 1: Clinical manifestations of HSV type1 infection[15]

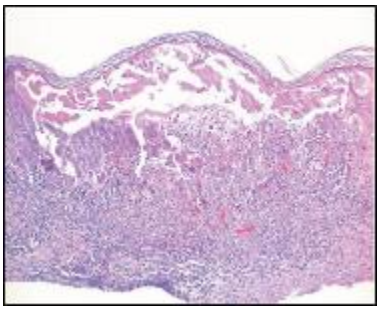

Fig 2: herpes keratinocytes and a mixed inflammatory infiltrate of the upper and mid dermis. [15]

Varicella-Zoster Virus

Chickenpox (varicella) results from primary infection, while reactivation of the virus is known as herpes zoster (shingles). Intra-oral vesicles of varicella, when present, 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 via the sensory nerves to the dorsal spinal ganglia or trigeminal ganglion, where it remains latent.

A number of predisposing factors can lead to a recurrence of the infection in the tissue supplied by the sensory nerve. Conditions leading to herpes zoster are usually those that cause immunosuppression, such as cytotoxic drugs, radiation, internal malignancies, malnutrition, old age, and alcohol and substance abuse. Occasionally, dental manipulation in a localised area can lead to reoccurrence. The first signs of herpes zoster are pain and tenderness in the dermatome corresponding to the affected sensory ganglion. In the head and neck area, vesicles form on one side of the face or in the oral mucosa in one of the divisions of Trigeminal nerve. These unilateral vesicles form clusters with areas of surrounding erythema, ending abruptly in the midline. The vesicles ulcerate and form pustules within three to four days. A crust lesion then forms, and healing takes place within seven to ten days. These lesions often heal with scarring and areas of hypo/hyperpigmentation may be seen. When the Facial Nerve and Auditory Nerve are involved (via the geniculate ganglion), facial paralysis, vesicles on the external ear, tinnitus, deafness and vertigo may follow. This is known as Ramsay-Hunt syndrome.[6]

Spontaneous bone necrosis of the mandible, occurring during an acute attack of herpes zoster, has been seen in immune-compromised patients.[7] The patients present with the unilateral vesicles of herpes zoster, with subsequent unilateral exfoliation of the teeth in the necrotic mandible.

A residual complication of herpes zoster is post-herpetic neuralgia. It occurs in 10% of patients with herpes zoster and affects the trigeminal nerve, most commonly the ophthalmic division. There is persistent, unilateral pain in the affected area. A history of previous skin lesions and possible scarring may aid in the diagnosis. The pain is not paroxysmal, as is seen in trigeminal neuralgia, although it may be just as severe.

Diagnosis and management

The clinical picture is often distinctive. Herpes zoster may be confused with recurrent Herpes simplex virus infection. Herpes zoster has a longer duration, a more severe prodromal phase, unilateral vesicles and ulceration, with abrupt ending at the midline and post-herpetic neuralgia.

The treatment is supportive and symptomatic, with topical or systemic anti-pruritics and analgesics that do not contain aspirin. A high dose of oral acyclovir (800 mg five times daily for seven days) is recommended for treating both primary and recurrent infections in immuno-compromised patients.[8]

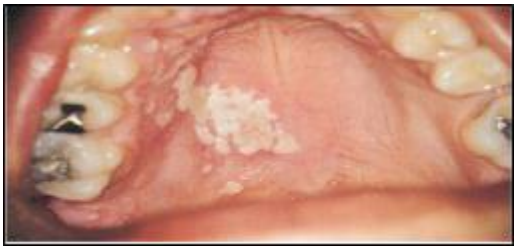

Fig 3: clusters of vesicles on palate.[16]

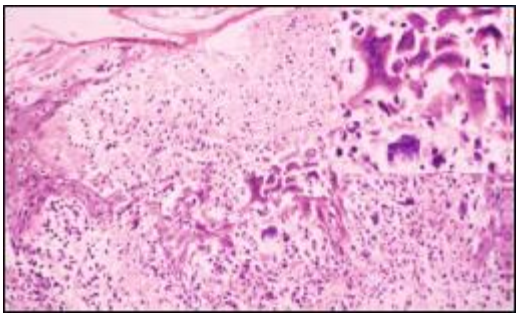

Fig 4: vesicle smear showing intercellular vacuolation & multinucleated epithelial cells.[17]

MUMPS

Mumps is a common childhood infection caused by the mumps virus. The hallmark of infection is swelling of the parotid gland. Aseptic meningitis and encephalitis are common complications of mumps together with orchitis and oophoritis, which can arise in adult men and women, respectively; other complications include deafness and pancreatitis. Clinical diagnosis can be based on the classic parotid swelling; however, this feature is not present in all cases of mumps and can also occur in various other disorders. Laboratory diagnosis is based on isolation of virus, detection of viral nucleic acid, or serological confirmation (generally presence of IgM mumps antibodies). Mumps is vaccine-preventable, and one dose of mumps vaccine is about 80% effective against the disease. Routine vaccination has proven highly effective in reducing the incidence of mumps, and is presently used by most developed countries; however, there have been outbreaks of disease in vaccinated populations.[9]

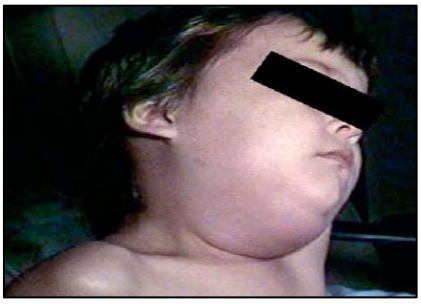

Fig 5: Hallmark swelling of parotid gland in a child with mumps.[18]

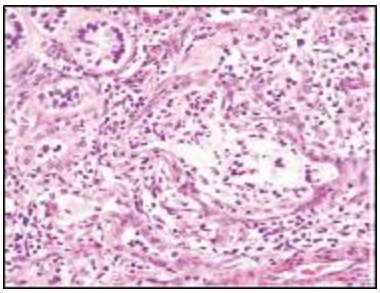

Fig 6: Mumps orchitis characterized by oedema, mixed inflammatory infiltrate and necrosis.[19]

MEASLES

Measles, a paramyxo virus infection, is most commonly seen in children as an acute febrile illness and erythematous maculo-papular skin rash. The incidence of measles has decreased dramatically in many communities due to successful vaccination programs although it has re-emerged in unvaccinated children, mostly amongst children of poor rural communities. Following an incubation period of 10 to 12 days, a prodromal phase consisting of fever, malaise, conjunctivitis, cough and coryza is seen. This is followed by a generalized exanthematous skin rash. The oral manifestation of measles is known as Koplik's spots. These occur early in the course of the infection and often precede the skin rash by 1 to 2 days. Koplik's spots are white-red macules on that appear on the buccal and labial mucosa. These macules represent foci of epithelial necrosis.[10]

Diagnosis and management

Diagnosis is based on the clinical features and history. Laboratory confirmation is possible for atypical cases. Supportive therapy including bed rest, fluids, adequate diet and non-aspirin antipyretics are recommended for symptomatic relief.

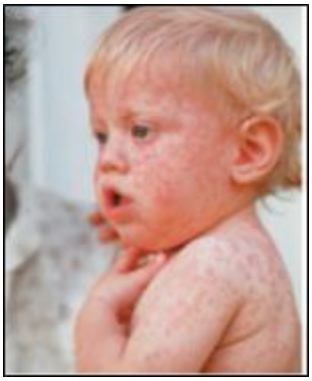

Fig 7: Child having generalised eruptions of measles.[20]

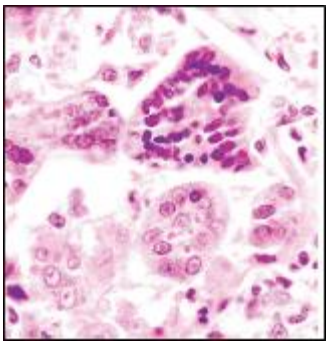

Fig 8: Measles infected cells are multinucleated and contain eosinophilic cytoplasmic & nuclear inclusion.[19]

Rubella (German Measles)

Rubella virus (family Togaviridae) is transmitted primarily via respiratory droplets and spreads haematogenously, with the ability to cross the placenta.[12] Children who are infected develop a pink rash spreading from the face to the rest of the body, and have low fever and cervical lymphadenopathy, whereas adults have a prodrome that often includes arthritis. Congenital infection may result in fetal loss or a syndrome including sensorineural deafness, cataracts, and heart defects. Infections are otherwise self-limiting and often asymptomatic. The MMR vaccine, containing an attenuated rubella virus strain, given at 12–15 months and 4–6 years, provides long-lasting immunity. Screening of women prior to conception is recommended. The diagnosis of rubella can be confirmed by serology, by RT-PCR (oronasopharyngeal swab, urine, blood, CSF, or amniotic fluid), or by viral culture, and skin lesions are rarely biopsied. The histology of congenital infections is characterized by non-inflammatory necrosis in the placenta with villous hypoplasia, and necrosis and inflammation of many fetal organs. 'Blueberry muffin' skin lesions are composed of erythrocytes. No characteristic VCPEs are observed.[13]

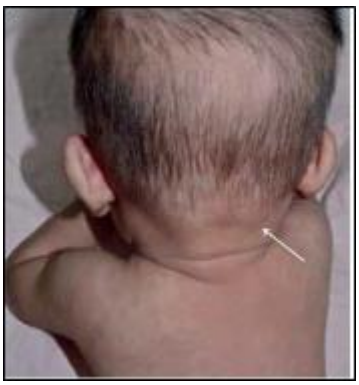

Fig 9: Bilateral suboccipital lymph nodes & a maculo papular rash on the back.[21]

Fig 10: Congenital rubella syndrome includes nuclear cataracts.[19]

Coxsackie Virus

Hand, foot and mouth disease

Hand, foot and mouth disease is most commonly seen amongst children aged one to five years. In 75% of cases it presents with an eruption of vesicles on the palms of the hands and on the feet. Occasional vesicles may also be found on the proximal extremities and buttocks. There are also vesicles in the anterior part of the mouth. An associated low-grade fever and malaise are usually present.

Diagnosis and management

The clinical features of Coxsackie virus are distinctive. The distribution of the lesions of herpangina differentiates it from primary herpetic gingivostomatitis, which affects the gingivae, whereas herpangina is an oropharyngitis. The systemic symptoms differentiate it from recurrent aphthous ulceration. The vesicles also help to distinguish herpangina from streptococcal pharyngitis.

In the case of hand, foot and mouth disease, the cutaneous vesicles can resemble chickenpox; however, in chickenpox the vesicles usually start on the face and trunk and then spread to the extremities. Involvement of the palms and soles is rare in chickenpox infections. Oral lesions are also rare in chickenpox.[2]

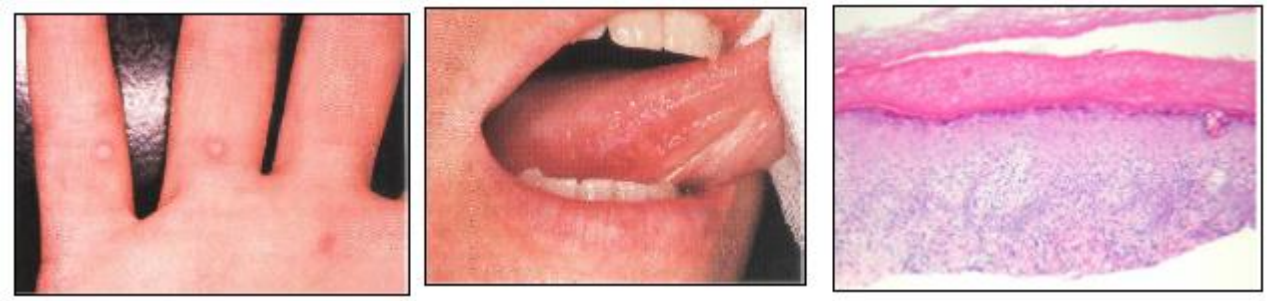

Fig 12: Lymphocytic infiltration & keratinocyte apoptosis in early lesions.[23]

Herpangina

Herpangina affects children, mainly during summer, and is characterised by a sudden onset of malaise, fever and a sore throat. Patients present with vesicles, ulcerations, and diffuse erythema on the soft palate, fauces and tonsillar areas. The systemic symptoms settle in two to three days and the ulcers heal in seven to ten days.

Herpangina and hand, foot and mouth disease are self-limiting, of short duration and need no treatment. Symptomatic treatment is advised.[12]

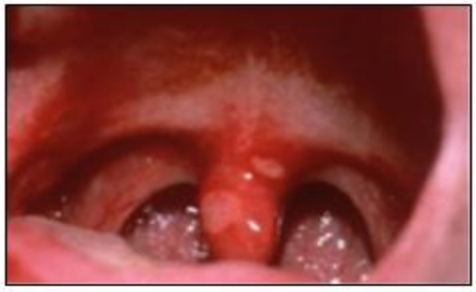

Fig 13: Shallow, apthous like ulcers of uvula and soft palate.[24]

Infectious Mononucleosis

Infectious mononucleosis, also known as “mono,” is an illness that usually affects adolescents and young adults.

Infectious mononucleosis (“mono”) is caused by an Epstein-Barr virus (EBV) infection. Epstein-Barr virus is a member of the herpes virus family and is one of the most common viruses that infects humans.

Most Americans have had an EBV infection by age 40 years. Epstein-Barr virus is spread through bodily fluids. It is most commonly transmitted through saliva, which is why mono is sometimes called “the kissing disease.” The virus can also be transmitted through mucus, blood, semen, or vaginal secretions. For some people, especially young children, an EBV

infection does not cause any symptoms. Others may develop a brief illness that is milder than mono. For those who develop mono, symptoms appear 4 to 6 weeks after the time of infection. The symptoms of mono are common to many infections. Fatigue is often more severe with mono than with other viral illnesses. Common symptoms of mono include fatigue, fever, sore throat, swollen lymph nodes, especially in the neck, body aches and loss of appetite. Rash is another common symptom.

Most symptoms go away in 2 to 4 weeks, but patient might continue to feel tired for several weeks or even months.

Diagnosis and Treatment

A doctor may suspect mono based on symptoms. A blood test can confirm the diagnosis. There are no medications to treat the infection itself. Antibiotics do not help because antibiotics do not work against viruses, including EBV.[14]

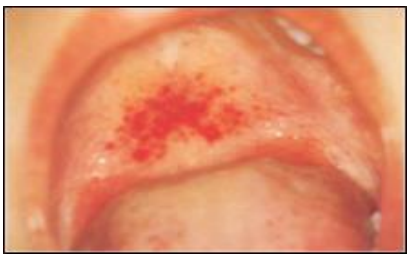

Fig 14: Petechiae on palate.[16]

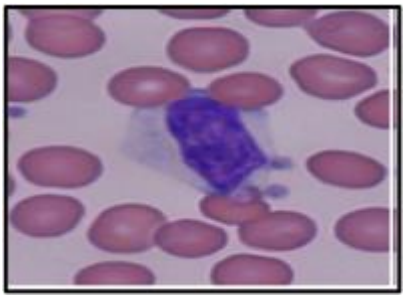

Fig 15: Downey cells surrounded by erythrocytes.[16]

Human Papillomavirus

Focal Epithelial Hyperplasia (Heck's Disease)

Heck's disease presents with multiple asymptomatic, slightly elevated, mucosa-coloured, smooth-surfaced nodules that occur on the labial or buccal mucosa gingivae or tongue of children. Individual lesions tend to be small (0.3 to 1 cm), but they frequently cluster and coalesce, giving the mucosa a cobblestone or fissured surface. Most lesions are found in children, although they occasionally can be found in older age groups. They usually regress spontaneously with age.[2]

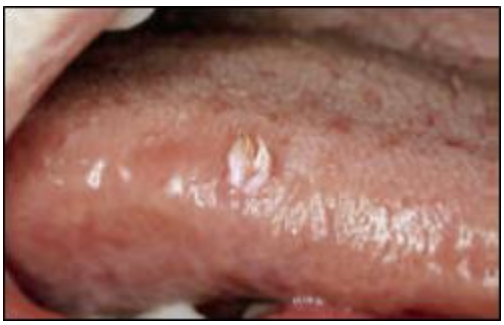

Fig 16: Papilloma on tongue.[25]

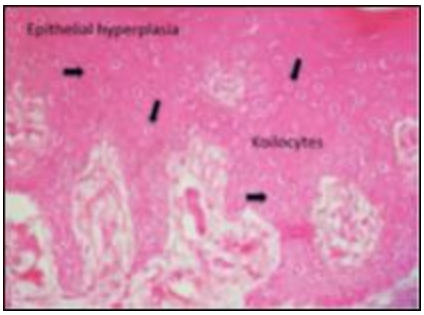

Fig 17: Epithelial hyperplasia and koilocytes.[25]

Conclusion

Examination of the oral cavity should routinely be performed as the oral mucosa is often the first site affected by viral infections. A thorough medical history together with a detailed examination will result in an accurate diagnosis for the majority of viral lesions affecting the oral cavity, resulting in appropriate patient care. Persistent lesions, especially if ulcerated, should be biopsied to exclude the possibility of a non-infective, more serious aetiology. Biopsies or other laboratory investigations should also be performed if a clinical diagnosis cannot be established. This is especially true in the setting of HIV/AIDS that can influence the typical clinical features of viral infections.

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