Case Based Oral Mucosal Diseases

Qianming Chen
Xin Zeng
Editors

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ISBN 978-981-13-0285-5 ISBN 978-981-13-0286-2 (eBook)
https://doi.org/10.1007/978-981-13-0286-2

The print edition is not for sale in China Mainland. Customers from China Mainland please order the print book from: People's Medical Publishing House

Library of Congress Control Number: 2018952230

Printed on acid-free paper

This Springer imprint is published by the registered company Springer Nature Singapore Pte Ltd.
The registered company address is: 152 Beach Road, #21-01/04 Gateway East, Singapore 189721, Singapore

Preface

The catch-all term, oral mucosal diseases, refers to various diseases of the oral mucosa and related soft tissues. Aside from certain individual cases that can be attributed to local factors, a majority of oral mucosal diseases occur due to a combination of both local and systemic factors. In recent years, the model of biological-psychological-social medicine has become especially significant in studying the pathogenicity and management of oral mucosal diseases.

Since an increase has been recorded in the incidence rate and the number of complicated cases of oral mucosal diseases, the Department of Oral Mucosal Diseases has been tasked with the regular development of novel diagnostic and treatment methods. As a result, we have left no exceptions in exploring clinical cases. In addition to a large number of common cases, an increasing number of rare, anomalous cases of oral mucosal diseases have been recorded. Often, it is difficult to provide immediate and definitive diagnoses for the latter type of cases. In order to provide definitive diagnoses, as well as out of curiosity, we took the initiative to review pictures, books, and other literature, as well as communicate with experts in relevant disciplines. Based on the information from such data and communications, we further examined patients to provide an accurate diagnosis and treatment. We feel gratified and accomplished because our expertise has allowed us to help patients who seek medical attention from us. Such experiences have left us even more intrigued by the complexity of oral mucosal diseases, further igniting our strong interest in this discipline.

"A picture is worth a thousand words." This is an inspirational quote that comes to our mind every time we review the collected images of clinical cases. Looking back at medical records and recalling the situation of each patient, the educational process of diagnosis and treatment, as well as our experiences after reaching a definitive diagnosis on the disease, we realize that each picture has a story. Therefore, we have also gained a deeper insight into two criteria that need to be fulfilled to be a good physician: (1) medical skills and (2) empathy toward patients. This brings to memory the epitaph of an American physician, Dr. Edward Livingston Trudeau: "To Cure Sometimes, To Relieve Often, To Comfort Always." Truly, this is particularly the case with medical practitioners working on rarely studied oral mucosal diseases.

We are passionate about this profession. We enjoy the ideas and discoveries in the diagnosis and treatment of each patient. Besides, we also enjoy the

recognition of our careers, as well as the sentiment behind the story of each patient.

Due to the abovementioned reasons, we desired to write a reference book on the clinically common and rare cases of oral mucosal diseases. One of our students, Jin Xin, also repeatedly suggested, while arranging the image resources of clinical cases, that we should not leave them as they are. After careful consideration, we began to write a book about oral mucosal diseases based on those pictures of clinical cases with the involvement and support of Dr. Jin Xin, Assoc. Prof. Jiang Lu, Assoc. Prof. Zhou Yu, and Assoc. Prof. Dan Hong-Xia from the Department of Oral Mucosal Diseases; Professor Wu Lan-Yan and Assoc. Prof. Geng Ning from the Department of Oral Pathology; as well as Assoc. Prof. Li Wei from the Department of Dermatology, West China College of Stomatology, Sichuan University. We look forward to seek an appropriate way to reveal, share, and discuss with our colleagues and students the clinical manifestations of oral mucosal diseases and the process of diagnosis and treatment for such cases. Besides, we also aim to provide a desk reference book for freshmen in this discipline.

On the occasion of completing this book, we would like to thank our mentor, Prof. Li Bing-Qi, for his care, support, and enlightenment. We would also like to express our gratitude to Dr. Jin Xin for his participation and great effort throughout the entire writing process, as well as Li Xiao-Ying (Deputy Chief Nurse) and Wu Yuan (Nurse) from the Department of Oral Mucosal Diseases, West China College of Stomatology, Sichuan University, for the photography of all the clinical pictures used in the book. Last but not least, we would also like to express our appreciation to all colleagues at the Department of Oral Mucosal Diseases, West China College of Stomatology, Sichuan University.

Chengdu, China

Qianming Chen
Xin Zeng

Contents

Oral Infectious Diseases

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Xin Jin, Xin Zeng, and Qianming Chen

Keywords

Herpes Simplex · Acute Herpetic Gingivostomatitis · Herpes Labialis · Herpes Zoster · Varicella · Hand-Foot-Mouth Disease · Herpangina · Oral Candidosis · Pseudomembranous Candidosis · Acute Erythematous Candidosis · Chronic Erythematous Candidosis · Chronic Hyperplastic Candidosis · Coccigenic Stomatitis · Oral Tuberculosis

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1.1 Herpes Simplex

Case 1 Acute Herpetic Gingivostomatitis (Children)

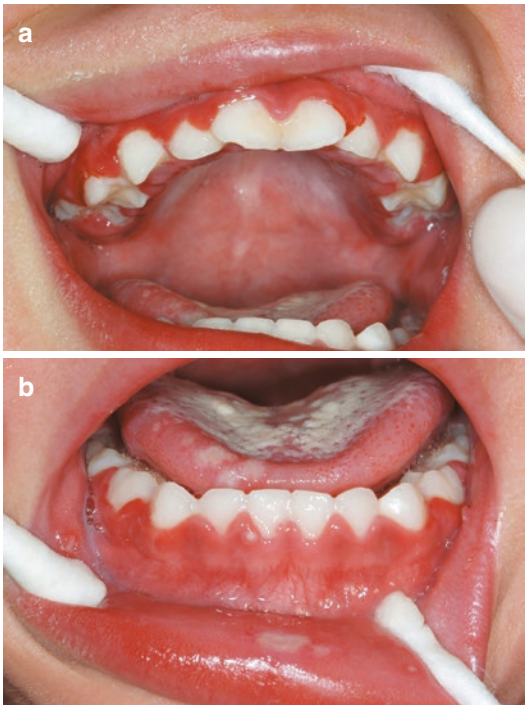

Fig. 1.1 (**a**) Red and swollen gums with erosions in clusters on the gingiva. (**b**) Red and swollen gums with erosions in clusters on the gingiva and tongue

Q. Chen, X. Zeng (eds.), *Case Based Oral Mucosal Diseases*,
https://doi.org/10.1007/978-981-13-0286-2_1

Age: 23 months
Sex: male
Chief Complaints:
23-month-old boy with a fever for 7 days, with ulcers in the mouth for 3 days
History of Present Illness:
A 23-month-old boy had a fever 7 days ago, and his maximum body temperature is 40 °C. The body temperature decreased after intravenous infusion (detailed drugs were unknown). He was taken in local hospital, but still running a low-grade fever. Vesicles and ulcers were observed in his mouth, with swollen gums 3 days ago. He had a difficulty of eating due to oral pain.
Past Medical History: None.
Allergy: None.
Physical Examination:
Red and swollen gums were detected, and erosions in clusters could be seen on the gingiva, labial mucosa, and front dorsum of the tongue (Fig. 1.1).
Laboratories and Imaging Studies: None.
Diagnosis:
Acute Herpetic Gingivostomatitis
Diagnosis Basis:

1. Fever history.
2. Oral lesions were characterized by red and swollen gingiva and erosions distributed in clusters.

Management:

1. Medication
   Rp.: Kouyanning granules 3 g × 10
   Sig.: 1.5 g p.o.t.i.d.
   Vitamin C 0.1 g × 100
   Sig.: 0.05 g p.o.t.i.d.
   Compound chlorhexidine solution 300 ml × 1
   Sig.: 1:1 diluted and topical use t.i.d.
   Recombinant human epidermal growth factor hydrogel 20 g × 1
   Sig.: topical use t.i.d.
2. Drink extra fluids and take more breaks

Case 2 Acute Herpetic Gingivostomatitis (Adult)

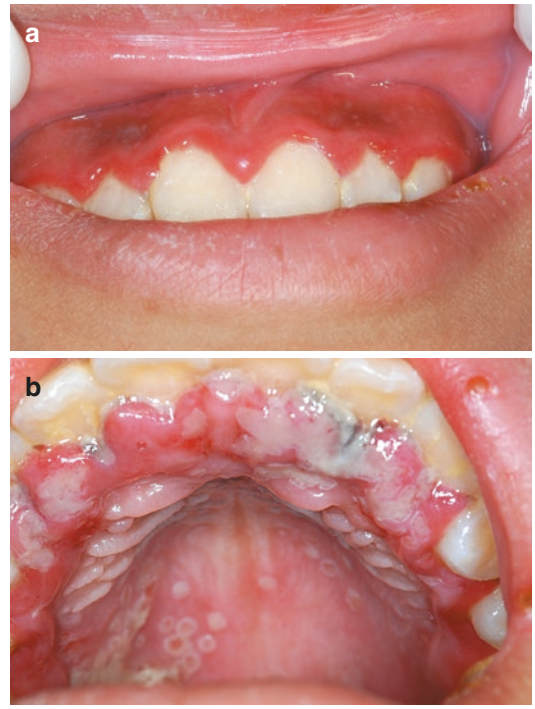

Fig. 1.2 (**a**) Widespread red and swollen gums. (**b**) Widespread red and swollen palatal gingiva, vesicles and ulcers distributed in clusters on the palate and palatal gingival mucosa

Age: 22 years
Sex: male
Chief Complaints:
Oral pain for 4 days
History of Present Illness:
A 22-year-old man presented to our clinic with inflamed, erosive, and painful gingiva for 4 days. He had a cold and cephalosporins were taken before the onset of oral lesions.
Past Medical History: None.
Allergy: None.
Physical Examination:
Generalized inflamed and swollen gingiva was detected, with vesicles and ulcers distributed in clusters on the palate and palatal gingival mucosa (Fig. 1.2).

Laboratories and Imaging Studies: None
Diagnosis:
Acute Herpetic Gingivostomatitis
Diagnosis Basis:

1. History of cold.
2. Oral lesions were characterized by red and swollen gingiva, with vesicles and ulcers distributed in clusters.

Management:

1. Aerosol therapy
   Rp.: Dexamethasone sodium phosphate injection 1 ml × 1
   Gentamycin sulfate injection 2 ml × 1
   Vitamin B12 injection 1 ml × 1
   Vitamin C injection 2.5 ml × 1
   Sig.: aerosol therapy q.d.-b.i.d. for 3 days
2. Medication
   Rp.: Valaciclovir hydrochloride tablets 0.3 g × 12
   Sig.: 0.3 g p.o. b.i.d.
   Kouyanning granules 3 g × 10
   Sig.: 6 g p.o. t.i.d.
   Vitamin C 0.1 g × 100
   Sig.: 0.2 g p.o. t.i.d.
   Compound chlorhexidine solution 300 ml × 1
   Sig.: rinse t.i.d.
   Dexamethasone sodium phosphate injection 1 ml × 5
   Sig.: 1:50 diluted and rinse t.i.d.
   Recombinant human epidermal growth factor hydrogel 20 g × 1
   Sig.: topical use q.d.
3. Drink extra fluids and take more breaks

Case 3 Recurrent Herpes Simplex (Herpes Labialis)

Age: 29 years
Sex: female
Chief Complaints:
Vesicles on the lower lip for 1 day
History of Present Illness:
A 29-year-old lady caught a cold 2 days ago, following symptoms such as burning and swelling on the lower lip. Within one day, small vesicles develop in clusters at the same site. She also complained of recurrent vesicles along the vermilion border of the lips once exposure to cold or spicy food, which could heal spontaneously.
Past Medical History: None.
Allergy: None.
Physical Examination:
Small vesicles were observed in clusters involving the left vermilion border of the lower lip and adjacent skin, surrounded by a mild erythematous rim (Fig. 1.3).
Laboratories and Imaging Studies: None.
Diagnosis:
Herpes Labialis
Diagnosis Basis:

1. History of recurrent vesicles along the vermilion border of the lips.
2. Small vesicles distributed in clusters.

Management:

1. Medication
   Rp.: Acyclovir eye drops 8 ml × 1
   Sig.: topical use t.i.d.
   Prednisolone acetate injection 125 mg × 1
   Sig.: topical use (without perioral skin) t.i.d.
2. We advised the patient to keep warm and reduce spicy food

Case 4 Recurrent Herpes Simplex (on the Palate)

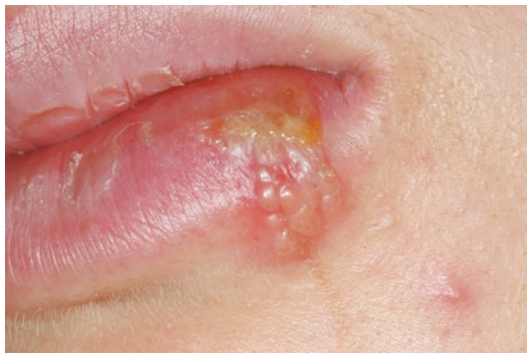

Fig. 1.3 Clusters of vesicles involving the left vermilion border of the lower lip and adjacent skin

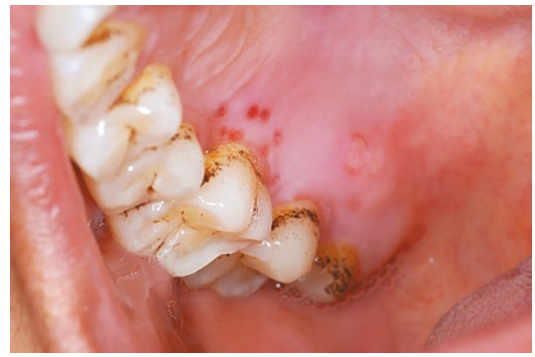

Fig. 1.4 Spotlike erosions in clusters on the right part of palate

Age: 53 years
Sex: female
Chief Complaints:
Repeated vesicles on the lip for 2 years and erosions on the palate for 2 days
History of Present Illness:
A 53-year-old woman presented to our clinic claiming the presence of recurrent vesicles on the lips and vermilion commissures. The clinical course usually lasts for about 1 week. Vesicles quickly rupture, leading to erosions that can heal spontaneously. Two days ago, vesicles appeared and ruptured, resulting in painful erosions.
Past Medical History: None.
Allergy: None.
Physical Examination:
Localized spotlike erosions were distributed in clusters on the right part of palate, with yellow pseudomembrane and hyperemia (Fig. 1.4).
Laboratories and Imaging Studies: None
Diagnosis:
Recurrent Herpes Simplex
Diagnosis Basis:

1. History of recurrent vesicles on the lips and vermilion commissures.
2. Oral lesion was located on the palate.
3. Erosions result from the rupturing vesicles distributed in clusters.

Management:

1. Medication
   Rp.: Compound chlorhexidine solution 300 ml × 1
   Sig.: rinse t.i.d.
   Prednisolone acetate injection 125 mg × 1
   Sig.: topical use t.i.d.

[Review] Herpes Simplex
Herpes simplex is caused by the herpes simplex virus type 1 (HSV-1). Herpes simplex virus (HSV) is a nuclear replicating enveloped DNA virus, with two strains of HSV-1 and HSV-2. Generally, HSV-1 is considered to give rise to infection "above the waist" including oral mucosa, perioral skin, and facial skin and HSV-2 "below the waist," which is associated with genital lesions [1]. In recent years, studies have shown that the predilection site of a specific viral subtype is changing, in part due to varying sexual practices [2–4].

This disease is contagious, especially in a closed community setting such as a daycare center or orphanage nursery. HSV is primarily transmitted by contact with infected oral secretions. Its distribution shows no sex or seasonal differences [5]. Studies reported that the prevalence of HSV-1 antibodies increased steadily with age and reached high levels of about 90% among subjects 40 years of age or older, indicating they had infection history [6]. HSV is thought to spread principally during the prodrome phase of the primary infection and is usually greater in immunocompromised individuals or in those undergoing oral surgery.

In the initial period of infection, HSV-1 infects the oral mucosa and enters the cell. Once inside the cell, virus replication causes plenty of virions produced that ultimately results in cell death, and finally primary infection symptom appears [1]. After primary infection and local replication on the oral mucosa, HSV-1 enters into sensory nerve endings, following transports to the neuronal cell bodies along retrograde axonal. The immune system limits the spread of virus infection at synaptic junctions through the establishment of latency, without neuronal damage. Recurrent infections arise in 30–40% of HSV-1 seropositive patients, which have been associated with exposure to sunlight, stress, fatigue, cold, spicy food, menstruation, and orofacial trauma [2]. When HSV-1 reactivation occurs, newly generated virions spread from the infected neurons to mucocutaneous sites and saliva by anterograde axoplasmic transport, resulting in mild mucocutaneous disorders.

Primary herpetic stomatitis is a primary infection by herpes simplex virus, also known as acute herpetic gingivostomatitis. Onset of it is usually during childhood from 6 months to 3 years old, and the peak incidence appears between 9 months and 28 months of age [7, 8]. The incubation period is about 2–12 days (average 4 days); symptoms such as cold, fever, or

cough can arise. One to 3 days later, mucocutaneous vesicle ruptured. It typically affects the lips, tongue, gingiva, buccal mucosa, and palate. The oral lesions manifest as blisters with 1–2 mm in diameter, which rupture rapidly and coalesce to shallow, painful, and usually irregular ulcers. They are often covered by a yellowish-gray pseudomembrane, with surrounding hyperemia. The ulcers gradually heal in 10–14 days, without scarring. The swelling gingiva is one of the gingival features, which may be misdiagnosed as gingivitis caused by dental plaque and calculus. Perioral lesions are found in approximately 2/3 of affected children. Most children have a fever of >38.0 °C for approximately 4 days, with enlarged cervical lymph nodes, increased saliva secretion, dehydration, coated tongue, bad breath, and skin rash. The severity of illness is associated with the host immunoreactions [1]. Virus spread widely or secondary bacteremia is rare [7].

Recurrent herpes simplex typically affects the lips, vermilion commissures, and perioral skin, termed as recurrent herpes labialis (RHL) [9]. RHL is preceded by premonitory symptoms such as burning, tingling, soreness, or swelling at the site where the lesions will occur [2]. In about 6 h, the lesions are usually red macules that rapidly become vesicular, following scabs and ulcers. Healing happens in 10 days from initial symptom onset, without scarring [1, 2]. The intraoral recurrent herpes simplex often occurs on the palate and gingival mucosa, which is characterized by erosions in clusters.

The diagnosis of herpes simplex is based on the clinical history and features [7]. Laboratory tests such as tissue culture techniques and detection of viral DNA are not the conventional diagnostic methods. All the cases of this unit are diagnosed by the typical history and clinical features.

Treatments of acute herpetic gingivostomatitis include systemic therapy and topical treatment. Topical treatment is mainly applied in recurrent herpes simplex.

Oral drugs include antiviral drugs (acyclovir and valaciclovir), Kouyanning granules, and vitamin C. If the course of disease is more than 5 days, antiviral drugs are not recommended. The usage of acyclovir is as follows: for children younger than 2 years old, 100 mg orally, five times per day, for 5 days, is the course of treatment, and for children older than 2 years old, 200 mg orally, five times per day, for 5 days, is the course of treatment [10]. Because it is a self-limiting illness with short disease course, acyclovir is not recommended if the symptom is mild. For adults, 200 mg orally, five times daily, for 5–7 days, is the course of treatment. Adult patients can also take valaciclovir hydrochloride tablets orally, 300 mg, on an empty stomach before meal, twice a day, for 7 days. Kouyanning granules should be taken as follows: 3–6 g, three times a day, for 3–5 days, with a gradual dosage reduction according to weight and age in children.

Topical treatments include gargarism (compound chlorhexidine solution, three times a day, 1:1 diluted for children use), topical-use drug (recombinant human epidermal growth factor hydrogel, once daily, compound ulcer paste or glucocorticoids such as 0.1% triamcinolone acetonide dental paste, 0.1% dexamethasone ointment, prednisolone acetate injection, triamcinolone acetonide injection, 1:5 diluted or dexamethasone paste, three times a day), and spray (stomatitis spray, three times a day). Acyclovir eye drops can be topically used on herpes labialis three times a day. Glucocorticoids should be used with caution for children under 6 years because they can cause growth retardation and bone loss, even the topical application is not suitable for long-term and extensive use. Moreover, glucocorticoids for herpes labialis should not be used on the perioral skin to avoid hyperpigmentation on the orofacial skin.

Aerosol therapy could have additional use for serious cases, including dexamethasone sodium phosphate injection, gentamycin sulfate injection, vitamin C injection, and vitamin B12 injection, once or twice a day. For children younger than 6 years old, gentamycin sulfate injection is not recommended for aerosol therapy.

1.2 Herpes Zoster and Varicella

Case 5 Herpes Zoster (Lip, Buccal Mucosa, Tongue and Skin)

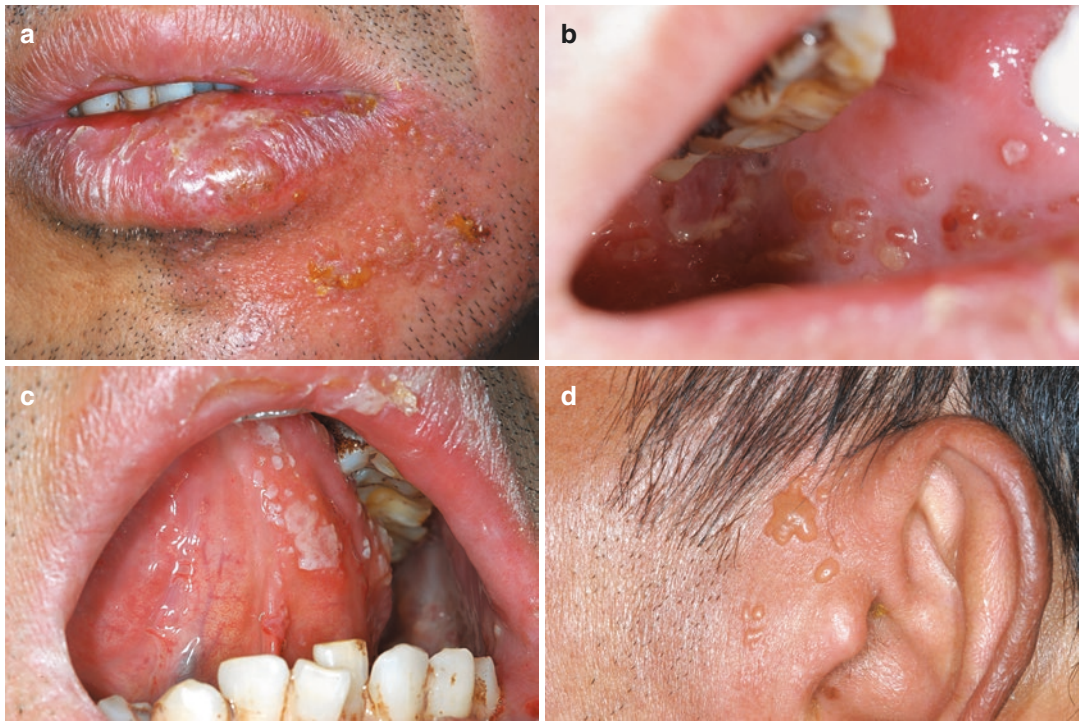

Fig. 1.5 (**a**) Vesicles in clusters involving the left vermilion border of the lower lip and adjacent skin. (**b**) Multiple blisters distributed on the left buccal mucosa. (**c**) Multiple erosions on the left lateral and ventral tongue, covered by a yellowish pseudomembrane, and the rash does not cross the midline. (**d**) Vesicles on the left preauricular region

Age: 46 years
Sex: male
Chief Complaint:
46-year-old man with oral ulcers for 1 week
History of Present Illness:
A 46-year-old man presented to our clinic with painful ulcers on the oral mucosa for 1 week after a cold, and painful blisters on the preauricular region appear 3 days ago.
Past Medical History: None.
Allergy: None.
Physical Examination:
Multiple blisters and erosions were distributed on the left dorsum, lateral and ventral tongue, left buccal mucosa, and the left mandibular lingual gingiva, and part of them coalesced covered by a yellowish pseudomembrane. Many vesicles appeared on the left lower lip and perioral and preauricular region (Fig. 1.5).
Laboratories and Imaging Studies: None.
Diagnosis:
Herpes Zoster
Diagnosis Basis:

1. Oral and cutaneous lesions are unilateral and do not cross the midline.
2. Multiple blisters and erosions are observed.

Management:

1. Aerosol therapy
   Rp.: Dexamethasone sodium phosphate injection 1 ml × 1
   Gentamycin sulfate injection 2 ml × 1
   Vitamin B12 injection 1 ml × 1

Vitamin C injection 2.5 ml × 1
Sig.: aerosol therapy q.d. or b.i.d. for 3 days

2. Medication
Rp.: Acyclovir 100 mg × 48
Sig.: 200 mg p.o. 5 times a day
Pidotimod 0.4 g × 12
Sig.: 0.4 g p.o. b.i.d.
Zhongtong'an capsules 0.28 g × 72
Sig.: 0.56 g p.o. t.i.d.
Vitamin C 0.1 g × 100
Sig.: 0.2 g p.o. t.i.d.
Compound chlorhexidine solution 300 ml × 1
Sig.: rinse t.i.d.
Dexamethasone sodium phosphate injection 1 ml × 5
Sig.: 1:50 diluted and rinse t.i.d
Prednisolone acetate injection 125 mg × 1
Sig.: topical use t.i.d.
3. Advising to the dermatological department for local treatment of cutaneous lesions.

Case 6 Herpes Zoster (Lip and Palate)

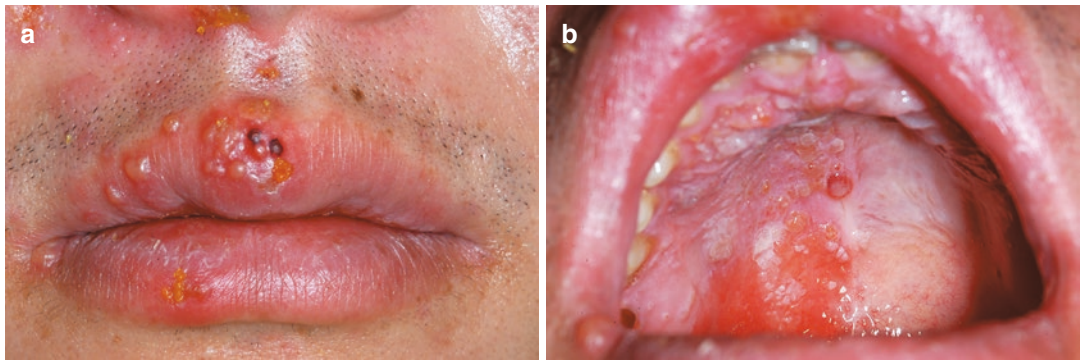

Fig. 1.6 (**a**) Clear vesicles in clustered at the right perioral skin and lips, and do not cross the midline. (**b**) Blisters and erosions on the right palate, and do not cross the midline

Age: 23 years
Sex: male
Chief Complaint:
23-year-old man with oral and facial blisters for 2–3 days
History of Present Illness:
A 23-year-old man presented to our clinic with oral and facial blisters for 2–3 days, with unbearable pain. He caught a cold 1 week ago.
Past Medical History: None.
Allergy: None.
Physical Examination:
The clear vesicles were clustered at the right nose, perioral skin, and lip; bead-like blisters on the right palate can also be noticed. All the vesicular rashes were unilateral and do not cross the midline. There were erosions in clusters on the right buccal mucosa covered by a yellowish-white pseudomembrane (Fig. 1.6).
Laboratories and Imaging Studies: None.
Diagnosis:
Herpes Zoster
Diagnosis Basis:

1. Oral and cutaneous lesions are unilateral and do not cross the midline.
2. Multiple blisters and erosions are observed.

Management:
The same as Case 5

Case 7 Varicella (Adult)

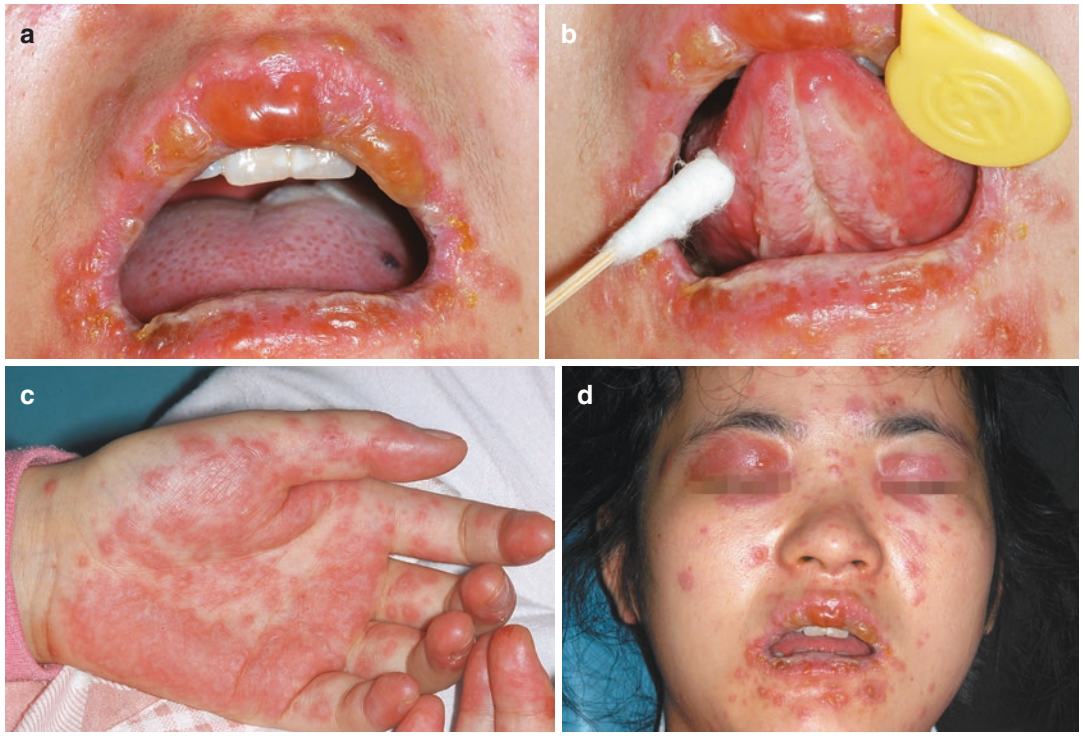

Fig. 1.7 (**a**) Widespread fluid-filled vesicles of different sizes on the lips. (**b**) Multiple erosions coalesced on the ventral tongue, covered by a yellowish pseudomembrane. (**c**) Miliary blisters and erythematous macules spread all over the palms. (**d**) Erythematous macules and vesicles on the face

Age: 20 years
Sex: female
Chief Complaint:
20-year-old woman with widespread oral ulcers for 3 days
History of Present Illness:
A 20-year-old woman presented to our clinic with widespread oral ulcers and unbearable pain for 3 days after a fever. The erythematous lesions and fluid-filled vesicles were observed involving the face, chest and palms. No medicine was taken prior to the illness onset.
Past Medical History: None.
Allergy: None.
Physical Examination:
Widespread small, fluid-filled vesicles with 1–8 mm in diameter involved the face, perioral skin, lips, dorsum and ventral tongue, buccal mucosa, and palate, with some of them ruptured to form irregular ulcers. Miliary blisters and erythematous macules were spread all over the face, neck, and palms (Fig. 1.7).
Laboratories and Imaging Studies: None.
Diagnosis:
Varicella
Diagnosis Basis:

1. The case begins with a prodrome of fever.
2. Erythematous macules and vesicular lesions appeared involving the scalp, face, and trunk 1–2 days after the fever.

Management:

1. Aerosol therapy
   Rp.: Dexamethasone sodium phosphate injection 1 ml × 1
   Gentamycin sulfate injection 2 ml × 1

Vitamin B12 injection 1 ml × 1
Vitamin C injection 2.5 ml × 1
Sig.: aerosol therapy q.d. or b.i.d. for 3 days

2. Medication
Rp.: Compound chlorhexidine solution 300 ml × 1
Sig.: rinse t.i.d.
Dexamethasone sodium phosphate injection 1 ml × 5
Sig.: 1:50 diluted and rinse t.i.d.
Prednisolone acetate injection 125 mg × 1
Sig.: topical use t.i.d.
3. Hospitalization in the dermatological department is recommended due to her severe condition. Exclusion from others in order to avoid infection.

Case 8 Varicella (Children)

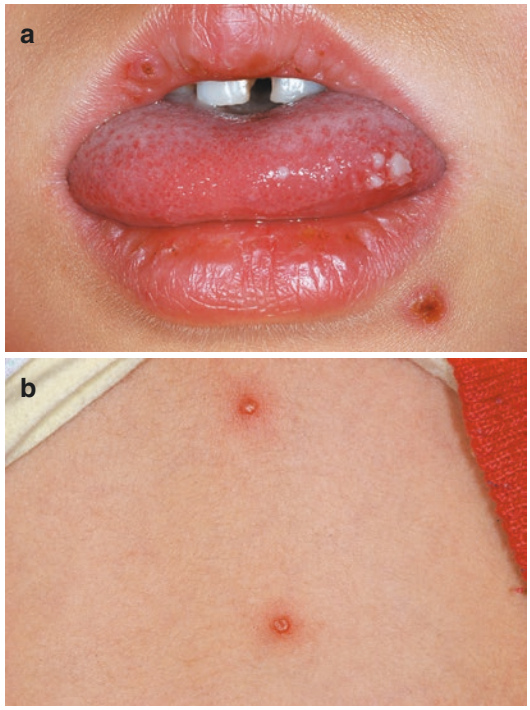

Fig. 1.8 (**a**) Several erosions covered by white pseudomembranes on the tip of the tongue, with crusting on the left perioral skin. (**b**) Erythema and vesicles on the skin of chest and abdomen

Age: 5 years
Sex: female
Chief Complaint:
5-year-old girl with oral ulcers for 3 days
History of Present Illness:
A 5-year-old girl presented to our clinic with multiple painful oral ulcers for 3 days after a fever. The fluid-filled vesicles were observed involving the back and abdominal skin.
Past Medical History: None.
Allergy: None.
Physical Examination:
Several blisters and erosions covered by white pseudomembranes appeared on the right side of retromolar trigone and tip of the tongue, with miliary erosions and crusting on perioral skin. Scattered fluid-filled vesicles with 3 mm in diameter were detected on the skin of back, chest, and abdomen. There were no obvious abnormalities on the hands and feet (Fig. 1.8).
Laboratories and Imaging Studies: None.
Diagnosis:
Varicella
Diagnosis Basis:

1. The case begins with a prodrome of fever.
2. Blisters of skins distributed centripetally.

Management:

1. Medication
Rp.: Kouyanning granules 3 g × 10
Sig.: 3 g p.o. t.i.d.
Vitamin C 0.1 g × 100
Sig.: 0.1 g p.o. t.i.d.
Compound chlorhexidine solution 300 ml × 1
Sig.: rinse t.i.d.
Recombinant human epidermal growth factor hydrogel 20 g × 1
Sig.: topical use q.d.
2. Hospitalization in the dermatological department is recommended. Exclusion from childcare in order to avoid infection until the blisters disappeared.

[Review] Herpes Zoster and Varicella

Herpes zoster is the manifestation of herpes varicella-zoster virus (VZV) infections. It occurs when the varicella-zoster virus, which causes both varicella and herpes zoster, is reactivated and spreads through the afferent nerve to the skin, with intense pain [11]. Herpes zoster can develop in anyone who has had varicella, and the frequency increases with increasing age [12]. Some patients, who have not suffered varicella in childhood, may manifest when varicella when infected with VZV as adults.

Primary VZV infection (varicella) causes VZV-specific antibody to be produced and VZV-specific T cell-mediated immune response, which can be detected within 1–2 weeks after appearance of lesions. The response is essential for recovery from varicella, due to both CD4 and CD8 effectors and memory T cells included. The memory T cell response during varicella will protect against infection during reexposure to VZV [13]. Varicella also results in lifelong latency of VZV in neurons of cranial nerve and dorsal root ganglia [14]. VZV-specific T cell-mediated immune response is also essential to maintain VZV latency in sensory ganglia at a subclinical state. When these responses are impaired, as occurs with aging or immunosuppression, the latent VZV will be reactivated. It will cause a ganglionitis with associated dermatomal neuropathic pain and following painful dermatomal vesicular rash, leading to herpes zoster [13].

Incubation period of varicella is generally ranging from 14 to 16 days. The initial cutaneous manifestations often involve the scalp, face, and trunk. They are pruritic erythema, with systemic symptoms of fever, fatigue, and anorexia. Then the maculopapular phase progresses to a vesicular phase, during which small fluid-filled vesicles occur with the range of number from 100 to 300 lesions. Approximately 24–48 h after the appearance of each lesion, crusting phase begins. Hypopigmentation is common and scarring is rare during healing. The cutaneous rash is centripetally distributed, starting with the face, following the trunk and limbs. Ulcerative and painful lesions appear on mucous membranes, such as the oropharynx and conjunctivae [15]. Varicella lesions in adult are more serious than in children; the specialist should be alert to complications such as pneumonia, neurologic disease, and bacterial infection. Hospitalization for further treatment is required if serious complications are noticed.

Herpes zoster is characterized by a band-like rash in the skin that corresponds to the affected nerve. The rash is unilateral and does not cross the midline. Chest herpes zoster is most commonly involved, followed by trigeminal herpes zoster. Localized sensations are ranging from mild itching or tingling to severe pain that precedes the development of the skin lesions by 1–5 days. As the cutaneous disease progresses, vesicles usually coalesce into larger fluid-filled lesions, following postulation and scabbing. Unilateral blisters are common oral lesions, which break down and coalesce to form extensive ulcers covered by a thick pseudomembrane. The lesions usually heal within 2–4 weeks, with complications of fatigue, headache, and photophobia; fever is unusual [11].

The Ramsay Hunt syndrome is a rare disease caused by an infection of the geniculate ganglion by the varicella-zoster virus. The main clinical features of the syndrome are as follows: Bell's palsy, unilateral or bilateral, vesicular eruptions on the ears, and ear pain [16].

The diagnosis of herpes zoster is usually based on the clinical history and features. All the cases of this unit are diagnosed by the typical history and clinical features.

Systemic treatment in the dermatological department is recommended due to band-like rash presenting as the typical cutaneous lesions. The treatment agents include antiviral drugs, immunomodulatory drugs, painkillers, and neurotrophic drugs. Acyclovir (200 mg orally, five times a day, for 5–10 days, or 400 mg orally, three times a day, for 5 days), valaciclovir (300 mg orally, twice a day for 7 days), and famciclovir (250 mg orally, three times a day for 7 days) are all effective antiviral drugs for treating herpes zoster. For patients with renal impairment, dose reduction is required. Immunomodulatory drugs include pidotimod (0.4 g orally, twice a day), transfer factor capsules (6 mg orally, three times a day), and thymopeti-

dum enteric-coated tablets (20 mg orally, one to three times a day). Neurotrophic drugs include vitamin B1 (10 mg orally, three times a day), vitamin B12 injections (0.025–0.2 mg, intramuscular injection, q.o.d.), and mecobalamin (0.5 mg orally, three times a day).

Topical treatment of oral lesions for varicella and herpes zoster includes gargle, coated drugs, and spray. Gargle includes compound chlorhexidine solution, three times a day (1:1 diluted for children). Coated medicine includes recombinant human epidermal growth factor hydrogel or recombinant bovine basic fibroblast growth factor gel, once daily, or compound ulcer paste and glucocorticoids such as prednisolone acetate injection, triamcinolone acetonide injection (1:5 diluted), triamcinolone acetonide dental paste, and 0.1% dexamethasone ointment or dexamethasone paste, topical use three times a day. Spray such as stomatitis spray can be used three times a day. Painkiller such as compound chamomile and lidocaine hydrochloride gel or compound benzocaine gel can be applied as well, topical use three times a day. For children younger than 6 years old, glucocorticoid is not recommended.

Zostavax is a concentrated formulation of Varivax that the US Food and Drug Administration (FDA) has approved to prevent herpes zoster and its complications in immunocompetent adults aged ≥60 years. The vaccine was designed to boost cell-mediated immune responses, which should keep latent varicella-zoster virus from reactivating and thus prevent herpes zoster [17]. A randomized, double-blind, placebo-controlled trial of 38,546 adults 60 years of age or older discovered that the zoster vaccine markedly reduced morbidity from herpes zoster and postherpetic neuralgia among older adults, with a median of 3.12 years of follow-up [18]. Varicella vaccine is an effective means for prevention, and it plays a vital role in controlling the outbreaks for varicella. Therefore, the vaccine is recommended to prevent varicella in all children and adults who are seronegative for antibodies to varicella-zoster virus [11]. The great majority of vaccine recipients were under prolonged protection, which were supervised for 7 years from clinical trial. Some subjects with vaccine injected develop mild infections after exposure to natural virus, but the rashes are fewer with no fever in most cases [19]. However, it is unclear if the vaccine can affect the morbidity and severity of herpes zoster.

1.3 Hand-Foot-Mouth Disease

Case 9 Hand-Foot-Mouth Disease

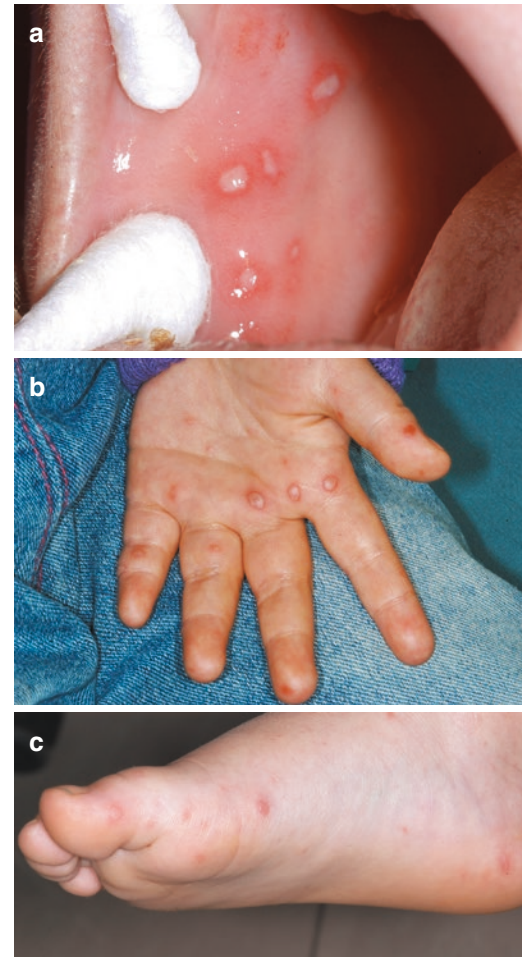

Fig. 1.9 (**a**) Scattered ulcers or erosions on the right buccal mucosa. (**b**) Blisters on the palms and fingers. (**c**) Blisters on the toes and soles

Age: 7 years
Sex: female
Chief Complaints:
Oral ulcers and red spots on the hands for 1 day

History of Present Illness:
The parents found oral ulcers accompanied with slight pain and red spots on her hands for 1 day. She had a history of cold before any symptoms.
Past Medical History: None.
Allergy: None.
Physical Examination:
There were scattered ulcers or erosions on the right buccal mucosa and tip and bilateral ventrum of the tongue, with about 2 mm in diameter. And blisters appeared with 1–3 mm in diameter on the palms, fingers, toes, and soles (Fig. 1.9).
Diagnosis:
Hand-Foot-Mouth Disease
Diagnosis Basis:

1. Little ulcers scattered on the oral mucosa.
2. The ulcers were accompanied with blisters on the hand and foot.

Management:

1. Medication
   Rp.: Kouyanning granules 3 g × 10 packets
   Sig.: 3 g t.i.d. p.o.
   Vitamin C 0.1 g × 100 tablets
   Sig.: 0.1 g t.i.d. p.o.
   Recombinant human epidermal growth factor hydrogel 20 g × 1
   Sig.: topical use, q.d.
2. Exclusion from childcare in order to avoid infection until the blisters disappeared.

[Review] Hand-Foot-Mouth Disease
Hand-foot-mouth disease (HFMD) is a common viral illness of infants and children. It is a syndrome characterized by vesicular stomatitis and cutaneous lesions of the distal extremities, which usually affect children under 10 years of the age. The incidence of HFMD is greatest in summer and early autumn [20]. It is often caused by Coxsackie A virus (A16) but may be caused less commonly by Coxsackie B and enterovirus 71 (EV71). A domestic study showed that the incidence of HFMD was increased year by year. EV71 and Coxsackie virus A16 were both the major etiologic agents of HFMD. The younger ones had higher risk of becoming severe and death cases [21]. Enterovirus 71 is often associated with a worldwide outbreak of HFMD, which can cause severe complications such as meningitis and myocarditis [22–25]. In a study in Thailand, A16 and EV71 strains obtained from outbreaks were characterized. Based on sequence analysis, nucleotide changes were found to cluster in the internal ribosome entry site (IRES) element of the 5′-untranslated region (5-UTR), which indicated the molecular basis of EV71 and CA16 outbreaks [26]. Infection sources of the HFMD are patients or virus carriers. Viruses usually spread through direct contact and droplets. It should be noted that HFMD is not related to foot and mouth disease of animals [27].

The incubation period is 3–6 days, with prodrome of fever, sore throat, and anorexia. One to two days later, red spots and blisters appear on the buccal mucosa, gingiva, and lateral or ventral tongue, which usually easily break into erosions and ulcers. The blisters and skin rash appear in 75% of patients without itchiness, which mainly occurs on the palm, fingers, toes, soles, and buttocks, at the same time or later after the oral lesion. The illness usually lasts 7–10 days. Infection causes immunity to the specific virus, but other enterovirus group could result in a second episode [27]. Most patients are only with oral, hand, and foot lesions; however, if headache, vomiting, cyanosis, abnormal heart rate, or other abnormal symptoms are detected, physicians should be especially alert to the complications such as meningitis or myocarditis.

Adults can also suffer from hand-foot-mouth disease. If the infection occurs late in pregnancy, enterovirus infection can be transmitted to the fetus. Subsequently, the newborn may have meningitis, thrombocytopenia, disseminated intravascular coagulation, myocarditis, or hepatitis, and disease appears to be more severe than if it is postnatally acquired [28].

Diagnosis is usually based on the clinical features alone. Diagnosis of HFMD in Case 9 was based on the typical lesions that occurred on the oral mucosa, hands, and feet.

Different treatments should be applied according to the degree of patients' conditions. Patients with mild symptoms take Kouyanning gran-

ules orally, 1.5–3.0 g continuous for 3–5 days, and vitamin C tablets, 0.05–0.1 g orally three times a day; vitamin B tablets can also be taken orally, 0.5–1 tablet a day. Topical medications include rinse (cleansing) solutions, spreads, and sprays. Compound chlorhexidine solution (1: 1 diluted for children) can be used as rinse solution, three times a day. Liniment such as recombinant human epidermal growth factor hydrogel, once a day, or compound ulcer paste can be applied. Stomatitis spray can be selected as the spray, three times a day. At the same time, parents should be especially alert to the general conditions of children; hospitalization for further treatment is required if severe clinical status or serious complications are noticed.

Exclusion from school or childcare is suggested to avoid infecting others.

1.4 Herpangina

Case 10 Herpangina

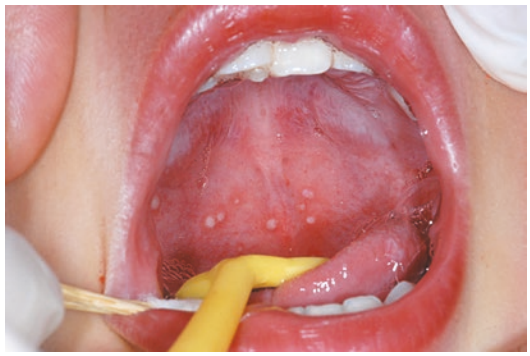

Fig. 1.10 Ulcers and erosions on posterior soft palate

Age: 2 years 8 months
Sex: male
Chief Complaints:
Oral pain for 1 day
History of Present Illness:
The teacher noticed that oral ulcers were located on their child's throat, with pain for 1 day. He had a history of cold 5 days ago.
Past Medical History: None.
Allergy: None.
Physical Examination:
There were several ulcers and erosions with 1–2 mm in diameter on posterior soft palate with mild hyperemia. Gingival redness and swelling were not detected, and there were no obvious abnormalities on the hands and feet (Fig. 1.10).
Diagnosis:
Herpangina
Diagnosis Basis:

1. The history of catching cold.
2. Several superficial round small ulcers were all in the posterior oral cavity.

Management:

1. Aerosol therapy
   Rp.: Dexamethasone sodium phosphate injection 1 ml × 1
   Gentamycin sulfate injection 2 ml × 1
   Vitamin B12 injection 1 ml × 1
   Vitamin C injection 2.5 ml × 1
   Sig.: aerosol therapy q.d. or b.i.d. for 3 days
2. Medication
   Rp.: Kouyanning granules 3 g × 10 packets
   Sig.: 3 g t.i.d. p.o.
   Vitamin C 0.1 g × 100 tablets
   Sig.: 0.1 g t.i.d. p.o.
   Compound chlorhexidine solution 300 ml × 1
   Sig.: rinse t.i.d.
   Recombinant human epidermal growth factor hydrogel 20 g × 1
   Sig.: topical use q.d.

[Review] Herpangina
Herpangina is an oral lesion mainly caused by the infection of Coxsackie virus A (CV-A). The virus types vary with the outbreak year and the area, and the main types are CV-A2, CV-A4, CV-A5, CV-A6, CV-A8, CV-A9, CV-A10, CV-A16, CV-A22, etc. [29–31]. The illness is highly infectious and spreads fast, which usually affects children. The incidence of herpangina is greatest in summer and autumn. It is characterized by an acute onset of fever and sore throat with mild precursory and general symptoms [32]. The clinical features are blisters with 1–2 mm in diameter on

the posterior oral mucosa, which often become erosions or ulcers. The site of lesions is limited to the posterior oral cavity, such as the soft palate, uvula, and tonsil. The disease usually lasts about 7 days. Diagnosis is mainly based on the history of the disease and the typical lesions on the posterior oral cavity.

Systemic treatment of the disease can use Kouyanning granules orally, 1.5–3.0 g continuous for 3–5 days, and vitamin C tablets, 0.05–0.1 g orally three times a day; vitamin B tablets can also be taken orally, 0.5–1 tablet a day. Topical medications include rinse (cleansing) solutions, spreads, and sprays. Compound chlorhexidine solution (1:1 diluted for children) can be used as rinse solution, three times a day. Liniment such as recombinant human epidermal growth factor hydrogel, once a day; or compound ulcer paste, 0.1% triamcinolone acetonide dental paste, and 0.01% dexamethasone compound three times a day; or prednisolone acetate injection and triamcinolone acetonide injection (1:5 diluted), three times a day, can be applied. Stomatitis spray can be selected as the spray, three times a day. Glucocorticoids should be used with caution for children under 6 years because they can cause growth retardation and bone loss, even the topical application is not suitable for long-term and extensive use.

1.5 Oral Candidosis

Case 11 Pseudomembranous Candidosis

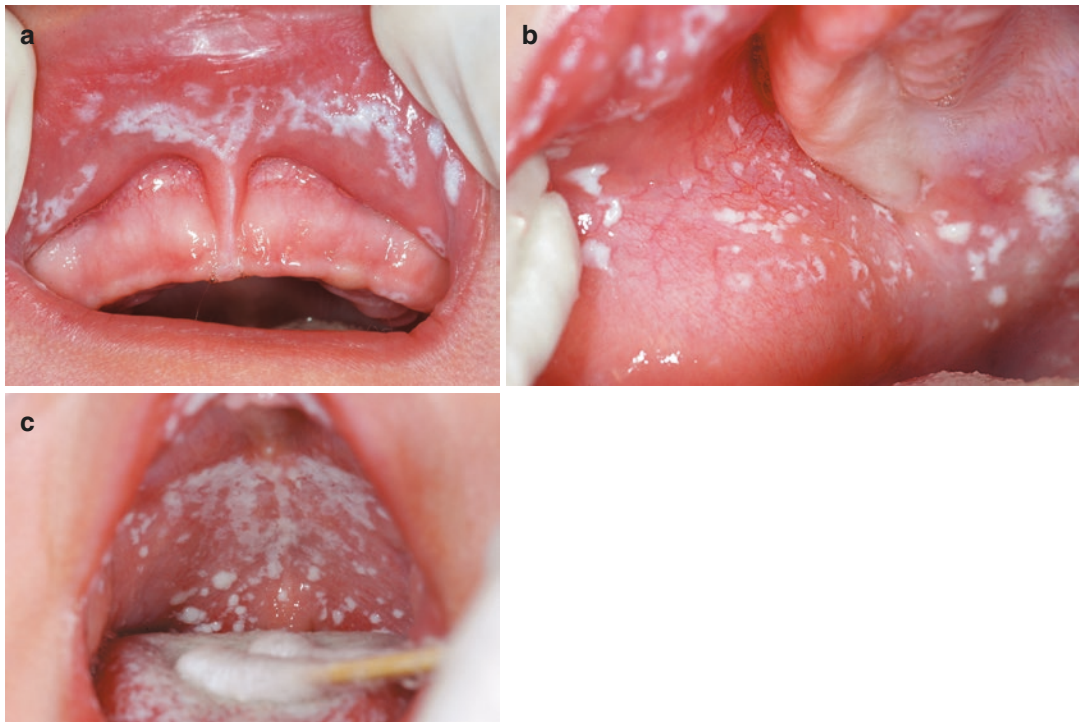

Fig. 1.11 (**a**) Widespread confluent white velvety plaques on the upper labium mucosa, which can be removed by gentle rubbing of the lesion. (**b**) White velvety plaques on the right buccal mucosa, which can be removed by gentle rubbing of the lesion. (**c**) Widespread confluent white velvety plaques on the palate, which can be removed by gentle rubbing of the lesion

Age: 3 months
Sex: male
Chief Complaints:
3-month-old boy with white patch for 4 days
History of Present Illness:
A 3-month-old boy presented to our clinic with oral white plaques for 4 days. No obvious discomfort was found. He had a fever 3 days ago, which had gone after unknown treatment.
Past Medical History: None.
Allergy: None.
Physical Examination:
Widespread confluent white velvety plaques were observed on the labium mucosa, dorsum of the tongue, palate, and buccal mucosa which can be removed by gentle rubbing of the lesion, leaving an erythematous surface (Fig. 1.11).
Diagnosis:
Pseudomembranous Candidosis

Diagnosis Basis:

1. The patient was an infant.
2. Oral lesions showed white velvety plaques which can be easily removed.

Management:

1. Medication
   Rp.: 1% sodium bicarbonate solution 250 ml × 4
   Sig.: topical use t.i.d. and soak the contact items
   Nystatin liniment 15 g × 2
   Sig.: topical use t.i.d.
2. Not only boil the contact items (such as bottles, spoon, cup, bowl and toys) following soaked with 1–2% sodium bicarbonate solution disinfectant, but also adhere to medication after the lesions regression for 10–14 days should be noted.

Case 12 Acute Erythematous Candidosis

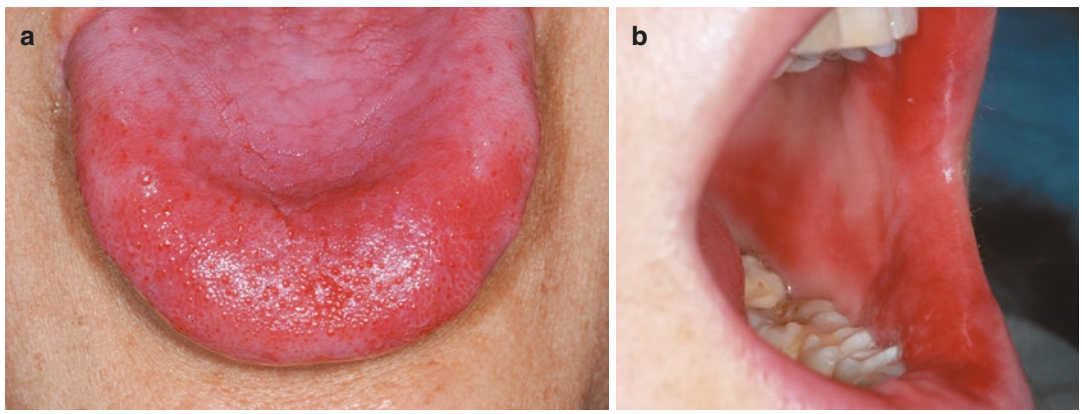

Fig. 1.12 (**a**) Disperse and irregular reddened lesions on the dorsum of the tongue. (**b**) Disperse hyperemia on the left buccal mucosa

Age: 51 years
Sex: female
Chief Complaints:
51-year-old woman with painful reddened mouth for 3 days
History of Present Illness:
A 51-year-old woman presented to our clinic complaining of multiple painful reddened lesions 3 days ago. It tends to develop after the receipt of broad-spectrum antibiotics for 1 week due to the cold he caught. Blood routine examination and blood sugar were normal.
Past Medical History: None.
Allergy: None.
Physical Examination:
Widespread reddened lesions with disperse and irregular appearance were noticed, with especially serious manifestations on the tongue and buccal

mucosa. Fungi were detected from samples taken from the buccal mucosa, dorsum of the tongue, and the palate by smear method (Fig. 1.12).

Diagnosis:

Acute Erythematous Candidosis

Diagnosis Basis:

1. History of antibiotics application to rule out anemia.
2. Oral reddened lesions with disperse appearance.
3. Fungi were detected by smear method.

Management:

1. Medication
   Rp.: Pidotimod 0.4 g × 18 tablets
   Sig.: 1 tablet p.o.
   Compound vitamin B 100 tablets
   Sig.: 2 tablets t.i.d. p.o.
   2% sodium bicarbonate solution 250 ml × 2
   Sig.: rinse t.i.d.
   Nystatin liniment 15 g × 2
   Sig.: topical use t.i.d.
2. Cessation of antibiotics abuse

Case 13 Chronic Erythematous Candidosis

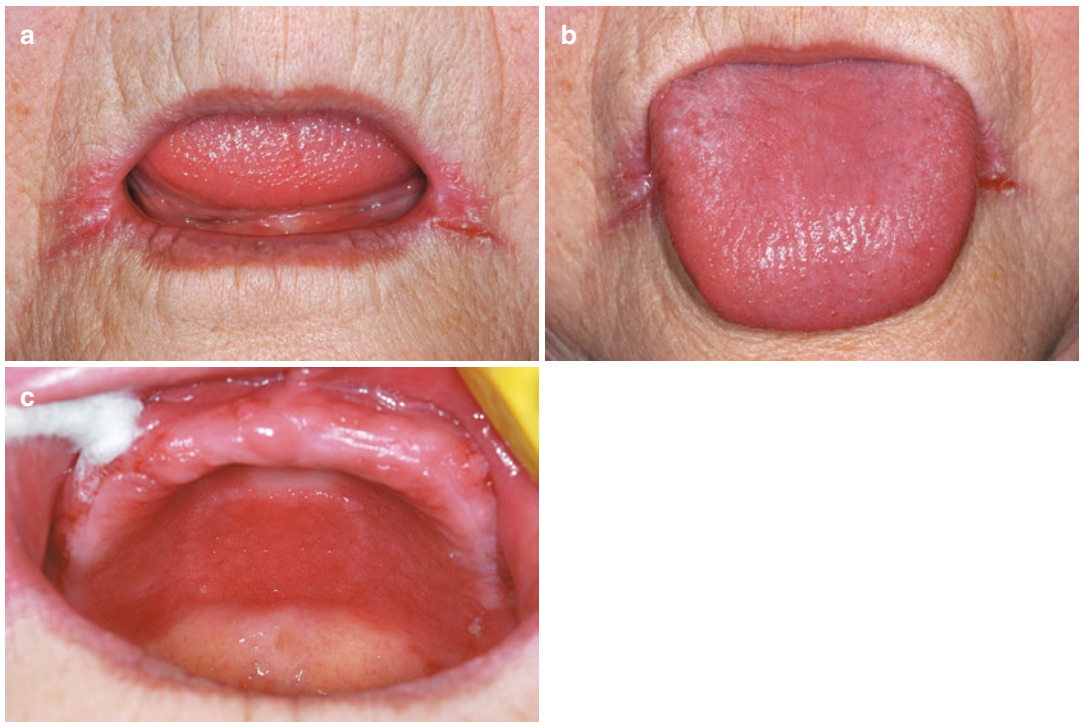

Fig. 1.13 (**a**) Fissures running in the corner of the mouth. (**b**) Atrophic dorsum of the tongue. (**c**) Widespread reddened lesions on the palate, with edema and papillary hyperplasia on the alveolar ridges and the palate

Age: 79 years

Sex: female

Chief Complaints:

79-year-old woman with painful reddened mouth for 4 years and fissure running in the corner of the mouth for 1 year

History of Present Illness:

A 79-year-old woman presented to our clinic complaining of painful reddened lesions with atrophic area on the dorsum of the tongue 4 years ago. Fissures running in the corner of the mouth occurred 1 year ago. Blood routine examination and blood sugar were normal.

Past Medical History: Hypertension.

Allergy: None.

Physical Examination:

Complete denture and low jaw spacing were observed. Widespread reddened lesions were noticed

on the palate, with edema and papillary hyperplasia on the alveolar ridges. The dorsum of the tongue was atrophic, and fissures running in the corner of the mouth occurred. Fungi were detected from samples taken from the corner of the mouth, dorsum of the tongue, and the palate by smear method (Fig. 1.13).

Diagnosis:

Chronic Erythematous Candidosis; Candidal Angular Cheilitis

Diagnosis Basis:

1. The patient was an old lady with complete denture.
2. Widespread reddened lesions with edema and papillary hyperplasia were observed on the maxillary denture-supporting area.
3. Fungi were detected by smear method.

Management:

1. Medication
   Rp.: Pidotimod 0.4 g × 18 tablets
   Sig.: 1 tablet b.i.d. p.o.
   Compound vitamin B 100 tablets
   Sig.: 2 tablets t.i.d. p.o.
   2% sodium bicarbonate solution 250 ml × 4
   Sig.: rinse t.i.d.
   Nystatin liniment 15 g × 2
   Sig.: topical use t.i.d.
2. Attention to clean dentures followed by soaked with 2% sodium bicarbonate solution

Case 14 Chronic Hyperplastic Candidosis

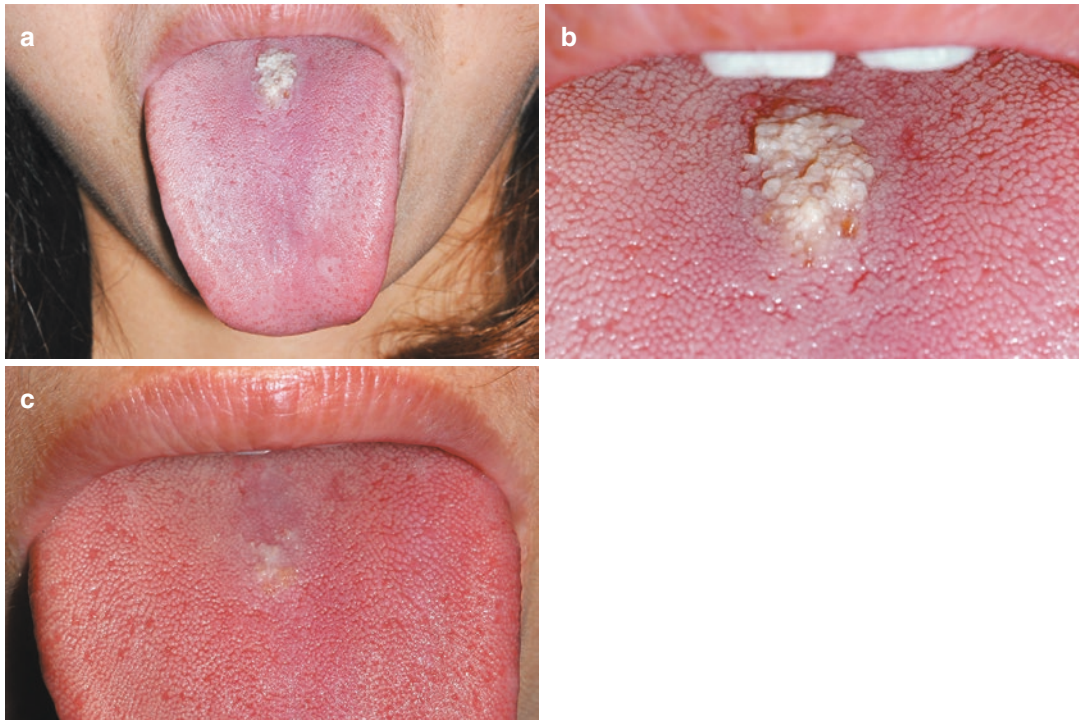

Fig. 1.14 (**a**) A 14 mm × 11 mm plaque on the posterior and middle dorsum of the tongue. (**b**) The plaque with white granular surface that protrudes from the mucosal surface. (**c**) The white lesion recessed mostly 1 week later

Age: 50 years

Sex: female

Chief Complaints:

White plaque on the dorsum of the tongue for 10 days

History of Present Illness:

The patient came across a painless white plaque on the posterior of the dorsum of the tongue with foreign body sensation. There was no obvious increase of this growth.

Past Medical History: None.
Allergy: None.
Physical Examination:
There was a 14 mm × 11 mm plaque on the posterior and middle dorsum of the tongue, with white granular surface. No local hyperemia or erosion was observed. It cannot be removed by gentle rubbing of the lesion. Smear method failed to detect fungi from the lesion (Fig. 1.14a, b).
Clinical Impression:
Chronic Hyperplastic Candidosis?
Management:

1. Medication
   Rp.: Pidotimod 0.4 g × 18 tablets
   Sig.: 1 tablet b.i.d. p.o.
   Compound vitamin B 100 tablets
   Sig.: 2 tablets t.i.d. p.o.
   2% sodium bicarbonate solution 250 ml × 4
   Sig.: rinse t.i.d.
   Nystatin liniment 15 g × 2
   Sig.: topical use t.i.d.
   Fluconazole 50 mg × 6 tablets
   Sig.: 50 mg b.i.d. suck
2. Subsequent visit 1 week later was suggested. Excision or biopsy would be considered if no remission occurred

Subsequent Treatment:
One week later, the white lesion recessed mostly (Fig. 1.14c); 2 weeks later, the lesions disappeared completely.
Diagnosis:
Chronic Hyperplastic Candidosis
Diagnosis Basis:

1. The dorsum of the tongue is a predilection site of chronic hyperplastic candidosis.
2. The plaque presented as white granular appearance.
3. Although definite diagnosis requires biopsy, complete recovery was achieved by antifungal therapy in this case.

[Review] Oral Candidosis
Oral candidosis is a fungal infection of *Candida* species on the mucous membranes of the mouth. In recent decades, the incidence of oral candidosis has markedly increased, mainly owing to the escalation of human immunodeficiency virus (HIV) infection, organ and bone marrow transplantation, and increasing use of immunosuppressive therapies as well as broad-spectrum antibiotics [33].

A change from the harmless commensal existence of *Candida* to a pathogenic state appears following alteration of the oral environment to one that favors the growth of *Candida*. The causes of such alterations are the so-called predisposing factors including host factors for *Candida* infection. With regard to the opportunistic pathogenic nature of *Candida*, candidiasis is often described as being "diseases of the diseased" [34]. *Candida albicans* is the most common in everyone, and mycological studies have revealed that *C. albicans* represents more than 80% of the specimen from all types of human candidosis [35]. It is noteworthy that the incidence of non-*C. albicans* species is increased in human candidosis. The reasons may partly relate to improved diagnostic methods. However, it could also reflect that more and more antifungal drug resistance was observed in some non-*Candida albicans* species compared with *C. albicans* [36]. The most predilection mucosa is superficial and moist, which is common in the vagina and oral cavity. Systemic infections are rare but are severe if they do develop, with mortality rates of up to 60% [37]. In the past 10 years, candidemia that has increased fivefold has been reported, with susceptible individuals suffering from leukemia or blood stem cell transplantation. In addition to candidosis, it has been considered that *Candida* species may be pathogenic factors in some oral disorders, including oral cancer, burning mouth syndrome, taste disorders, and endodontic disease, although the pathogenesis remains unclear [38–41].

C. albicans is heat-labile and is stable in acidic conditions. The pathogenic significance of being able to generate hyphae could associate with the greater enhanced adherence to host surfaces and invade epithelial layers resulting in tissue damage. Putative virulence factors have been identified, including adherence to host by cell surface hydrophobicity and expression of cell surface

adhesins; through high-frequency phenotypic switching, hyphal generated, secreted aspartyl proteinase production, and complement binding to reduce phagocytosis, destruct secretory IgA and mask antigen; through hyphal development and hydrolytic enzyme production, to promote entry of oral mucosa, resulting in destruction of host cell and extracellular matrix [34].

A change from the harmless commensal existence to a pathogenic state relates to lots of predisposing factors. Local host factors include wearing denture, using steroid inhaler, declined salivary flow, high sugar diet, and smoking. Systemic host factors include extremes of age, diabetes, immunosuppression, receipt of broad-spectrum antibiotics, etc. [42].

Candidiasis is rare in immunocompetent populations; the incidence of fungal infection appears to increase in individuals presenting clinical features of acquired or primary immunodeficiencies. The HIV infection, immunosuppressive therapy, use of broad-spectrum antibiotics, and invasive surgical procedures such as solid organ or bone marrow transplantation are the main factors related to acquired immunodeficiencies. The primary immunodeficiency diseases are hereditary disorders involving one or multiple components of the immune system, which could lead to recurrent or persistent bacterial, fungal, and viral infections. Primary immunodeficiencies are usually diagnosed during early life, with more than 80% of cases diagnosed before the age of 20 years [43]. The diseases vary in the severity and spectrum of symptoms which need early diagnosis and treatment. There are many types of primary immunodeficiencies, such as familial/diffuse chronic mucocutaneous candidosis, candidosis-endocrinopathy syndrome, candidosis-thymoma syndrome, DiGeorge syndrome, chronic granulomatous disease, etc. Most of them manifest as chronic oral candida infections and other systemic symptoms, involving the oral mucosa, skin, and nail [44]. The initial skin lesions are usually erythema, verrucous proliferation, and scab formation, following marked hyperkeratosis and acanthosis, rarely, cutaneous horns.

Oral candidosis is mainly present as stomatitis, angular cheilitis, and cheilitis. Candida stomatitis includes two acute types, namely, pseudomembranous candidosis and acute erythematous candidosis, and two persistent forms, known as chronic erythematous candidosis and chronic hyperplastic candidosis.

Pseudomembranous candidosis is also known as the oral thrush and is mostly in neonates and 5–10% of the elderly. It is characterized by the painless confluent white velvety plaques that are easily removed by gentle rubbing of the lesion, leaving an erythematous surface which may easily bleed. The feature that plaques can be removed is a diagnostic point that differentiates pseudomembranous candidosis from other oral patch lesions. Histological inspections show fungal materials in the yeast and filamentous forms, together with food debris, leukocytes, and epithelial cells [45]. The adjacent oral mucosa is of normal color and texture. In the majority of immunocompromised patients, pseudomembranous candidosis often seems to be more extensive with thicker and widespread pseudomembranes, and the lesions will invariably relapse when treatment ceases.

Acute erythematous candidosis is often known as antibiotic sore mouth, as it tends to develop after the receipt of broad-spectrum antibiotics, resulting in a reduced bacterial level of the oral microflora [34]. It presents as a painful reddened lesion, the most common infection site is the dorsum of the tongue, and the palate or buccal mucosa may be involved. Cessation of antibiotic therapy results in the normal balance of the microflora, which subsequently resolves the candidosis without intervention. Inhaled corticosteroids are an additional factor.

Chronic erythematous candidosis is also known as *Candida*-associated denture stomatitis, which is almost exclusively encountered on palatal tissues beneath the fitting surface of a denture. It often presents as a reddened lesion, sometimes with papillary hyperplasia on the palate. The main host factors related to this disorder are poor oral hygiene, not removing dentures while sleeping, or bad denture fit. Up to 75% of

denture wearers have clinical signs of this condition [46].

Chronic hyperplastic candidosis mainly manifests as a thickened white plaque, most commonly on the dorsum of the tongue. It has the potential of squamous cell carcinoma development at lesion locations, although the function of *Candida* in carcinogenesis remains unclear [47]. Several studies have shown that antifungal treatment may alter the clinical features of this lesion from a nonhomogeneous to a homogeneous leukoplakia, while others have demonstrated that part of the lesions completely disappears after antifungal therapy alone, thus confirming its fungal etiology [34].

Candidal angular cheilitis manifests as erythematous lesions at one or both of the angles of the mouth. The spectrum of microorganisms discovered from this disorder includes *Staphylococcus aureus*, streptococcal species, etc., other than *Candida*. As a result, the exact role of *Candida* in angular cheilitis remains uncertain [34].

Candidal cheilitis lacks the specific clinical features, which could manifest as erosions, crusting, or small granular lesions on the lips.

The diagnosis of oral candidosis is usually based on the clinical history and features; laboratory examinations are also needed [43]. The common tests include smear method, isolated culture, and histopathological examination. Generally, pseudomembranous and erythematous candidosis can be diagnosed without a biopsy.

A characteristic feature of chronic hyperplastic candidosis is hyperparakeratosis on the superficial mucosa with inflammatory cell infiltration and microabscesses formed. Epithelial cell edema, mild to moderate epithelium dysplasia, and a dense infiltration of lymphocytic cells into the mesenchyme of lamina propria were also found. The penetration of the oral mucosa by *C. albicans* hyphae, which are detected in biopsy sections following Periodic Acid-Schiff (PAS) or equivalent staining methods. Case 11 was diagnosed by the typical pseudomembranous lesions; Cases 12 and 13 were diagnosed by the typical history, clinical features, and smear method; and Case 14 was diagnosed by the clinical features and good response to antifungal therapy.

Management of oral candidosis requires identification and correction of the specific underlying predisposing factors in an individual patient, such as cessation of antibiotics and glucocorticoid abuse, cleaning the denture, and appropriate oral hygiene practices.

Local treatment has good effect on oral candidosis. Commonly used is 2–4% sodium bicarbonate solution and nystatin liniment. Nystatin liniment is a tetraene antibiotic, and 1 mg is equivalent to 2000 U. Aqueous suspensions of 0.05–0.1 million U/ml can be used for topical use, once every 2–3 h, and it can be swallowed after coated. For infants and young children with oral thrush, the lesions will regress after the application of the above drugs but are easy to relapse. Not only boiling the contact items (such as bottles, spoon, cup, bowl, and toys) followed by soaking with 1–2% sodium bicarbonate solution disinfectant but also adhering to the medication after the lesion regression for 10–14 days should be noted. In addition, if the child is still in the breastfeeding stage, the mother's nipple should also be cleaned with 1–2% sodium bicarbonate solution and coated with nystatin liniment or water suspension.

For patients with stubborn condition, combination of oral drugs that include antifungal agents, immunoenhancers, and vitamins can be effective. Oral antifungal drugs such as fluconazole tablets are suggested to be taken on the first day by 200 mg, followed by 50 mg, two times daily for 7–14 days, or itraconazole capsules, 100–200 mg orally, one time per day. However, it is critical to notice that the abovementioned oral antifungal drugs should not be used in infants and patients with serious systemic diseases. Immunoenhancers include pidotimod, 0.4–0.8 g each time, two times per day for 7–14 days; or thymopetidum enteric-coated tablets, 20 mg orally, two to three times daily, for 15–30 days; or transfer factor capsule, 6 mg each time, two to three times daily, for 15–30 days. Vitamin drugs include compound vitamin B, mecobalamin, folic acid, vitamin C, and so on.

1.6 Coccigenic Stomatitis (Membranous Stomatitis)

Case 15 Coccigenic Stomatitis (Membranous Stomatitis)

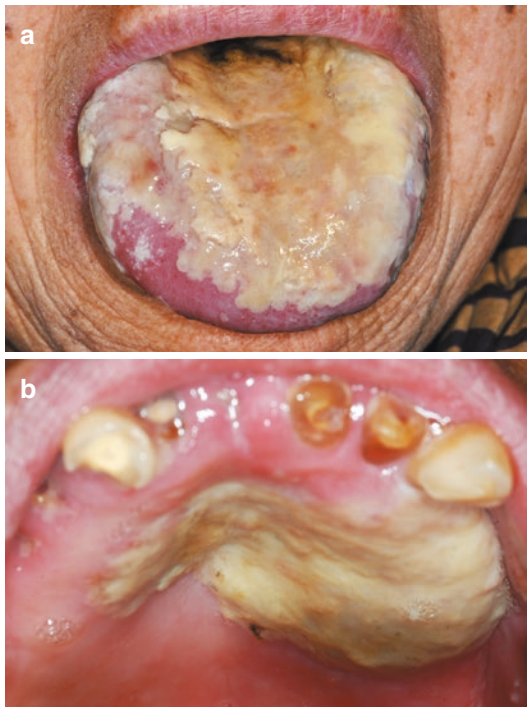

Fig. 1.15 (**a**) Widespread dense, smooth, thick, and yellowish-brown pseudomembrane on the dorsum of the tongue. (**b**) Widespread dense, smooth, thick, and yellowish-brown pseudomembrane on the palate

Age: 72 years
Sex: female
Chief Complaints:
72-year-old woman with an ulcerated tongue for 3 days
History of Present Illness:
A 72-year-old woman presented to our clinic with painful oral ulcers for 3 days, which impaired eating and speech. She had taken antibiotic drugs (unknown details) due to bronchitis 1 week ago in the local hospital.
Past Medical History: Bronchitis, hypertension.
Allergy: None.
Physical Examination:
Widespread dense, smooth, thick, and yellowish-brown pseudomembrane was observed on the dorsum of the tongue and palate, which can be removed by rubbing of the lesion. The floor of the mouth and ventral tongue were also involved (Fig. 1.15). White blood cell count was normal. The percentage of neutrophils increased slightly (75.84%), but the rate of lymphocytes decreased (11.74%).
Diagnosis:
Membranous Stomatitis
Diagnosis Basis:
Widespread dense, smooth, and thick pseudomembrane appeared on the oral mucosa.
Management:

1. Medication
   Rp.: Pidotimod 0.4 g × 12 tablets
   Sig.: 0.4 g b.i.d. p.o.
   Compound vitamin B 100 tablets
   Sig.: 2 tablets t.i.d. p.o.
   Compound chlorhexidine solution 300 ml × 1
   Sig.: rinse t.i.d.
   Dequalinium chloride buccal tablet 0.25 mg × 18 tablets
   Sig.: 0.25 mg 4–6 times/day suck
   2% sodium bicarbonate solution 250 ml × 2
   Sig.: rinse t.i.d.
   Nystatin liniment 15 g × 2
   Sig.: topical use t.i.d.

Subsequent Treatment:
One week later, the lesion was recession mostly, leaving superficial erosive surface. So the medications were adjusted to 2% sodium bicarbonate solution, oral rinse, three times daily; nystatin liniment, topical use, three times per day; and topical use of prednisolone acetate injection on the erosion to promote healing.

[Review] Coccigenic Stomatitis (Membranous Stomatitis)
The oral cavity is colonized by several hundred types of microorganisms. In healthy individuals, they are usually harmless and in balance. Oral microflora mainly consists of *Streptococci*,

Staphylococci, and *Diplococcus pneumonia*. The balance between the host and oral microflora breaking down relates to lots of predisposing factors, including cold and fever, acute infectious disease, radiotherapy and chemotherapy for malignancies, and long-term use of immunosuppressants, which could reduce the immune function, resulting in abnormal proliferation and virulence increase of bacteria responsible for coccigenic stomatitis. Advanced age, suffering from other oral mucosal disorders, dentures, and orthodontic materials may also be predisposing factors [48, 49].

Primary coccigenic stomatitis is uncommon, often occurred in weak patients with low resistance. Secondary coccigenic stomatitis is commonly seen in clinical practice occurring following other oral mucosal lesions, such as herpes simplex, allergies stomatitis, or erosive oral lichen planus. The anti-infectious treatment together with the treatment of primary lesions should be considered. Patient in Case 15 of this unit had medication history before oral erosion; therefore, drug allergic stomatitis initially, followed by secondary coccigenic stomatitis, was considered.

Coccigenic stomatitis can occur in any part of the oral mucosa, mainly for hyperemia and local erosions or ulcers. The ulcers and erosions are covered by a gray or yellowish-brown pseudomembrane, which is dense, smooth, and thick that are not easily removed by gentle rubbing of the lesion, leaving an erosive surface. So it is also called membranous stomatitis. The surrounding mucosal hyperemia and swelling could be observed, with obvious inflammatory reaction. The patients show significant pain and increased saliva, with bad breath, and lymphadenopathy may be accompanied by systemic symptoms such as fever. Coccigenic stomatitis may be the mixed infection that is caused by several kinds of *Coccus* coexistence. If necessary, smear or bacterial culture can be made to determine the main pathogens.

Increased permeability of the mucosal barrier because of mucositis may result in microbial dissemination into the bloodstream. Bacteremia poses a lethal threat to individuals with impaired immune mechanisms, leading to systemic infections, which should be noticed in clinical practices [50].

A patient accompanied by the systemic infection should be evaluated firstly. Targeted antibiotics should be chosen based on results of bacterial culture and drug sensitivity test, including penicillins, cephalosporins, and macrolides. The following drugs can be applied if without systemic infection: pidotimod, 0.4 g orally, twice a day for 1–2 weeks; compound vitamin B, two tablets orally, three times a day; 1% povidone iodine solution or compound chlorhexidine solution for oral rinse, three times a day; and topical use of compound ulcer paste. Lozenges can also be used, such as the cydiodine tablets, 1.5 mg suck, four to six times a day; lysozyme hydrochloride tablets, 20 mg suck, four to six times a day; and dequalinium chloride buccal tablet, 0.5 mg suck, four to six times a day. During the medication process, 2–4% sodium bicarbonate solution for oral rinse and topical use of nystatin liniment should be administrated to avoid fungal infection.

1.7 Oral Tuberculosis

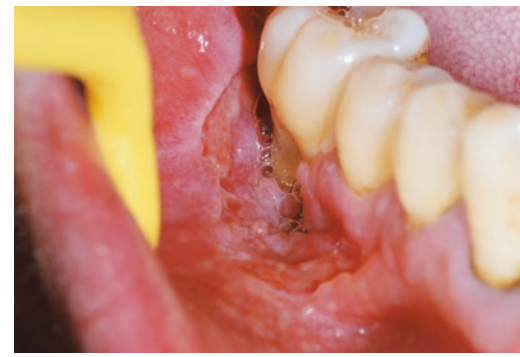

Fig. 1.16 A 20 mm × 10 mm ulcer with undermined edges, clear boundary, and a granulating floor on the right mandibular buccal gingival sulcus

Case 16 Tuberculosis Ulcer
Age: 46 years
Sex: male
Chief Complaints:
46-year-old man with ulcers on the right mandibular gingiva for 6 months

History of Present Illness:
A 46-year-old man complained of painless ulcers on the right mandibular gingiva, with weight loss for 6 months. He denied the history of hot flashes, night sweats, and tuberculosis.
Past Medical History: None.
Allergy: None.
Physical Examination:
There was a 20 mm × 10 mm ulcer on the right mandibular buccal gingival sulcus. It was stellate with undermined edges and clear boundary. After removing purulent exudates of the superficial ulceration, a granulating floor can be noticed (Fig. 1.16).
Clinical Impression:
Tuberculosis Ulcer?
Laboratories and Imaging Studies:

1. Routine blood test, blood glucose, and serological tests for syphilis and HIV were normal.
2. Tissue biopsy of the ulcer was performed. Histopathology exam showed chronic granulomatous inflammation with unstructured caseous material. The bacilli were identified by acid-fast stains, and *Mycobacterium tuberculosis* DNA was detected by DNA-qPCR. Tuberculosis ulcer was confirmed by pathological diagnosis.
3. Chest X-ray showed infectious disorder of bilateral lung.

Diagnosis:
Tuberculosis Ulcer
Diagnosis Basis:

1. The painless ulcer was stellate with undermined edges. A granulating floor can be noticed after removing purulent exudates of the superficial ulceration.
2. It was confirmed by histopathological examination.

Management:

1. He was advised to the department of infectious diseases for antituberculosis therapy.
2. Intralesional injection was adopted for oral tuberculosis ulcers: isoniazid 0.1 g, every other day, for ten times as the treatment course.
3. Topical use of compound chlorhexidine solution, oral rinse, three to four times daily.

[Review] Oral Tuberculosis
Oral tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*. It can be classified as primary and secondary oral TB. Primary oral TB was detected in 42% and secondary oral TB in 58% (of which 54% pulmonary, 4% extrapulmonary) of patients. The secondary oral lesion is more common in elder patients, whereas the primary type mainly affects the young. It has been reported that approximately 50% of patients with oral manifestation of TB has led to the diagnosis of a previously unknown systemic infection, which resulted in a timely and effective treatment [51].

Oral TB is rare and has been reported to occur in 0.05–5% of all TB infections, but it should be considered if particular oral ulcers encountered due to more drug-resistant TB and acquired immunodeficiency syndrome (AIDS) occur. Oral TB accounted for up to 1.33% of human immunodeficiency virus (HIV)-associated opportunistic infections, based on a cohort of 1345 patients [52].

Mycobacterium tuberculosis can survive in human adipocytes for a long time. Recent researches have indicated that radical cure for tuberculosis is difficult, for antituberculosis drugs are hard to get into the adipocytes directly. The mechanism of the oral *Mycobacterium tuberculosis* infection is not clear yet, but it is generally believed that oral mucous membrane presents a natural resistance to *Mycobacterium* invasion. This resistance has been attributed to the integrity and thickness of the oral epithelium, the cleansing action of saliva, and the presence of salivary enzymes and tissue antibodies. Any break or loss of this natural barrier, which may be a result of trauma, inflammation, tooth extraction, or poor oral hygiene, and preexisting lesions such as leukoplakias, periapical granulomas, periodontitis, etc., may provide an invasion route of *Mycobacterium*. Immunosuppression and nutritional deficiencies may also be the systemic predisposing factors [53, 54].

Mycobacterium tuberculosis infects all parts of the mouth. Oral tuberculous lesions include tuberculous chancre, tuberculosis ulcers, and lupus vulgaris, among which the most common symptoms are tuberculosis ulcers.

Tuberculous chancre (primary tuberculosis syndrome) is rare and more widely in children and adolescents [55]. The dorsal surface of the tongue is affected most commonly, followed by the buccal mucosa and lips. For those with negative tuberculin skin test, oral mucosa may be the first area invaded by *Mycobacterium tuberculosis*. Following an incubation period of 2–3 weeks, a nodule occurs at the entry part and develops into an intractable painless ulcer with surrounding induration, which is called tuberculous chancre. Enlarged cervical lymph nodes are common in primary infection.

Tuberculosis ulcer is the most common secondary tubercular lesion in the mouth. It tends to occur in the middle-aged and elderly, with the tongue and hard palate as the predilection sites. In addition, gums, floor of the mouth, lips, and buccal mucosa can also be involved. The typical oral lesions consist of a stellate ulcer with undermined edges and clear boundary. After removing purulent exudates of the superficial ulceration, a granulating floor can be noticed. There are yellowish-brown miliary nodules at the margin of the ulcers, which ruptured to form dark red mulberry-like granulomas, following the increased ulcers accordingly. Irregular appearance of tuberculosis ulcers is caused by variable locations of these nodules. The pain degree varies, but the lingual ulcers are obviously painful [54]. If the patients have poor resistibility, lesions can appear at the junction of the oral mucosa and skin. It is characteristic of superficial granulomatous ulcer initially, followed by widespread tissue damages and deformation tendency, which is called tuberculosis cutis ulcerosa with poor prognosis.

Lupus vulgaris are rare cutaneous tuberculosis skin lesions and appear mostly in adolescent or children with good immune function. It begins as painless reddish-brown nodules which is soft with clear boundaries. On diascopy, it shows characteristic "apple-jelly" color in the central area of the nodules, surrounded by pale normal skin. The term "lupus" may be derived from the rapacity and virulence of the disease. Tissue necrosis and defect resembling wolf bites can be observed if combined with secondary infection.

The differential diagnoses of oral tuberculous ulcers include recurrent aphthous ulcers, traumatic ulcers, squamous cell carcinoma, lymphoma, metastatic tumors, and so on [56].

The diagnosis of oral tuberculosis is mainly confirmed by the histopathological examination. The lesion is consisted of small tubercles, the center of which is unstructured caseous material, surrounded by multiple epithelioid cells and Langhans-type giant cells, with dense inflammatory cellular infiltration. Proliferation of fibroblasts among tubercles can be observed. For confirmation and differential diagnosis, the bacilli could be identified by acid-fast stains and culture. In addition, sputum culture, history of tuberculosis, tuberculin skin test, and chest X-ray would be beneficial in the diagnosis of oral tuberculosis [57].

Patients with oral tuberculosis should be advised to the department of infectious diseases for further inspection and antituberculosis therapy. Most oral lesions can be healed after receiving generalized anti-TB treatment. Intralesional injection can be adopted for oral tuberculosis ulcers simultaneously: streptomycin 0.5 g, once daily, or isoniazid 0.1 g, once daily or every other day, for ten times as a treatment course. Topical therapeutic options are mainly symptomatic treatment, including compound chlorhexidine solution, oral rinse, three to four times daily. The patients still need to finish the course of anti-TB treatment in the department of infectious diseases, although oral lesions are healed.

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