Case Report

Finding the pathognomonic clinical features, do we still need supporting examinations?: two case reports

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ABSTRACT

Introduction: Pathognomonic symptoms often allow for the extablishment of a clinical diagnosis without laboratory-supporting examinations. This article discusses two cases of oral mucosal disease presenting with typical symptoms and pathognomonic clinical features. Through anamnesis, history taking, and physical examination led to the clinical diagnosis of primary herpetic gingivostomatitis and pseudomembranous oral candidiasis. **Case report**: The first case involved a 30-year-old woman with primary herpetic gingivostomatitis, characterized by multiple ulcers in the oral cavity and lips. The second case was that of a 4-year-old girl with pseudomembranous oral candidiasis, characterized by wipeable whitish plaques on the oral mucosa, which left an erythematous area. Antiviral therapy was given to the herpetic gingivostomatitis patient, while the patient wih pseudomembranous candidiasis received antifungal treatment. Significant clinical improvement was observed within 1-2 weeks following adequate treatment. Supporting examinations were not performed due to the pathognomonic clinical features. **Conclusion**: Primary herpetic gingivostomatitis and acute pseudomembranous candidiasis exhibit pathognomonic clinical features that are typical and generally sufficient for clinical diagnosis without laboratory-supporting confirmation. If clinical diagnosis-based treatment results in improvement, supporting examination may not be necessary. Therefore, strict supervision from a doctor is mandatory in this situation.

KEYWORDS

Candidiasis, herpes, herpetic gingivostomatitis, oral candidiasis, pathognomonic

INTRODUCTION

Two of several oral mucosal diseases that are often found in the community and have pathognomonic clinical features are Primary Herpetic Gingivostomatitis (PHGS) and pseudomembrane-type Oral Candidiasis (POC).[1,2] Pathognomonic symptoms are often a strong marker in diagnosing a particular disease because they show signs or clinical features typical of that disease.[3] In clinical practice, if these pathognomonic symptoms are present and aid in diagnosis and management, supporting examinations may not be required to confirm the diagnosis.

Prodromal symptoms are often the only indications of PHGS infection in youngsters, but they can be so mild or even non-existent, that infected patients are unable to recognize them. Only 10-12% of PHGS cases in children are severe enough to be noticed by the parents. The global incidence of PHGS in adults is high, with an estimated 67% of the global population affected, particularly in Africa, Southeast Asia, and Asia Pacific region. It is believed that PHGS infection is relatively common in Indonesia. Primary infection can cause PHGS in some people who did not have childhood exposure to the virus, even though the

majority of infections are symptomless. Research indicates a relatively high incidence of herpes infection in Indonesian children; however, a significant portion of PHGS cases remain undiagnosed, as the symptoms are often mistaken for common oral conditions.[4–6]

Pseudomembranous candidiasis is more common in children, especially infants, and children with weakened immune systems. Its prevalence is estimated to reach 10-20% in healthy infants, but it may be higher in vulnerable groups, including children with HIV/AIDS, cancer, or those receiving immunosuppressive therapy. In Indonesia, specific data on the prevalence of pseudomembranous candidiasis in children may be limited, but this fungal infection has been reported as a health problem in several studies. Research shows that Candida infections are more common in children with certain conditions, such as malnutrition and systemic diseases. The incidence of candidiasis in Asia from several epidemiological studies in Hong Kong stated that C. albicans is the most frequently identified species with an average of 56% of candidiasis cases. Several studies in Indonesia found the prevalence of oral candidiasis ranging from 10–30% in children, with higher rates in those with risk factors, such as antibiotic use and underlying medical conditions.[7–10]

PHGS can also occur in patients with underlying medical conditions. PHGS is the clinical manifestation of a primary infection by Herpes Simplex Virus type 1 (HSV-1) in the oral cavity.[11–13] The disease usually occurs in children under five years old but can also occur in adolescents and adults. HSV-1 is transmitted through direct contact with oral secretions or respiratory droplets, and the virus penetrates the mucosa or broken skin.[14] After an incubation period of 3 to 9 days, a prodromal phase appears with symptoms such as malaise, fatigue, muscle pain, and enlarged submandibular lymph nodes.[12,15] This is followed by the onset of oral lesions, starting with gingival inflammation that appears red and edematous. Subsequently, small vesicles form, which rupture and develop into shallow yellowish ulcers with a surrounding erythematous halo. PHGS is known as a very typical condition with pathognomonic clinical symptoms and features, which can facilitate clinical diagnosis.[11]

The diagnosis of PHGS is generally clinical, based on the patient's medical history and physical examination. The presence of vesicular and ulcerative lesions in the oral cavity is tyically sufficient to establish the diagnosis.[16,17] However, if additional confirmation is required, herpes gingivostomatitis can be confirmed by direct immunofluorescence examination of ulcer scrapings or vesicle fluid, the Tzanck smear, which detects cytological changes due to herpes virus infection, or a complete blood count which will show leukocytosis or neutropenia associated with viral infection.[11,12] Serological examination of specific anti-HSV-1 antibodies can also be performed to determine the status of reactive infection,[18] but unfortunately, the costs required are quite high and are not covered by insurance in Indonesia. PHGS in adults can recur due to the patient's weak immune system. This is because the HSV-1 virus that causes it is dormant in the dorsal trigeminal ganglion. One of the key strategies for preventing recurrence is maintaining an adequate immune system.[19]

POC is an opportunistic infection that commonly affecting the oral mucosa, with Candida albicans being the most common cause.[20] Candida infections are more common in the very young, the elderly, or those with serious health problems. Factors such as the use of broad-spectrum antibiotics, oral corticosteroids, and an underdeveloped immune system increase the risk of fungal infections, especially in infants and children.[21] Pseudomembranous candidiasis is characterized by the presence of multiple white plaques that can be lifted. These plaques consist of fungal hyphae, which can be identified through KOH staining, and the underlying mucosa often appears erythematous.[22–25]

The clinical diagnosis of candidiasis can typically be established through subjective and objective examinations. However, supporting tests such as wet mount microscopy and fungal culture can provide definitive confirmation. Similar

to PHGS, POC is an infectious disease that can potentially recur. The most distinguishing feature between PHGS and POC is the type of lesion found. PHGS is characterized by ulcerative lesions, while POC is marked by plaque lesions. Supporting examinations become necessary if there is no positive response to antivirals in PHGS and antifungals in POC.[20]

Overall, the novelty of these case reports lies in its detailed exploration of the clinical pathognomonic of PHGS and POC, as well as its procedural recommendations for comprehensive diagnosis and management without supporting examinations when there is diagnostic certainty and predisposing conditions. This article aims to discuss two cases of oral mucosal disease with typical symptoms and pathognomonic clinical features.

Case Reports

First case

A 30-year-old woman presented with complaints of painful ulcers on the lip that had appeared six days prior, accompanied by multiple ulcers inside her mouth. The patient also had a fever every morning, felt weak due to difficulty eating, and had used antibiotics as well as Triamcinolone acetonide 0.1% (Kenalog® in orabase). History-taking revealed that the patient had an irregular eating pattern, insufficient water intake, and was in a state of fatigue in caring for a toddler. The physical examination showed vital signs within normal limits. The extraoral examinations found red-yellowish serosanguinous crusts on the upper and lower lips (Figure 1A), accompanied by pain. Meanwhile, the intraoral examinations revealed multiple round ulcers with erythematous edges on the labial and buccal mucosa, gingiva, tongue, and palate (Figures 1B, 1C, 1D, and 1E). An erythematous macule with inflammation signs was observed along the gingival margin in the region 13–23. The oral lesions found had no bleeding tendency.

Based on examination results, the diagnosis was Primary Herpetic Gingivostomatitis (PHGS). The differential diagnoses for this case included Herpes Associated Erythema Multiforme (HAEM) and Recurrent Intraoral Herpes (RIH). The treatment plan consists of antivirals and multivitamins. The coated tongue was also observed and classifieed as Miyazaki scale 3. Non-pharmacological management included instructions to maintain oral hygiene and improve a healthy lifestyle to enhance immune function. Pharmacological therapy given included acyclovir 200 mg taken orally 5 times a day, acyclovir 5% cream followed by petroleum jelly applied topically 5 times a day for the extraoral lesions, and multivitamins (Surbex-Z®) once a day, for 14 days. The prognosis for this condition is generally favorable with appropriate treatment, as most patients respond well to antiviral therapy and supportive care.

Two weeks after adequate treatment, the patient reported no subjective complaints. Extra and intraoral examinations showed good improvement (Figures 2A – 2E). Hyaluronic acid 0.2% (Aloclair®) gel was given 3 times a day on the labial mucosa and gums region 38 and 12 because it remains small erythematous lesions due to inflammation. Communication via WA chat was carried out every three days to monitor the progress of therapy both subjectively based on complaints reported by the patient and objectively through photos of the oral mucosal condition sent by the patient. Due to time and financial constraints, the patient was unable to return to the hospital. Therefore, the final evaluation was conducted remotely via WhatsApp chat, confirming that the patient had fully recovered without any clinical signs or symptoms, a few days later.

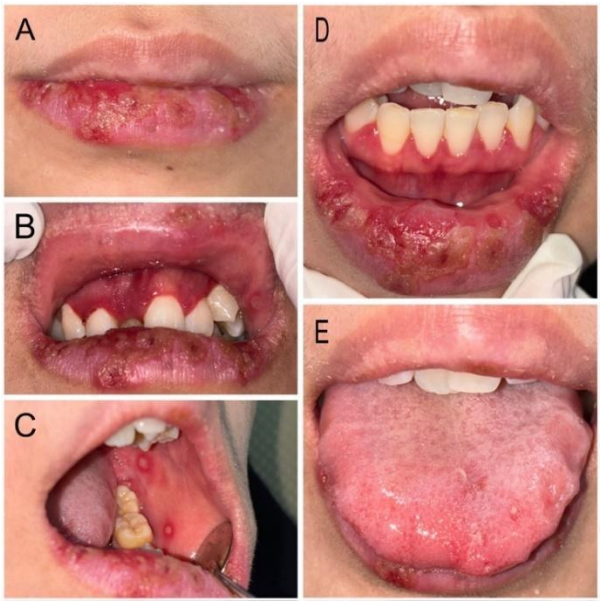

Figure 1. Multiple ulcers in the PHGS patient, first visit: (A) on the lip; (B) on the upper anterior gingiva; (C) on the left buccal mucosa; (D) on the lower labial mucosa; and (E) on the dorsum of the tongue.

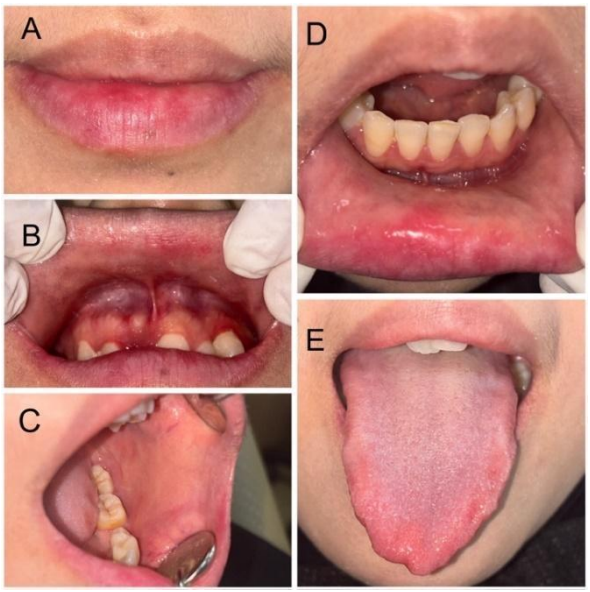

Figure 2. The second visit of the PHGS patient revealed good improvements on (A) lip; (B) upper anterior gingiva; (C) left buccal mucosa; (D) lower labial mucosa; and (E) tongue (E).

Second case

In the second case, a 4-year-old girl presented with slightly painful white patches on her mouth and lips that had persisted for seven days. The symptoms had improved but had not yet fully resolved, despite treatment with Povidone-iodine 1% (Betadine®) mouthwash, nystatin, and Interlac D which were prescribed by a previous doctor. She has allergic rhinitis and was undergoing treatment by an ear, nose, and throat (ENT) specialist. Her current medications included cetirizine (an antihistamine) and a nasal spray, which she used routinely, especially when allergy symptoms recur. A physical examination revealed that the patient's vital signs were normal. Extraoral examination showed dry lips with exfoliative lesions (figure 3A). The intraoral examinations revealed whitish pseudomembranous plaques on the dorsum of the tongue (Figure 3A), left buccal

mucosa (Figure 3B), and also upper and lower labial mucosa (Figure 3C and 3D), which can be wiped off and leave an erythematous area with tenderness.

The patient was diagnosed with pseudomembranous oral candidiasis (POC), based on examinations. The differential diagnoses of this case are Oral Lichen Planus and Hyperplastic Candidiasis. The treatment plan consisted of antifungal and multivitamins. Oral hygiene instruction and maintaining a healthy lifestyle were given as non-pharmacological management. Pharmacological therapy included nystatin oral suspension 100.000 IU/ml (4x1 ml/day), multivitamins (Becomvit® syrup) once a day, and probiotics (Interlac-D ®) once a day given again to continue the previous treatment. Prognosis for these conditions is generally favorable with appropriate management, as many patients respond well to antifungal therapy and lifestyle modifiactions. Detailed instructions regarding medication use, dosage, and the importance of adherence were provided to ensure effective treatment. One week after treatment, the patient's subjective complaints had improved. Extraoral and intraoral examinations also showed improvement, the lip is moist, and no white lesions were found (Figures 4A – 4D).

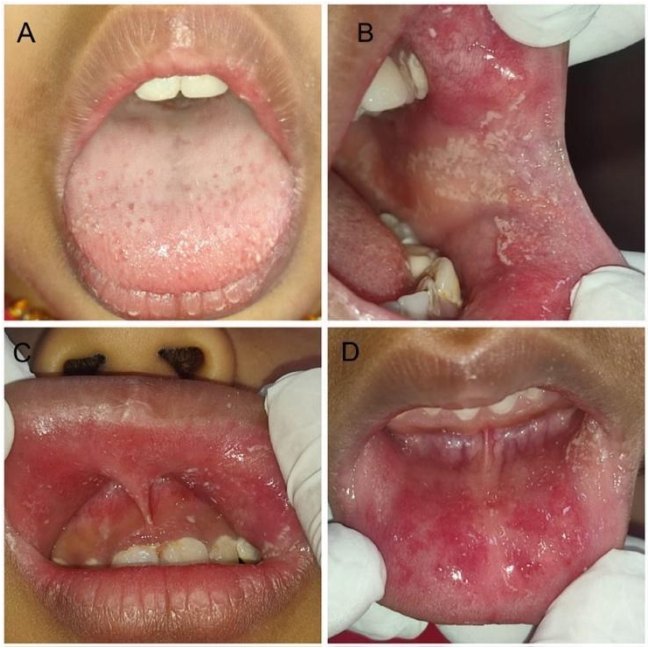

Figure 3. POC lesions found on the first visit: (A) dorsum tongue; (B) left buccal mucosa; (C) upper labial mucosa; and (D) lower labial mucosa

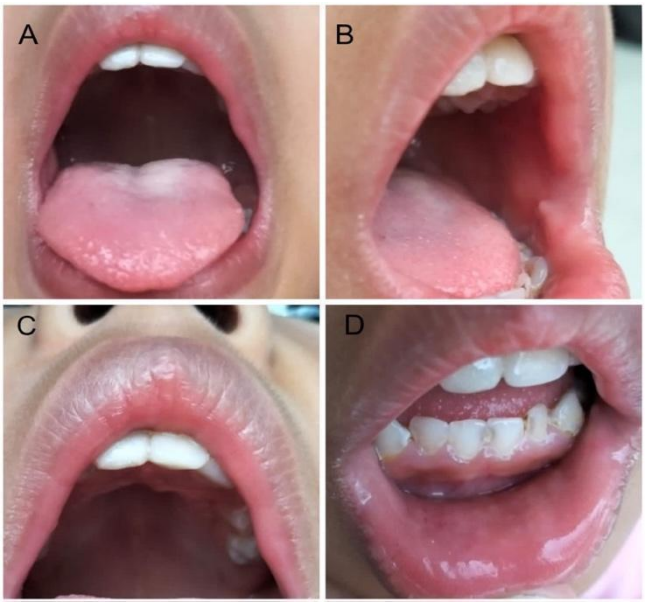

Figure 4. Extraoral and intraoral examinations of the POC patient at the second visit showed improvement, the lip is moist, and no white lesions were found.

Both patients expressed satisfaction with the services and treatments they had received. They also demonstrated an understanding of the efforts that should be made independently to prevent the recurrence of the disease, based on the education and information we provided. Additionally, the patients provided both verbal and written consent for the publication of this case report and the planned scientific dissemination, while ensuring the confidentiality of the patient's identity and adherence to code of ethics.

DISCUSSION

This case report discusses a 30-year-old female patient who was diagnosed with primary herpetic gingivostomatitis. She presented with fever accompanied by sores on the lips and multiple ulcers in the oral cavity. Extraoral and intraoral examinations revealed typical clinical features of ulcerative lesions, leading to the clinical diagnosis of ulcerative lesions caused by viral infection. Serosanguinous crusted lesions on the lips and multiple ulcerative lesions, most of which were located on the non-keratinized oral mucosa, were pathognomonic clinical features of PHGS found in this patient. This finding is consistent with the literature which states that the presence of oral vesicular and ulcerative lesions is pathognomonic and is sufficient for diagnosis.[9,10]

Primary herpetic gingivostomatitis is the initial manifestation of Herpes simplex virus (HSV) type 1 infection. The incubation period for this disease is 3–7 days, followed by a prodromal period characterized by clinical symptoms such as fever, anorexia, malaise, and myalgia.[19] Several days after the onset of prodromal symptoms, erythema and clusters of vesicles and ulcers appear on the hard palate, attached gingiva, dorsum of the tongue, and non-keratinized mucosa such as the buccal mucosa, labial mucosa, ventral tongue, and soft palate.[11,12] Damage to epithelial cells causes vesicle rupture, leading to the formation of ulcerations measuring 1–5 mm, which can merge to form larger ulcers with wavy edges and surrounding erythema.[11,20]

The gingiva often appears very red, and the mouth becomes highly painful, resulting in difficulty eating. The cervical, submental, and submaxillary lymph nodes may become enlarged.[11,26] The inability to swallow often causes saliva accumulation, which can result in drooling. The number of lesions and the degree of discomfort vary significantly among patients. In severe cases, intense pain

causes the patient to become restless and sensitive. Fever, drooling, and fluid deprivation can also contribute to dehydration, which in some cases requires hospitalization.[12]

The treatment provided to the first-case patient included systemic and topical antiviral therapy, which the patient adhered to cooperatively and consistently, leading to significant improvement after two weeks. The administration of multivitamins also supported the healing process of this disease. PHGS is an infectious disease that is a self-limiting disease, so when the patient's immune system increases, it will lead to healing. Several studies also stated that the recommended therapy for PHGS is adequate nutrition to support recovery, analgesics to manage pain and malaise, and the use of antiviral drugs (acyclovir, valacyclovir, or famciclovir) as the causative therapy.[11] Therefore, the therapy provided to the patient aligns with the existing literature.

Pseudomembranous oral candidiasis (POC) is an opportunistic infection of the oral cavity that primarily occurs under certain conditions, such as decreased immunity. *Candida spp*. are normally part of the oral flora and are found in 20–75% of the general population without causing symptoms.[27] However, in individuals with certain predisposing factors, *Candida* can become pathogenic and cause infection.[2,28] In children, systemic predisposing factors that can trigger POC include age, nutritional intake, use of systemic drugs, immune disorders, and congenital conditions. *Candida* infections generally do not occur in individuals with healthy immune systems because acquired immunity will prevent the development of mucosal colonization into symptomatic infection.[22] An intact mucosa serves as a barrier against the penetration of pathogens and antigenic macromolecules. However, in individuals with compromised mucosal immune responses, pathogens such as *Candida albicans* can colonize more easily and cause infection.[29]

Clinically, POC is characterized by the presence of yellowish-white plaques resembling milk curd that can be removed by gently rubbing, leaving an erythematous mucosal surface.[30] The plaque consists of hyphae that invade the inner layer of the stratum spinosum, desquamated epithelial cells, fibrin, debris, and necrotic material.[22,24]

In this case, a 4-year-old girl was diagnosed with POC. The oral complaints, including mild pain that interfered with appetite and the white patches in the mouth and lips, are pathognomonic signs and clinical features of POC and lead to this clinical diagnosis.[10,11] This is the basis for the fact that supporting examinations were not performed on this patient.

The antifungal therapy Nystatin prescribed for this patient led to significant improvement. This is thought to be because the patient was very cooperative and understood how to use the drug, the dosage, and the importance of compliance based on our instructions. Nystatin is a broad-spectrum antifungal compound that is effective against candidal infections. The use of topical nystatin is the most common in dentistry because its systemic exposure is minimal. Nystatin can also be used as a prophylactic to prevent oral and systemic candidiasis in patients with weakened immune systems because its interactions with other drugs are minimal.[2,31] Providing multivitamins and probiotics have also been proven to support recovery in these patients with the mechanism of action to increase the body's immunity.[32] Consultation with a nutritionist should be recommended to patients if nutritional imbalance or deficiency problems are found which may at any time trigger a relapse or worsen the immune system's condition.

The two cases presented illustrate the strong role of pathognomonic clinical features in establishing the diagnosis. The clinical picture is often considered pathognomonic because it is so specific for this condition. While supporting examinations are the golden standard in disease management, they may not always be feasible due to limited facilities, financial constraints, or lack of insurance coverage.[33]

The most commonly performed and sufficient supporting examination for the diagnosis of PHGS is the serological examination of specific anti-HSV-1 antibodies

(ELISA method). Meanwhile, the potassium hydroxide (KOH) staining on lesion swabs is one of the several supporting examinations for POC. Even though pathognomonic symptoms can be the primary guide in establishing the diagnosis, supporting examinations still have an important role in situations where there is doubt or complications or in patients with predisposing conditions that require additional confirmation. A comprehensive assessment of the patient's condition, clinical history, and risk factors is essential in determining whether supporting examinations are needed. The limitation of this case report is that it does not have supporting laboratory examination data that can be used as a confirmatory diagnosis. However, this case report still brings benefits to dentists in daily clinical practice.

This article discusses two cases demonstrating pathognomonic clinical features of two different oral mucosal diseases, primary herpetic gingivostomatitis (PHGS) and pseudomembranous oral candidiasis (POC). Both cases were clinically diagnosed based on subjective and objective findings without supporting examination and showed successful recovery following appropriate treatment. Typical clinical features and symptoms of each disease are the main aspects that can lead to a diagnosis.

The limitation of this case report is that only one patient was examined in each case so there is no comparison with other cases. However, the typical clinical picture is actually sufficient to make a diagnosis if the patient does not have accompanying systemic diseases that make it doubtful in making a diagnosis and providing therapy.

CONCLUSION

Primary herpetic gingivostomatitis and acute pseudomembranous candidiasis exhibit pathognomonic clinical features that are typically sufficient for clinical diagnosis without laboratory-supporting confirmation. If treatment based on clinical diagnosis leads to improvement, then supporting examination may not be necessary. However, close supervision by a doctor is essential in this situation. However, supporting examinations are important if any doubts, complications, or predisposing conditions require verification. The implication of this case report can be applied clinically by dentists in diagnosing oral diseases that have pathognomonic clinical features. It also can become a guideline for the management of the PHGS and POC, offering a cost-effective approach while ensuring that necessary supporting examinations are not overlooked in certain cases.

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