Majalah Kedokteran Gigi Indonesia Vol 9 No 2 – August 2023 ISSN 2460-0164 (print), ISSN 2442-2576 (online) Available online at https://jurnal.ugm.ac.id/mkgi DOI: http://doi.org/10.22146/majkedgiind.79883

### CASE REPORT

# Management of herpangina: a viral infection in infants

Caecilia Dewi Ratna Prathiwi\*, Indra Bramanti\*\*⊠

- \*Study Program of Pedodontic, Faculty of Dentistry, Universitas Gadjah Mada, Yogyakarta, Indonesia
- \*\*Department of Paediatric Dentistry, Faculty of Dentistry, Universitas Gadjah Mada, Yogyakarta, Indonesia
- \*\*JI Denta No 1 Sekip Utara, Yogyakarta, Indonesia; ⊠ correspondence: bramantikg@ugm.ac.id

Submitted: 7th December 2022; Revised: 17th February 2023; Accepted: 20th July 2023

#### **ABSTRACT**

Herpangina is a self-limiting disease caused by coxsackievirus. The manifestation consists of acute febrile with small ulcerative or vesicular lesions on the tonsillar, soft palate, uvula and buccal mucosa. The disease mostly affects children. The aim of this case report is to discuss the oral symptoms of herpangina based on current literature for dental and health practitioners. In our case, a 15-month-old baby girl presented with high fever reaching 40.2 °C for 2 days with no seizures, cold and cough. Intra oral examination showed several well-defined whitish round lesions on the soft palate and one on the upper left lip. The patient was prescribed 3ml of methisoprinol 250 mg 3 times a day, 4 ml of paracetamol 125 mg every 6 hours, hyaluronic acid spray 3 times a day, and 1ml of vitamin C 40 mg taken once a day. The patient showed no sign of bacterial infection. Lesion disappeared after 7 days of treatment. Upon follow-up visit after 2 weeks, the lesion had completely disappeared. Dentists should be able to recognize and manage herpangina cases in infants.

Keywords: herpangina; infant; oral ulcer; viral infection

#### INTRODUCTION

Herpangina is a self-limiting infection that is caused by coxsackievirus and is manifested clinically as an acute febrile illness followed by small ulcerative or vesicular lesions on the soft palate, tonsillar area, uvula and sometimes buccal mucosa.1 Herpangina mostly occurs in infants under 5 years old, but it can occur in any age group, including adolescents and young adults.2 The disease is contagious due to droplet transmissions and most cases increase in the summer because the rising temperature may speed the increased transmission of the virus.3 Herpangina is often found in schools and childcare facilities.<sup>1,4</sup> Infants and immunocompromised patients must be wary of the disease because its complication can cause serious illness which can lead to multiple organ failure.3

Enterovirus A71 (EV-A71) infections are one of the main etiological agents of herpangina worldwide.<sup>5,6,7</sup> Enterovirus is non-envelope RNA virus that has unique physical and biological properties.<sup>8</sup> It can cause a contagious viral

infection through faecal-oral transmission of oropharyngeal secretions and the respiratory droplets dissemination.<sup>7,9</sup> The prevalence of herpangina is rarely reported. Since 2009 there have been multiple outbreaks in Asian countries including China, Thailand, Japan and Korea.<sup>6,7,10</sup> Epidemic of herpangina has occurred in Japan with several conditions reported to be fatal. The most common area involved in severe or fatal cases of EV-A71 is the brain stem.<sup>7,11</sup>

Herpangina generally resolves completely within 5–7 days post infection. 1,3,6 Seen clinically, herpangina resembles hand, foot, and mouth disease (HFMD) and herpetic gingivostomatitis. Herpangina is characterized by high fever and oral ulcers without any lesions appearing on the skin, while HFMD is typically a brief, febrile illness, oral exanthem followed by vesicular rash on soles, palms and sometime buttocks. 12

Patients having ulceration of the oral cavity might consult primarily to a dental practitioner or a general physician. During the COVID-19 pandemic,

all forms of viral infections of the oral cavity should be suspected. Local or systemic factors play role in developing ulcers. <sup>13</sup> A thorough assessment of clinical symptoms that appear may help establish a correct diagnosis. Because the virus has the potential to cause high morbidity and mortality among children, it is critical to understand the disease for better treatment. The aim of this case report is to discuss oral symptoms of herpangina based on current literature for dental and health practitioners.

### **CASE DESCRIPTION**

A 15-month-old baby girl presented to the Department of Paediatric Dentistry of Prof. Soedomo Dental Hospital, Yogyakarta in early August 2022 with oral conditions. According to the patient's parents, the patient suddenly had a high fever reaching 40.2 °C in the previous morning and had been given medication for fever every 4 hours. There was no sign of seizures, cough, nor cold and the patient was still able to eat or drink. However, on the second day her parents found a whitish spot on the oral cavity (Figure 1) followed by malaise and fuzziness.

Oral clinical examination found several round lesions measuring ± 2 mm on the soft palate and one large lesion measuring ± 4 mm in the deeper part. A question arose as to whether it was associated with any systemic condition. After the examination and a consultation with a paediatrician, the patient's provisional diagnosis was a viral infection with a clinical suspicion of herpangina and the differential diagnosis was hand, foot and mouth disease (HFMD) and herpetic gingivostomatitis. The patient was required to return for a follow-up visit on day 3 to examine additional symptoms and for laboratory



**Figure 1.** There were several well-defined whitish round lesions in the soft palate area

tests. Based on the previously described symptoms, the patient was prescribed methisoprinol and paracetamol by the paediatrician and hyaluronic acid spray and vitamin C by the dentist for 7 days.

On the third day, the lesion had reduced in size, from 2 mm to 1 mm and from 4 mm to 2 mm (Figure 2). Blood test showed normal numbers (Table 1). Additional symptoms were not observed, and body temperature was 37.5 °C. The patient's appetite slowly increased. Based on the holistic approach, the final diagnosis was herpangina. There was no limitation on food intake, but soft diet was suggested. After 7 days all lesions had disappeared and the patient could return to normal activities (Figure 3).

### **DISCUSSION**

Herpangina is an acute viral disease accompanied by sudden fever and is associated with vesicles and ulcers around oropharynx. Manifestations

Table 1. Blood test result

Result	References value	Conclusion
11.8 g/dL	11-15 g/dL	N
31.9%	36-44%	< N
8,300x10³/µl	5,000-13,500x10 <sup>3</sup> /µI	N
219,000x10 <sup>3</sup> /µl	150,000-440,000x10 <sup>3</sup> /µI	N
	11.8 g/dL 31.9% 8,300x10³/µl	11.8 g/dL 11-15 g/dL 31.9% 36-44% 8,300x10³/µl 5,000-13,500x10³/µl



Figure 2. Lesion on day 3

of herpangina are often present with sudden pharyngeal pain and high fever, also multiple ulcers in the posterior pharyngeal area, 14 such as soft palate, uvula and tonsil.8,15 In this case, the patient came with a fever of 39.6 °C. The fever developed a day before coming to the hospital. This elevated body temperature occurs as the body's response to fight against a recent viral infection. In any infectious conditions, whether caused by a virus or bacteria, the body will give an inflammatory response. Fever is one of the responses that may occur. The patient's parents also reported that the patient looked lethargic and malaise. No cold nor cough was present.

Similar to herpetic lesion, herpangina is wellcharacterized by multiple vesicular exanthema and ulcers on the soft palate. The lesions initially appear as reddish macules that turn into vesicles and finally to ulcerations, which can be 2-4 mm in size. 14,16 Within two days of infection, an average of four or five (but sometimes up to twenties) greyish bumps 1 to 2 mm in diameter are formed and developed into vesicles surrounded by a reddish ring.4 Over the next 24 hours, these become superficial lesions, rarely larger than 5 mm in diameter and heal within 7 up to 10 days. These lesions most commonly appear on the tonsillar pillars (adjacent to the tonsils) and occasionally found on the soft palate, tonsils, uvula, or tongue. A small number of lesions (two to six) are usually formed at posterior oropharyngeal especially soft palate or tonsil. The number of lesions in our case was more than 10 on the soft palate and tonsillar



Figure 3. The condition of the oral cavity at day 7

pillar. As a result, the patient had difficulty in chewing and swallowing.

Differential diagnoses of herpangina are HFMD and herpetic gingivostomatitis. Herpangina can be distinguished from herpetic gingivostomatitis. The location of vesicles in herpangina is usually around the posterior oropharynx, whereas in herpetic gingivostomatitis, the they usually appear in the anterior oropharynx and the oral cavity. Herpangina differs from HFMD, in which other reddish lesions occur on the extremities of hands and feet.

Herpangina is caused by enteroviruses (EV), 4,5,10,17 particularly coxsackievirus (CV). 17 Geographical locations, seasons and population susceptibility play important roles in etiological spectrum of herpangina. 18,19 Major outbreaks have been reported in many Asian countries, and cases have often been found in schools and childcare facilities.20 However, herpangina infection in our case was presumably because the patient was in the oral phase of development, one of the most important stages of child development.<sup>20</sup> Children begin to recognize their environment through their mouth while fulfilling their curiosity and personal satisfaction. In this phase, they would generally be more active to put anything into their mouth using both hands,21,22 thus making them more susceptible to enteroviruses than adults.

Diagnosis was made based on anamnesis as well as clinical and laboratory examinations. Differential diagnosis with HFMD and herpetic gingivostomatitis was omitted because there were

no other accompanying symptoms, such as red rashes on the palms of the hands and feet and no ulcers in facial area.

Herpangina is a viral infection that can normally heal within 7-10 days. 1,11 Providing good nutrition and adequate food intake would further accelerate the healing process of herpangina. The type of therapy given is usually a supportive therapy to help relieve symptoms and provide comfort for the patient. Methisoprinol is an antiviral drug of choice that works by inhibiting the growth and spread of viruses in the body. This drug can also improve the immune system. It helps the body to fight infection and is recommended to be taken even though the condition has improved to avoid reinfection. 23 Adequate fluid intake may prevent dehydration from painful oral lesions. Cold liquids are usually preferred.

The prognosis of herpangina is generally good, but a few children may develop more severe disease and can be afflicted with encephalitis, aseptic meningitis, acute delayed oedema, paralysis, pulmonary myocarditis and other complications.5,7,17 Although serious complications are rare, one should be aware of the course of herpangina associated with EV 71 infection. Risk factors for EV 71 infection with disease progression to CNS involvement are associated with younger age, fever, vomiting, mouth ulcers, difficulty breathing, cold locomotion and poor urine production. CNS involvement may require adequate treatment because the disease progression tends to be fast and can be fatal due to heart-lung failure.

# CONCLUSION

Herpangina is an acute viral infection that is common in childhood. Herpangina may lead to various fatal complications such as meningitis, encephalitis, cardiomyopathy, or even death. Because of its similarity to other viral infections, dental practitioners must be able to distinguish herpangina from other differential diagnoses to determine a final diagnosis through clinical examinations. Consultation with a paediatrician

for systemic therapy is necessary. This may help dental practitioners to provide appropriate clinical therapy for patients with herpangina.

# **CONFLICT OF INTEREST**

The authors declare no conflict of interest with the data contained in the manuscript.

#### **REFERENCES**

- Puenpa J, Mauleekoonphairoj J, Linsuwanon P, Suwannakarn K, Chieochansin T, Korkong S, Theamboonlers A, Poovorawan Y. Prevalence and characterization of enterovirus infections among pediatric patients with hand foot mouth disease, herpangina and influenza like illness in Thailand, 2012. PLoS One. 2014; 9(6): e98888. doi: 10.1371/journal.pone.0098888
- Xie MZ, Chen LY, Yang YN, Cui Y, Zhang SH, Zhao TS, Zhang WX, Du J, Cui FQ, Lu QB. Molecular epidemiology of herpangina children in Tongzhou District, Beijing, China, During 2019-2020. Front Med (Lausanne). 2022; 9: 822796. doi: 10.3389/fmed.2022.822796
- Oliveira DB, Campos RK, Soares MS, Barros RB, Batista TCA, Ferreira PCP, Bonjardim CA, Trindade GS, Abrahão JS, Kroon EG. Outbreak of herpangina in the Brazilian Amazon in 2009 caused by Enterovirus B. Arch Virol. 2014; 159(5): 1155–1157.

doi: 10.1007/s00705-013-1858-5

- Chansaenroj J, Auphimai C, Puenpa J, Mauleekoonphairoj J, Wanlapakorn N, Vuthitanachot V, Vongpunsawad S, Poovorawan Y. High prevalence of coxsackievirus A2 in children with herpangina in Thailand in 2015. Virusdisease. 2017; 28(1): 111–114. doi: 10.1007/s13337-017-0366-8
- Li W, Gao HH, Zhang Q, Liu YJ, Tao R, Cheng YP, Shu Q, Shang S. Large outbreak of herpangina in children caused by enterovirus in summer of 2015 in Hangzhou, China. Sci Rep. 2016; 6: 1–5. doi: 10.1038/srep35388
- Yao X, Bian LL, Lu WW, Li JX, Mao QY, Wang YP, Gao F, Wu X, Ye Q, Li XL, Zhu FC, Liang Z. Epidemiological and etiological

- characteristics of herpangina and hand foot mouth diseases in Jiangsu, China, 2013–2014. Hum Vaccin Immunother. 2017; 13(4): 823–830.
- doi: 10.1080/21645515.2016.1236879
- Chang YK, Chen KH, Chen KT. Hand, foot and mouth disease and herpangina caused by enterovirus a71 infections: A review of enterovirus a71 molecular epidemiology, pathogenesis, and current vaccine development. Rev Inst Med Trop Sao Paulo. 2018; 60: 1–8. doi: 10.1590/S1678-9946201860070
- Pons-Salort M, Parker EPK, Grassly NC. The epidemiology of non-polio enteroviruses: Recent advances and outstanding questions. Curr Opin Infect Dis. 2015; 28(5): 479–487. doi: 10.1097/QCO.0000000000000187
- Xie MZ, Chen LY, Yang YN, Cui Y, Zhang SH, Zhao TS, Zhang WX, Du J, Cui FQ, Lu QB. Molecular epidemiology of herpangina children in Tongzhou District, Beijing, China, During 2019-2020. Front Med (Lausanne). 2022; 9: 1–10. doi: 10.3389/fmed.2022.822796
- Zhao TS, Du J, Li HJ, Cui Y, Liu Y, Yang Y, Cui F, Lu QB. Molecular epidemiology and clinical characteristics of herpangina children in Beijing, China: a surveillance study. PeerJ. 2020; 8: 1–15. doi: 10.7717/peerj.9991
- Chang LY, Lin TY, Hsu KH, Huang YC, Lin KL, Hsueh C, Shih SR, Ning HC, Hwang MS, Wang HS, Lee CY. Clinical features and risk factors of pulmonary oedema after enterovirus-71-related hand, foot, and mouth disease. Lancet. 1999; 354(9191): 1682–1686. doi: 10.1016/S0140-6736(99)04434-7
- 12. Romero JR. Hand, foot, and mouth disease and herpangina. UpToDate. 2022.
- Minhas S, Sajjad A, Kashif M, Taj F, Waddani H al, Khurshid Z. Oral ulcers presentation in systemic diseases: an update. Open Access Maced J Med Sci. 2019; 7(19): 3341–3347. doi: 10.3889/oamjms.2019.689
- Park K, Lee B, Baek K, Cheon D, Yeo S, Park J, Soh J, Cheon H, Yoon K, Choi Y. Enteroviruses isolated from herpangina and hand-foot-andmouth disease in Korean children. Virol J.

- 2012; 9: 1-6. doi: 10.1186/1743-422X-9-205
- 15. Thakkar P, Banks JM, Rahat R, Brandini DA, Naqvi AR. Viruses of the oral cavity: prevalence, pathobiology and association with oral diseases. Rev Med Virol. 2022; 32(4): e2311. doi: 10.1002/rmv.2311
- Koh WM, Bogich T, Siegel K, Jin J, Chong EY, Tan CY, Chen MI, Horby P, Cook AR. The epidemiology of hand, foot and mouth disease in Asia: a systematic review and analysis. Pediatr Infect Dis J. 2016; 35(10): e285-300. doi: 10.1097/INF.000000000001242
- 17. Yu H, Li XW, Liu QB, Deng HL, Liu G, Jiang RM, Deng JK, Ye YZ, Hao JH, Chen YH, Nong GM, Shen ZB, Liu CS, Zou YX, Wu JZ, Wu XD, Chen BQ, Luo RP, Lin AW, Chen Y, Liu XD. Diagnosis and treatment of herpangina: Chinese expert consensus. World J Pediatr. 2020; 16(2): 129–134.
  - doi: 10.1007/s12519-019-00277-9
- Puenpa J, Wanlapakorn N, Vongpunsawad S, Poovorawan Y. The history of enterovirus A71 outbreaks and molecular epidemiology in the Asia-Pacific region. J Biomed Sci. 2019; 26(1): 1-11. doi: 10.1186/s12929-019-0573-2
- 19. Yao X, Bian L, Lu W, Li J, Mao Q, Wang Y, Gao F, Wu X, Ye Q, Xu M, Li Z, Zhu F, Liang Z. Enterovirus spectrum from the active surveillance of hand foot and mouth disease patients under the clinical trial of inactivated Enterovirus A71 vaccine in Jiangsu, China, 2012-2013. 2015; 87(12): 2009-2017. doi: 10.1002/jmv.24275
- 20. Wang J, Hu Y, Zheng M. Enterovirus A71 antivirals: past, present, and future. Acta Pharm Sin B. 2022; 12(4): 1542-1566. doi: 10.1016/j.apsb.2021.08.017.
- 21. Kail R. Children and Their Development (Mydevelopmentlab Series). 2011.
- 22. Wardianti Y, Mayasari D. Pengaruh fase oral terhadap perkembangan anak. Jurnal Bimbingan Konseling Indonesia. 2016; 1(2): 36-37.
- 23. Apriasari ML. Methisoprinol as an immunomodulator for treating infectious mononucleosis. Dental Journal. 2016; 49(1): 1-4. doi: 10.20473/j.djmkg.v49.i1.p1-4