

CASE REPORT

Oral Aphthous-like Ulcers Response to Topical Therapy in Young Adult Woman with Beta-Thalassemia Intermedia

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ABSTRACT

Background: Beta thalassemia may have some oral manifestations. Oral mucosa ulcer may be one of the oral manifestations of beta-thalassemia. The oral ulcer may resemble recurrent aphthous stomatitis (RAS). This current case report aims to present an aphthous oral ulcer as a manifestation in young adult women with beta-thalassemia. **Case report:** A 28-year-old woman complained of recurrent painful oral ulcers in the labial mucosa. She was diagnosed with beta-thalassemia intermedia three years before. The ulcer may take 3-4 weeks to heal completely. Intraoral examination revealed two yellowish ulcers, 5 mm and 10 mm, surrounded by an erythematous halo, regular margin on left lips mucosa, oral ulcer pain scale measured medium level by visual analogue scale (VAS). The oral aphthous-like ulcer was taken for diagnosis in this case. Topical treatment was given to the oral ulcer using chlorine dioxide gel three times daily. After 10 days, the oral aphthous-like ulcer was healed. **Conclusion:** An oral aphthous-like ulcer may be the oral manifestation in beta-thalassemia patients, and the oral ulcer may respond well to topical treatment commonly used in recurrent aphthous stomatitis (RAS) patients. Hence, it is important to recognize oral conditions as one clinical manifestation in beta-thalassemia patients and choose the appropriate treatment to accelerate oral ulcer healing.

Keywords: Beta-Thalassemia, oral manifestation, oral ulcer, topical therapy

INTRODUCTION

Thalassemias are a group of inherited autosomal recessive hematologic disorders characterized by defects in one or more of the haemoglobin chain syntheses. Alpha thalassemia is caused by reduced or absent alpha globin chain synthesis, whereas beta-thalassemia is caused by reduced or absent beta globin chains. Approximately 1.5-1.7% of people in the world have both types of thalassemias. Both types of thalassemia are prevalent in African and Southeast Asian descent. However, beta thalassemia may also occur in the Mediterranean, Middle East, Central Asia, India, southern China, and South America. Both types of thalassemia may cause an imbalance of globin chains and cause hemolysis resulting in impaired erythropoiesis.¹ Beta-thalassemia is a syndrome group classified into thalassemia major or Cooley's Anemia, Thalassemia Intermedia (Mediterranean Anemia), and Thalassemia minor.¹ Other types of Beta thalassemia are Beta thalassemia with associated Hb anomalies (HbC, HbE, HbS), Hereditary persistence of Fetal Hb, and Beta-thalassemia, Autosomal dominant forms, beta thalassemia associated with other manifestations.¹ Beta-thalassemia minor may only have microcytosis and

mild anemia without any signs and symptoms, whereas Beta thalassemia major may have many signs and symptoms such as abdominal swelling, growth retardation, irritability, jaundice, pallor, skeletal abnormalities, splenomegaly, and requires lifelong blood transfusions. Beta-thalassemia intermedia may have variable severity signs and symptoms and be less severe than Beta-Thalassemia major.¹

Epidemiology studies showed that thalassemia has oral manifestations. A study showed that children and adolescents with thalassemia have low growth rates with an increase in age and significant delays in dental development.² The most common orofacial manifestations of beta-thalassemia are prominent frontal and parietal bones, sunken nose bridge, protruding zygomas and mongoloid slanting eyes, enlargement of maxilla and obliteration of maxilla sinus, depression of nose bridge that results in facial appearance chipmunk face.^{3,4} Furthermore, most Beta-thalassemia patients are children and young adults. Beta thalassemia may have oral manifestations such as lip incompetence, maxillary protrusion, and gingivitis.⁵ Some oral conditions or disorders are also associated with thalassemia, such as pale oral mucosa, halitosis, oral ulcer, oral mucosa pigmentation, cheilitis (angular cheilitis, actinic cheilitis), hypo mineralization, fungal infection (candidiasis), burning sensation, geographic tongue, fissured tongue and poor oral hygiene.^{6,7} Beta-thalassemia patients also have a poor oral health-related quality of life compared with healthy children.^{8,9}

There are also some case reports of Beta-thalassemia with various oral manifestations. Most case reports were Beta-thalassemia with dentofacial manifestation management, such as a case report of a young boy with Beta-thalassemia with dental and swelling in the upper teeth region,¹⁰ a case report of a young boy diagnosed with beta-thalassemia had skeletal class II tendency and protrusive appearance of maxillary growth.¹¹ Another case report of Beta-thalassemia was in young adult women with dental pain management in conjunction with Beta-thalassemia treatment.¹² Oral mucosa ulcer may also be an oral manifestation of Beta-thalassemia. There were few cases of oral ulcers in beta-thalassemia, although there was a case report of aphthous-like ulcers in beta-thalassemia intermedia patients.¹³ Here, we also would like to present the aphthous-like ulcers in young adult women with beta-thalassemia intermedia and responded well to topical therapy. Beta-thalassemia intermedia is a systemic disease; topical therapy may still be challenged for oral ulcer treatment since the β thalassemia intermedia may compromise oral ulcer healing due to anaemia. Hence, topical non-drug use with combination actions not only anti-inflammatory but also antiseptic, and another component such as aloe extract that accelerates wound healing may be useful.

CASE REPORT

A 28-year-old woman came to UGM Dental Hospital complaining of painful ulcers on her lower lip. She had felt the ulcers for 5 days. The ulcers appeared after her lips were unintentionally bitten. The ulcer's size was getting larger, and she felt the ulcers were more painful, especially when eating. She has had oral ulcers and recurrent history for more than 6 years. Typically, her ulcers need approximately 3-4 weeks to heal without any treatment. She had a scaling treatment 3 years ago, tooth filling 4 years ago, and wisdom teeth extraction 5 years ago with prolonged bleeding for 3 days. She also had orthodontic treatment for 5 years. She routinely brushes her teeth twice daily. For medical history, she was diagnosed with thalassemia at 3 years old, and she had been explicitly known as a Beta-Thalassemia intermedia patient in the past 3 years and required occasional blood transfusions for this condition. She does not have any allergy history. Her father and mother have hypertension. She is not married and lives with her parents. She does not smoke or drink alcohol.

In physical examination, she had a normal BMI (19.5), the vital signs were normal, and the pain severity of her ulcers was 5 when measured using a visual analogue scale (VAS). No

abnormalities were found in the extraoral examination. Intra-oral examination revealed two yellowish ulcers, 5 and 10 mm each; both were surrounded by an erythematous halo, the regular margin on the left lip's mucosa. Other lesions were physiological pigmentation, torus palatines, coated tongue, and gingivitis in some regions. A complete blood examination results from one month previously showed erythrocytes ($3.46 \times 10^6 \mu\text{L}$), Hb (7.8 g/dL), haematocrits (24.3%), MCV (70.2 fL), MCH (22.5 Pg), thrombocyte ($132 \times 10^3 \mu\text{L}$) all were low, and the other parameters were normal. The oral aphthous-like ulcer diagnosis was concluded. The ulcers were treated topically with chlorine dioxide gel three times daily. The ulcer regressed after 4 days of treatment (Figure 2) and healed after 10 days of treatment (Figure 3).



Figure 1. Yellowish ulcers on the left lower labial mucosal area are around 5 mm in double-round shape, with a well-demarcated margin, and the erythematous surrounding area (1st visit).



Figure 2. The left lower labial mucosal ulcer was reduced in size after being treated for 4 days using topically chlorine dioxide gel (2nd visit).

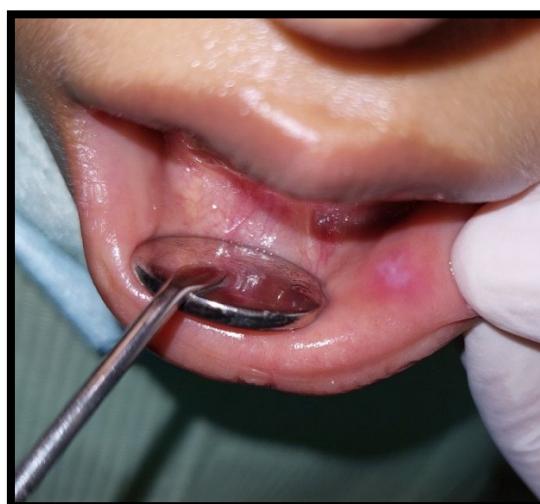


Figure 3. The ulcers showed a progressive healing process after 10 days of treatment using a topical application of chlorine dioxide gel on the site. The young epithelial tissue showed a pink colour (3rd visit)

DISCUSSION

Oral mucosa ulcer is among the most common oral manifestations of beta-thalassemia.^{6,7} The type of oral ulcer may resemble recurrent aphthous stomatitis (RAS) with the clinical characteristic of one or more well-demarcated, round oral ulcers, yellowish based, surrounded by an erythematous area, located in non-keratinized mucosa, with 1-10 mm size.¹⁴ The patient also had experienced recurrent oral ulcers after being diagnosed with Beta-thalassemia, which healed by itself within 3 weeks duration without accompanied or preceded symptoms and followed by any lesion on other parts of the body. This patient was diagnosed with beta-thalassemia intermedia in the last three years. This is quite common due to the nature of beta-thalassemia as non-transfusional dependent thalassemia (NTDT), so a patient might be diagnosed later in life.¹

This case is similar to the previous case report about aphthous-like ulcers in a man with Beta-thalassemia, which is also induced by trauma,¹³ However, in this case report, our patient is a female, and the ulcer may also be related to the decreased in her physical condition. The explanation of both factors may contribute to oral ulcers based on the patient's history. The oral ulcer will recur when the patient feels unwell physically and has trauma on-site. Trauma is the most precipitating factor of oral ulcers and may be the precipitating factor for RAS.¹⁴ Physical stress has been known as one of the precipitating factors of aphthous ulcers.^{15,16} Like psychological stress, the decreased physical condition may cause stress conditions that disrupt the immunity balance.¹⁷ The immunity imbalance (Th1/Th2) may dysregulate the immune response, altering the immune response to unknown antigens in oral mucosa and resulting in oral ulcers.¹⁸

The aphthous-like ulcer in beta-thalassemia may also be predisposed by an anaemia condition in thalassemia patients. The reduced Beta globin chains may lead to erythroid precursors in bone marrow, resulting in ineffective erythropoiesis. Haemolysis contributes to anaemia. The patient received a blood transfusion to correct the anaemia condition.¹ Prolonged anaemia may compromise oral mucosal turnover, make it vulnerable to any stimuli that precipitate oral ulcer development, and delay oral mucosal ulcer healing.¹⁹

Considering the thalassemia condition was not severe, the aphthous oral ulcer, in this case, was treated using a common topical drug such as topical chlorine dioxide gel.¹³ The main goal of oral ulcer treatment is to reduce pain and inflammation, lessen the duration of oral ulcers, and prevent local trauma and secondary infections.²⁰ The topical gel containing Chlorine dioxide (ClO₂) may help to accelerate oral ulcer healing by the antibacterial, antifungal, and fungicidal action without any serious adverse effects.²¹⁻²³ The zinc and aloe vera components may have antioxidant activity and increase re-epithelization and immunomodulation.^{24,25} Hence, it may facilitate faster healing of oral ulcers. It was shown that the aphthous-like ulcer in this patient was healed approximately only in 10 days. The important thing was that the patient admitted that the oral ulcer may be influenced by her systemic condition and that topical medication may help accelerate the healing of the oral ulcer. Although the oral ulcer may be one of the oral manifestations of Beta-thalassemia intermedia. This current case had a similar precipitating factor to recurrent aphthous stomatitis (RAS). Since the onset of oral ulcer of this case in adult age after she was diagnosed with Beta-thalassemia intermedia and recurrent. Further examination, such as histopathology and other factors, such as nutrition, is needed since the systemic condition may compromise nutrition status, which may be the limitation of this case report.

CONCLUSION

The oral ulcer in a patient with beta-thalassemia intermedia may resemble the clinical features of more common ulcerations, such as aphthous stomatitis. A thorough anamnesis and history taking are important to disclose the main factors contributing to a patient's condition. Topical Chlorine dioxide (ClO₂) may accelerate the healing of the ulcer in such a case.

CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this case report.

REFERENCE

1. Origa, R. (2017). β -Thalassemia. In *Genetics in Medicine* (Vol. 19, Issue 6, pp. 609–619). Nature Publishing Group. <https://doi.org/10.1038/gim.2016.173>
2. Hattab, F. N. (2013). Pattern of Physical growth and dental development in Jordanian children and adolescents with thalassemia major. *Journal of Oral Science*, 55(1), 71–77.
3. Raeesi, A., Kowash, S. B., & Halabi, A. (2017). Medical and Dental Implications of Patients with Beta Thalassemia Major. Part 2: Orofacial and Dental Characteristics: A Review. *JSM Dent*, 5(2), 1092-1–96.
4. Riyanti, E. (2008). Dental and oral management in beta major thalassemia in children. *Padjajaran Journal of Dentistry*, 20(1), 43–48.
5. Arora, A., & Sathyaprasad, S. (2022). Oro-facial Manifestations, Oral Health Status and Treatment Needs in Transfusion Dependent Children With β -thalassemia Major: A Cross-sectional Study. *Malaysian Journal of Medicine and Health Sciences*, 18(2), 76–80.
6. Abulsattar, M. S., & Al-Yassiri, A. M. (2014). Prevalence of Orofacial changes in patients with Beta-thalassemia major in Karbala City, Iraq. *Selwaimani Dental Journal*, 1, 64–67.
7. Rahim Abdulkarim, D., & M. Gaphor, S. (2023). Prevalence of Oral Manifestation of Thalassemic Patients in Sulaymaniyah Thalassemia Center. *Tikrit Journal for Dental Sciences*, 11(1), 93–104. <https://doi.org/10.25130/tjds.11.1.11>
8. Amirabadi, F., Saravani, S., Miri-Aliabad, G., & Khorashadi-Zadeh, M. (2019). The Association between Dental Health Status and Oral Health-Related Quality of Life of Children Diagnosed with β -Thalassemia Major in Zahedan City, Iran. *Int J Pediatr*, 7(2), 8985–8991. <https://doi.org/10.22038/ijp.2018.34517.3034>
9. Nabi, A., Muttu, J., Chhparwal, A., Mukhopadhyay, A., Pattnaik, S., & Choudhary, P. (2022). Implications of β -thalassemia on oral health status in patients: A cross-sectional study. *Journal of Family Medicine and Primary Care*, 11(3), 1174–1178. https://doi.org/10.4103/jfmpc.jfmpc_1215_21
10. Nagaveni, N. B., P. P., & Koley, P. (2017). Clinical Management of a Pediatric Patient Associated with Thalassemia Major: A Case Report. *CODS Journal of Dentistry*, 9(2), 55–58. <https://doi.org/10.5005/jp-journals-10063-0034>
11. Widodo, H. B., & Maharani, A. E. (2019). Oral manifestation of thalassemia Beta mayor: case study. *Journal of Case Reports in Dental Medicine*, 1(2), 32–35. <https://doi.org/10.20956/jcrdm.v1i2.90>
12. Vesna, A., Tina, K., & Zoran, N. (2021). Thalassemia-Beta Major-Case report. *Archives of Hematology Case Reports and Reviews*, 021–025. <https://doi.org/10.17352/ahcr.000034>
13. Riyanto, D., Soebadi, B., Hadi, P., & Radithia, D. (2020). Management of aphthous-like ulcer induce by trauma in a patient with thalassemia beta intermedia: a case report. *Journal of Case Reports in Dental Medicine*, 2(1), 5–8. <https://doi.org/10.20956/jcrdm.v2i1.110>
14. Namrata, M., & Abilasha, R. (2017). Recurrent Aphthous Stomatitis. *International Journal of Orofacial Biology*, 1(1), 43–47. <https://doi.org/10.4103/ijofb.ijofb>

15. Oyetola, E. O., Mogaji, I. K., Aghor, T. O., & O.A Ayilara. (2018). Pattern of Presentation of Oral Ulceration in Patients Attending an Oral Medicine Clinic in Nigeria. *Annals of Ibadan Postgraduate Medicine*, 16(1), 9–11.
16. Verma, S., Srikrishna, K., S., Shalini, K., Sinha, G., & Srivastava, P. (2023). Recurrent Oral Ulcers and Its Association with Stress Among Dental Students in the Northeast Indian Population: A Cross-Sectional Questionnaire-Based Survey. *Cureus*, 15(2), 1–10. <https://doi.org/10.7759/cureus.34947>
17. Seizer, L., & Schubert, C. (2022). On the Role of Psychoneuroimmunology in Oral Medicine. In *International Dental Journal* (Vol. 72, Issue 6, pp. 765–772). Elsevier Inc. <https://doi.org/10.1016/j.identj.2022.07.002>
18. Challacombe, S. J., Alshahaf, S., & Tappuni, A. (2015). Recurrent Aphthous Stomatitis: Towards Evidence-Based Treatment? *Current Oral Health Reports*, 2, 158–167. <https://doi.org/10.1007/s40496-015-0054-y>
19. Wu, Y. C., Wu, Y. H., Wang, Y. P., Chang, J. Y. F., Chen, H. M., & Sun, A. (2016). Hematinic deficiencies and anemia statuses in recurrent aphthous stomatitis patients with or without atrophic glossitis. *Journal of the Formosan Medical Association*, 115(12), 1061–1068. <https://doi.org/10.1016/j.jfma.2016.10.007>
20. Akintoye, S. O., & Greenberg, M. S. (2014). Recurrent Aphthous Stomatitis. *Dental Clinics of North America*, 58(2), 281–297. <https://doi.org/10.1016/j.cden.2013.12.002>. Recurrent
21. Kerémi, B., Márta, K., Farkas, K., Czumbel, L. M., Tóth, B., Szakács, Z., Csupor, D., Czimmer, J., Rumbus, Z., Révész, P., Németh, A., Gerber, G., Hegyi, P., & Varga, G. (2020). Effects of Chlorine Dioxide on Oral Hygiene - A Systematic Review and Meta-analysis. *Current Pharmaceutical Design*, 26(25), 3015–3025. <https://doi.org/10.2174/1381612826666200515134450>
22. Mani, S. (2012). Chlorine Dioxide: A Potential Mouth Rinse for Oral Health. *International Journal of Experimental Dental Science*, 1(2), 118–119. <https://doi.org/10.5005/jp-journals-10029-1029>
23. Peredo-Lovillo, A., Romero-Luna, H. E., Juárez-Trujillo, N., & Jiménez-Fernández, M. (2023). Antimicrobial efficiency of chlorine dioxide and its potential use as anti-SARS-CoV-2 agent: mechanisms of action and interactions with gut microbiota. *Journal of Applied Microbiology*, 134(7), 1–13. <https://doi.org/10.1093/jambio/lxad133>
24. Lin, P. H., Sermersheim, M., Li, H., Lee, P. H. U., Steinberg, S. M., & Ma, J. (2018). Zinc in wound healing modulation. *Nutrients*, 10(16), 2–20. <https://doi.org/10.3390/nu10010016>
25. Permatasanti, A., Fitriasaki, N., Sari, N. M., & Wahyuni, I. S. (2023). Antioxidant Effect of Mouthwash Containing Zinc, Aloe Vera, and Stabilized Chlorine Dioxide for Oral Manifestation of Acute Myeloblastic Leukemia (AML). *International Journal of Applied Pharmaceutics*, 15(Special Issue 2), 58–62. <https://doi.org/10.22159/ijap.2023.v15s2.11>