International Medical Case Reports Journal

Dovepress
open access to scientific and medical research

Open Access Full Text Article

CASE REPORT

Multidisciplinary Management of Oral Manifestations in Pregnant Women with Beta-Thalassemia Major: A Case Report

Dhini Karina[1], Nuri Fitriasari[2], Henry Yonatan Mandalas[3], Rizky Andhika[4], Indra Wijaya[5], Indah Suasani Wahyuni[6]

[1]Oral Medicine Residency Program, Faculty of Dentistry, Universitas Padjadjaran, Bandung, Indonesia; [2]Oral Medicine Division, Department of Dental and Oral Health, Hasan Sadikin Hospital, Bandung, Indonesia; [3]Periodontics, Department of Dental and Oral Health, Hasan Sadikin Hospital, Bandung, Indonesia; [4]Division of Nephrology and Hypertension, Department of Internal Medicine, Faculty of Medicine, Universitas Padjadjaran, Hasan Sadikin General Hospital, Bandung, Indonesia; [5]Division of Hematology and Oncology, Department of Internal Medicine, Faculty of Medicine, Universitas Padjadjaran, Hasan Sadikin General Hospital, Bandung, Indonesia; [6]Department of Oral Medicine, Faculty of Dentistry, Universitas Padjadjaran, Bandung, Indonesia

Correspondence: Indah Suasani Wahyuni, Email indah.wahyuni@unpad.ac.id

Introduction: Beta-thalassemia major is a blood disorder caused by impaired synthesis of hemoglobin beta chain. Oral manifestations of beta-thalassemia major in pregnancy have rarely been reported.

Objective: This study aimed to describe a case of oral manifestations in a pregnant woman with beta-thalassemia major for multidisciplinary management.

Case: A 27-year-old woman, suffering from beta thalassemia major who is undergoing therapy in the form of routine blood transfusions every month and taking anti-chelation drugs but is currently stopping this because she is pregnant, currently 16 weeks pregnant, complains complained of swollen gums, bleeding, and bad breath. Extraoral examination revealed dry, exfoliative lips. Intraoral examination revealed gingival hyperplasia with erythema, soft consistency, dark red rounded gingival margins, bleeding, true pockets and pain throughout the labial, buccal, palatal, and lingual. There was no history of systemic disease in this patient. Patient has never visited a dentist, either before or now, with complaints about her oral cavity. Hematological parameters showed abnormalities, and peripheral blood examination revealed an infection. The oral diagnoses included gingival enlargement and chronic periodontitis associated with pregnancy and β- thalassemia major.

Case Management: Dental management consisted of spooling with 3% hydrogen peroxide (H_2O_2) spooling, chlorine dioxide spray mouthwash, antibiotics, calculus removal, and oral hygiene instructions. Blood transfusions were administered once a month, and anti-chelation therapy was stopped during pregnancy. After three months of multidisciplinary management, the results were satisfactory.

Conclusion: Multidisciplinary, collaborative dental and medical management with non-surgical therapy of oral manifestations in pregnant women with beta-thalassemia major showed satisfactory results.

Keywords: anti-chelation drug, chlorine dioxide, gingival enlargement, hydrogen peroxide, blood transfusion

Introduction

Thalassemia is a genetically inherited autosomal blood disorder characterized by an impaired function of specific globin genes, resulting in specific globin chain insufficiency.[1] The classification of thalassemia based on the clinical severity, consisting of thalassemia major, thalassemia intermedia, and thalassemia minor.[2] The type of thalassemia major is beta thalassemia major (BTM) which appears early in life and requires lifelong blood transfusions and iron chelation therapy.[3] Clinical manifestations of beta thalassemia range from the silent carrier state to transfusion-dependent thalassemia major (TDTM). The silent carrier state occurs when one beta globin gene is only partially expressed (β/β+). Beta thalassemia trait results when beta globin expression is absent from one chromosome (β/β0).[4]

Received: 5 April 2024
Accepted: 4 July 2024
Published: 26 July 2024

Individuals diagnosed with BTM experience several abnormalities in various organs, as well as the reproductive system. These patients frequently have hypogonadotropic, hypogonadistic, infertile, delayed or nonexistent sexual development, as a result of iron overload and severe chelation therapy.[5] The poor survival of BTM patients past adolescence has led to a historical neglect of their reproductive and sexual health. Current developments in the early detection, care, and treatment of this illness greatly extend life expectancy and increased the chances of reproduction.[2,5]

The impact of pregnancy on the health of mothers with beta thalassemia is major in the form of preeclampsia, gestational hypertension, thrombosis, kidney failure, peripheral vascular resistance, placenta previa, pleural effusion and pulmonary hypertension.[5] Spontaneous abortion, fetal loss, prematurity birth, fetal growth restriction (FGR) and low birth rate Body weight (LBW) is the impact of pregnancy in BTM on the fetal.[5] Pregnancy does not have a negative impact on β-thalassemia major or fetal health, although many complications can occur, it is necessary to carry out careful monitoring by experienced obstetricians and hematologists.[6]

Pregnancy has oral manifestations, namely pyogenic granuloma and periodontal disease.[7,8] The clinical features are gingival hyperplastic or tooth mobility, and deposit of calculus. Hormonal changes in estrogen and progesterone levels during pregnancy greatly affect the development of gingival inflammation and periodontal disease.[8,9] Oral and facial manifestations of beta thalassemia major are skull protrusion, maxillary enlargement, and malar eminence. Expansion of the marrow cavity causes a "Chipmunk face" facial appearance, malocclusion and periodontal disease of which there is rare discussion.[10,11]

Oral manifestations in pregnant patients with β-thalassemia major are rare or unreported. Existing case reports only discuss gingival enlargement in patients with β-thalassemia and not in pregnant patients and vice versa.[9,10] This case report describes the multidisciplinary management of oral manifestations in pregnant women with beta-thalassemia major, which is crucial for successfully treating the patient's oral manifestations.

Case Report

A 27-year-old woman with beta-thalassemia major since 24 years and 16 weeks of pregnancy was referred from the Internal Medicine Department to the Oral Medicine Department with complaints of swelling, bleeding gums since early pregnancy, and bad breath. The patient was hospitalized with complaints of pain in her knee so he could not move. She was admitted to hospital with complaints of pain in her knees so she could not move and was diagnosed with Arthritis ar Genue Sinistra related to Thalassemia by an internal medicine specialist, sub division of rheumatology. General condition patient was weak, sick, and difficult to move during the approximately two weeks, when she was hospitalized. Patient has never visited a dentist, either before or now, with complaints about her oral cavity. The patient had a splenectomy in 2009. Her beta-thalassemia major was treated with routine blood transfusions once a month and iron anti- chelation drugs (deferoxamine); however, it was stopped due to pregnancy. There was no history of other systemic disease in this patient. A family history of the same disease was ruled out. History of recurrent stomatitis and drug or food allergies was ruled out.

The patient's general condition weak, with normal vital signs; however, the patient had fever. Intraoral examination revealed gingival hyperplasia; erythema; soft consistency; a dark red, rounded gingival margin; tendencies to bleed on the labial, buccal, palatal, and lingual areas; and pain. (Figure 1A–G) Oral hygiene index-simplified (OHIS) score was poor (5.7) and there were true pockets in all regions. Peripheral blood morphology result: (1) erythrocytes: polychromacy in anisochrome populations (hypochrome, normochrome), anisopoikilocytosis (ovalocytes, target); (2) leukocytes: sufficient quantity, hypersegmentation (+); (3) platelet count: numbers increase, spread out; Interpretation: moderate anemia et causa thalassemia major accompanied by signs of increased erythropoiesis activity with suspected infection. The results of blood tests at the first and last visits are shown in Table 1. The diagnosis was made based on the history, clinical features, and examination, as well as additional examinations, namely gingival enlargement accompanied by chronic periodontitis associated to pregnancy with β-thalassemia major and exfoliative cheilitis of the lips. The classification of periodontal disease in this patient is chronic periodontitis with gingival enlargement associated with pregnancy and beta-thalassemia major. The prognosis in this case was good because the patient was cooperative and followed the directions of the Oral Medicine Department. In this case, multidisciplinary therapy was a collaboration between an oral medicine specialist, a periodontist, and an internist. Dental therapy consisted of spooling with 3%

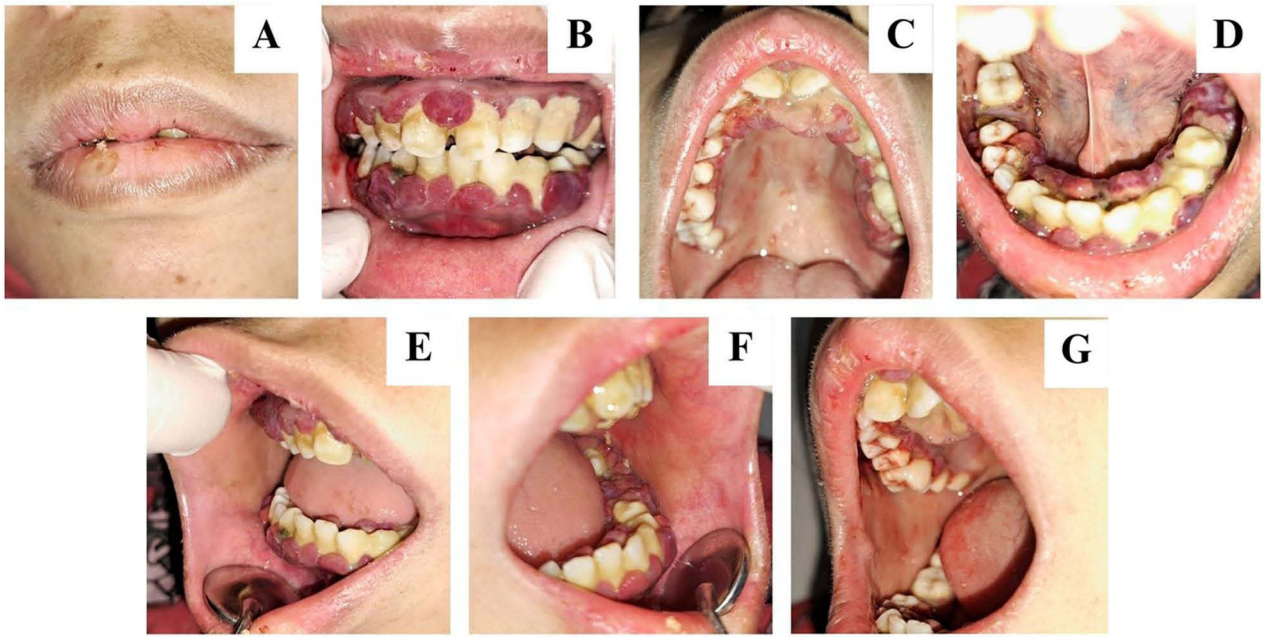

Figure 1 (**A**–**G**) Intraoral clinical feature at the first visit. The appeared gingival hyperplasia, erythema, soft consistency, a dark red, rounded gingival margin, and tendencies to bleed on the labial, buccal, palatal, and lingual regions.

hydrogen peroxide (H_2O_2) solution, chlorine dioxide spray mouthwash (Oxyfresh®, USA), antibiotics (amoxicillin 500 mg tablet, and metronidazole 300 mg tablet), and scaling/root planning. Spooling of H_2O_2 3% solution was performed at every visit; chlorine dioxide spray mouthwash was used three times a day after meals, and antibiotics were administered for seven days at third visit. Scaling and root planning were performed by the periodontist after the general condition was controlled and after the gingival hyperplasia and spontaneous bleeding improved. Blood transfusions to remove packed red cell buffy coat (PRC BCR) are also carried out routinely once a month. Non-pharmacological

Table 1 First and Last Visit Laboratory Test Results

Hematology Parameters	First Visit	Last Visit	Normal Range
Hemoglobin (Hb)	9.7 g/dl (L)	10.3 g/dL (L)	12.3–15.3 g/dL
Hematocrit (Ht)	30.2% (L)	32.0% (L)	36.0–45.0%
Erythrocytes	6.27 million/mL (H)	4.92 million/mL (N)	4.5–5.1 million/mL
MCV	74.9 fl (L)	81.2 fl (N)	80–96 fl
MCH	22.7 pg (L)	26.3pg (L)	27.5–33.2 pg
MCHC	30.3% (L)	32.2% (L)	33.4–35.5%
Leukocytes	14.11×10^3/uL (H)	5.4×10^3/uL (N)	4.4–11.3×10^3/uL
Lymphocyte	8% (L)	23% (N)	18–44%
Monocyte	10% (H)	5% (N)	2–8%
Platelets	720 ×10^3/uL (H)	514×10^3/uL (H)	150–450×10^3/uL
Serum Ferritin	3989.5 ng/mL (H)	3006.9 ng/mL (H)	15–150 ng/mL

Abbreviations: MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; L, low; N, normal; H, high.

therapy, including oral hygiene instructions, was still given to patients. Oral complaints in this case occurred due to the poor oral hygiene, β-thalassemia major, and pregnancy, were also informed to the patient as education.

This patient had eight follow-up visits, consisting of two inpatient and six outpatient visits, with the following details:

First Visit

The first visit was carried out one day after the initial inpatient visit (day +1). Intraoral bleeding still exists in the lingual-anterior part of the mandible, but bleeding in the anterior part of the maxilla has stopped (Figure 2A–F). The patient still had a fever. Medications previously provided were used accordingly. Pharmacological were continued, including spooling 3% H2O2 on all parts of the gingiva, using chlorine dioxide as a mouthwash, and applying a thin layer of petroleum jelly to the lips. A blood transfusion was carried out last night. Oral hygiene instructions are still given to patients.

Second Visit

The second visit was performed two days after the initial visit (day +2). Intraoral bleeding Follow-up visits should be conducted in outpatient settings (Figure 2G–M). Pharmacological therapy including spooling 3% H2O2 on all parts of the gingiva, using chlorine dioxide as a mouthwash, and applying a thin layer of petroleum jelly to the lips. A blood transfusion was carried out last night. Oral hygiene instructions are still given to patients.

Third Visit

Nine days after the initial visit (Day+9). First outpatient treatment. Oral symptoms appeared to improve; bad breath was greatly reduced, but the gums were still swollen (Figure 3A). The chlorine dioxide spray mouthwash was still being used and had run out. The patient could brush her teeth with a soft toothbrush but still experienced bleeding. Spooling was performed with 3% H2O2. The previous therapy was continued, antibiotics were prescribed 3x/day for seven days, and a blood transfusion was planned as a preparation for scaling the dental calculus. Oral hygiene instructions are still given to patients.

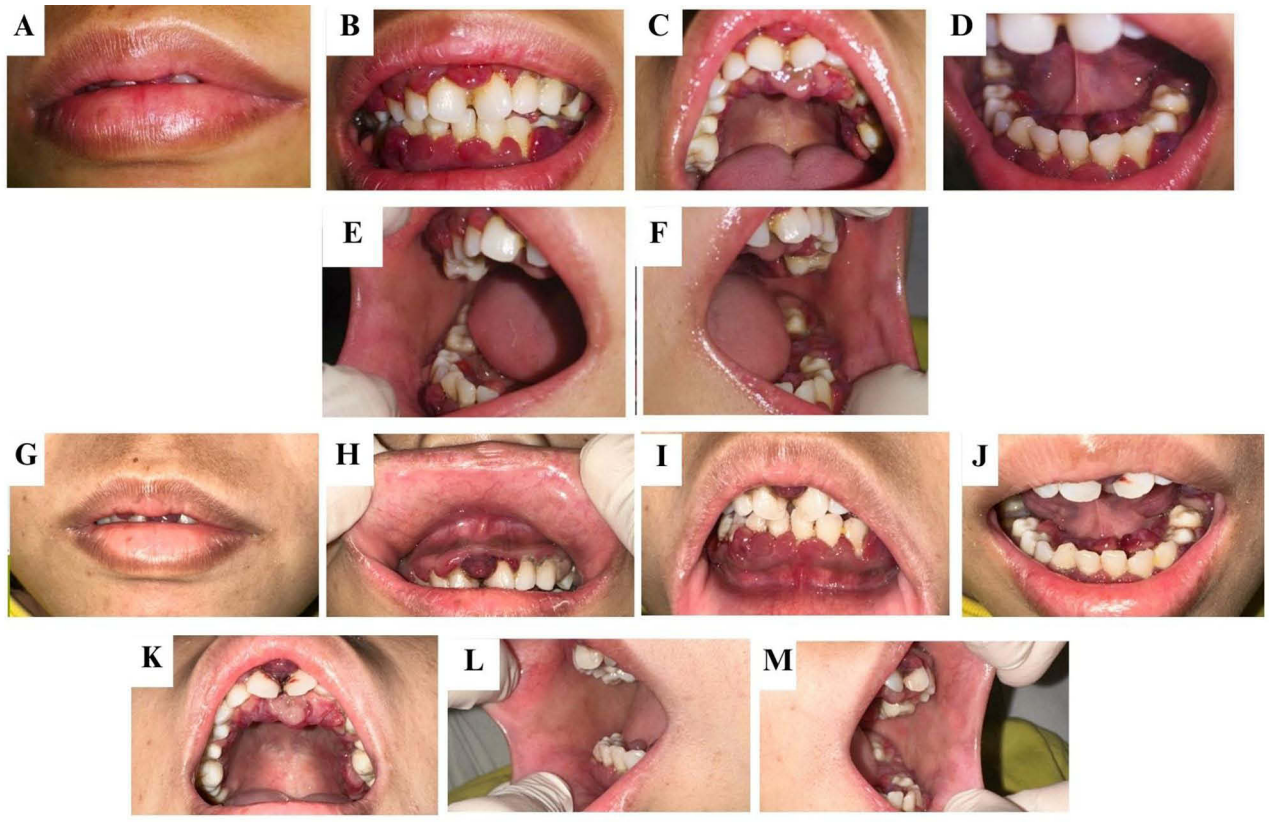

Figure 2 (**A**–**F**) The first follow-up visit. (**G**–**M**) The second follow-up visit. There has been no clinical change in the gingiva.

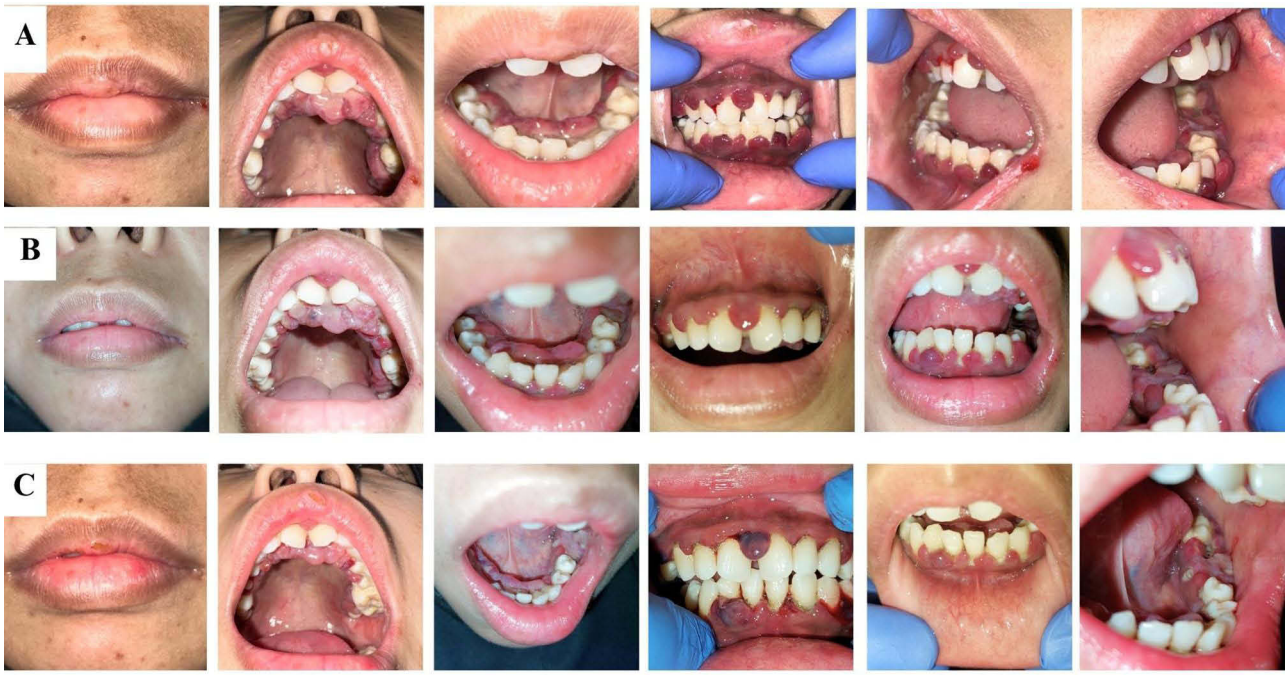

Figure 3 (**A**) The follow-up visit was nine days after the initial visit. (**B**) The follow-up visit was one month after the initial visit. (**C**) The follow-up visit was one week after the 4th visit. Gingival enlargement decreased in all regions.

Fourth Visit

One month after the first visit (Day+30). Oral complaints improved significantly, bad breath was absent, gingiva enlargement decreased, and spontaneous bleeding ceased (Figure 3B). The patient did not experience bleeding when brushing her teeth. Transfusions were performed between visits H+9 and H+30. During this visit, laboratory hematology tests and subsequent blood transfusions were performed. Antibiotics were no longer administered, 3% H_2O_2, chlorine dioxide, petroleum jelly and oral hygiene instructions were continued.

Fifth Visit

One week after the 4th visit (day +37), the oral complaints improved (Figure 3C), but pharmacological and non-pharmacological therapy continued, including spooling 3% H2O2 on all parts of the gingiva, chlorine dioxide as a mouthwash, and applying a thin layer of petroleum jelly to the lips. Oral hygiene instructions are still given to patients. Supragingival scaling was planned two weeks later or after routine transfusions were administered.

Sixth Visit

Two months after the initial visit (day +60), the oral complaints improved (Figure 4A). The gingival hyperplasia in some areas was no longer present, although in other areas still present, but they have undergone improvement. The transfusion had already been performed one week previously. Pharmacological therapy was continued, including 3% H2O2 spooling, chlorine dioxide spray mouthwash, and petroleum jelly. Non-pharmacological therapy namely oral hygiene instructions and an interdental toothbrush was suggested. Supra- and subgival scaling were performed.

Seventh Visit

Two weeks after the 6th visit (Day+74), all the complaints improved (Figure 4B). Gingival hyperplasia mostly resolved after scaling. Pharmacological includes 3% H2O2 spooling, chlorine dioxide spray mouthwash, and petroleum jelly as well as non-pharmacological therapy, consisting of oral hygiene instructions and the use of an interdental toothbrush.

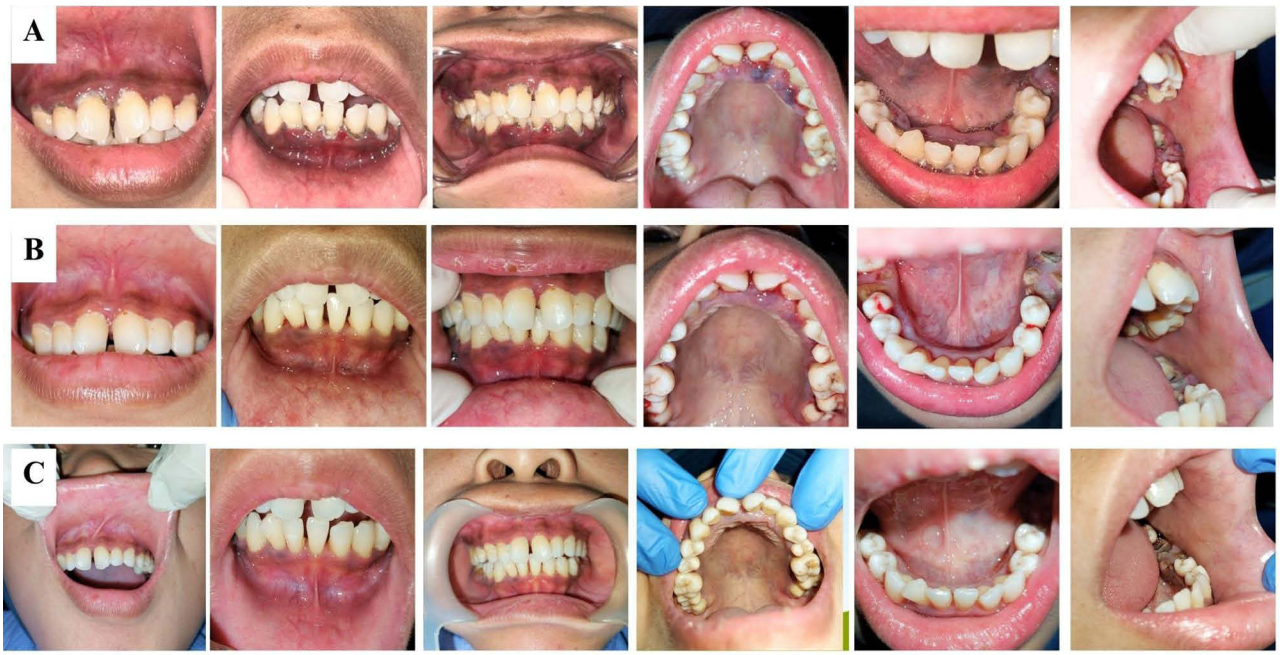

Figure 4 (**A**) The follow-up visit was two months from the initial visit. Gingival enlargement resolved in the anterior and posterior regions of the maxilla and mandible. (**B**) The follow-up visit was two weeks after the 6th visit. Gingival enlargement of all regions of the maxilla and mandible resolved, except for the palatal-anterior part of the maxilla. (**C**) The follow-up visit was three months of therapy after the initial visit, which showed significant improvement in the gingiva.

Eighth Visit

Three months after the initial visit (day +90), routine blood transfusions were performed one week before the visit. The patient is no longer presented with any oral complaints. All patients with gingival hyperplasia recovered optimally (Figure 4C). The spooling process was stopped with 3% H2O2. Supra- and subgival scaling were performed again in all maxillary and mandibular regions. Instructions for the use of an interdental toothbrush, chlorine dioxide spray mouthwash, and petroleum jelly are still provided. The summary of the collaborative management and therapy is depicted in Figure 5.

The clinical features after three months of treatment are shown in Figure 4C. The patient agreed to have her case written in a case report and published it scientifically while maintaining confidentiality. The patient has approved and written informed consent for the case details to be published included publication of the image, and the institution has also approved for publication. This case had complied with the Declaration of Helsinki.

Discussion

The patient had low Hb and Ht levels and elevated erythrocyte, leukocyte, and serum-ferritin levels. Serum ferritin levels were high because the anti-chelation drugs were not consumed, as iron was dispersed into the endothelial reticulum, stimulating the release and synthesis of ferritin into the circulation. According to Fadel et al, causes the patient to experience a high risk of infection, including gingival inflammation and periodontal disease.[11–13] Ferritin is used by the bacterium *Porphyromonas gingivalis* to increase the virulence of periodontal disease and thrives because of changes in salivary components, especially lysozyme and salivary immunoglobulin A (sIgA). This interferes with the binding of oxygen by the salivary glands and causes damage to them. Bacteria accumulation and increase of ferritin levels has resulted in an increase in pro-inflammatory cytokines (IL1, IL6, and IL8) and the periodontal tissue will be more susceptible to infection and inflammation.[14] The morphological peripheral blood result interpretation showed anemia with increased erythropoiesis activity due to a suspected infection. Infection may associate with gingival hyperplasia, which is an oral manifestation of beta thalassemia.

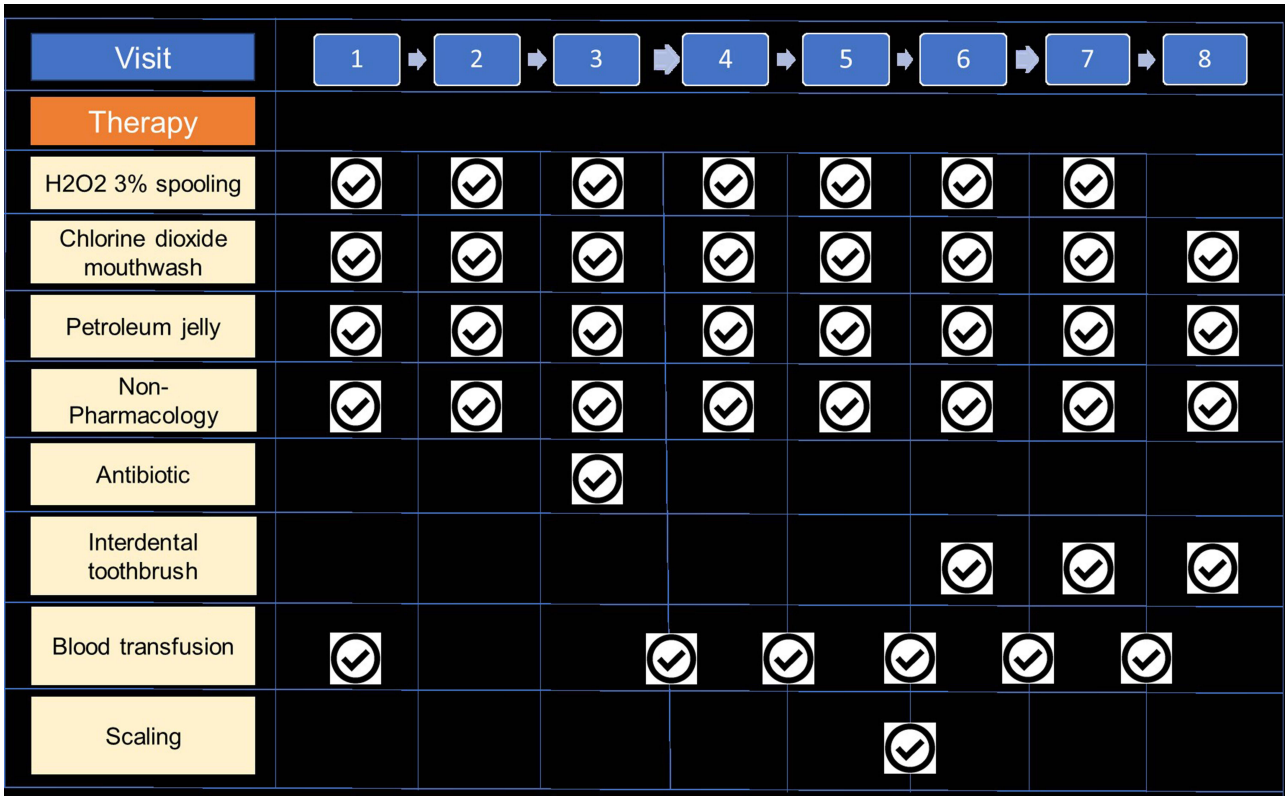

Figure 5 Summary of the multidisciplinary management.

The oral manifestation of pregnancy, mild chronic gingival hyperplasia, is an inflammatory response to local irritant factors and is influenced by pregnancy hormones. This condition begins with inflammation of the papilla and spreads to the gingival margins. It is bluish or dark red, has a brittle, soft consistency, has a smooth, shiny surface, and tends to bleed.[9] The oral condition in this patient was affected by multifactorial, included: stopping anti-chelation drugs, hormonal changes during pregnancy, and local irritating factors of the oral cavity (bad oral hygiene).

A solution of 3% H_2O_2 was used for spooling therapy and was useful for decreasing the number of bacteria in the gingival pockets. Gingival bleeding and inflammation can be controlled, and the gingival attachment can be improved. H_2O_2 exhibits broad antimicrobial properties (against bacteria, viruses, and fungi). The oxidative properties of the 3% H2O2 solution can kill pathogenic bacteria, reduce inflammatory exudates, increase gingival attachment, and promote periodontal tissue repair. This solution is expected to reach the subgingival areas that are difficult to handle with patient self-cleaning and can only be performed in the hospital.[15,15] The use of 3% H_2O_2 is safe for pregnant women because it is used for topical use in this case.[16]

Another mouthwash, chlorine dioxide, was administered to the patient so that she could use it independently. Chlorine dioxide spray mouthwash is an antimicrobial (bacterial, viral, and fungal) used to treat halitosis. It is a water-soluble, odorless, analgesic antibiotic for gram-negative bacteria that penetrates the biofilm layer.[15,17,18] This mouthwash is effective in small concentrations and is not toxic even if the concentration is increased.[17]

The patient was also administered petroleum jelly to moisturize dry lips. Petroleum jelly or petrolatum is a mixture of mineral oil, paraffin, and microcrystalline wax, which melts and seeps into the skin, into the spaces between cells and gaps in lipids, and then refreezes and settles inside.[19,20] This moisturizer is often used to prevent skin infections after outpatient surgery and as a maintenance therapy for atopic dermatitis. The function of petroleum jelly is to help protect the outer skin from the effects of weather and exposure to sunlight, as well as help to protect the inner skin by preventing natural water loss from the skin.[19] Petrolatum administration also induces the expression of filaggrin and loricrin which

play a role in increasing the thickness of the stratum corneum and reducing T-cell infiltrates in inflammatory conditions. Petrolatum potentially modulates antimicrobial properties and acts as a barrier to epidermal differentiation.[20]

This patient was administered antibiotics as an additional therapy to decrease the number of bacteria and support the improvement of inflammation and periodontal pockets. In addition, antibiotics are generally administered to patients with periodontal disease to prevent secondary infections.[10,21]

Scaling and root planning are non-surgical periodontal therapies that can be performed in patients with controlled beta-thalassemia to remove local irritant factors (plaque, debris, and calculus). These procedures accelerate tissue repair and significantly improve the gingival conditions.[21,22] This case is in line with the results of the research reported by Hanif et al in 2022, which stated that supra- and subgingival scaling in patients with beta-thalassemia will help produce significant improvements in gum condition, even in patients without antibiotics.[23] The oral cavity problems were resolved optimally and the patient was satisfied. About 2 months later, the patient gave birth to a healthy child. A limitation of this case report is that it was limited to only one patient. However, it can still become a source of scientific information for dental practitioners conducting multidisciplinary, comprehensive management of patients with beta-thalassemia major and pregnancy.

Conclusion

Multidisciplinary, collaborative dental and medical management with non-surgical therapy of oral manifestations in pregnant women with beta-thalassemia major shows satisfactory results.

Acknowledgments

The authors would like to thank Universitas Padjadjaran for the article processing charge (APC) funding provided for the publication of this article. We would also like to thank the Department of Internal Medicine and Department of Dental and Oral Health, Hasan Sadikin Hospital Bandung, Indonesia, for their collaboration in providing therapy to the patient.

Disclosure

The authors state no conflicts of interest in this work.

References

1. Lee JS, Cho SI, Park SS, Seong MW. Molecular basis and diagnosis of thalassemia. *Blood Res*. 2021;56(April):39–43. doi:10.5045/br.2021.2020332
2. Viprakasit V. Clinical Classification, Screening and Diagnosis for Thalassemia. *Hematol Oncol Clin N Am*. 2018;32:193–211. doi:10.1016/j.hoc.2017.11.006
3. Anurogo D, Budi NYP, Ngo MHT, Huang YH, Pawitan JA. Cell and gene therapy for anemia: hematopoietic stem cells and gene editing. *Int J Mol Sci*. 2021;22(12):1–28. doi:10.3390/ijms22126275
4. Lawrence C, Riehm E. *Biochemical and Molecular Basis of Pediatric Disease. In: Biochemical and Molecular Basis of Pediatric Disease*. Elsevier Inc; 2021:529–560. doi:10.1016/c2018-0-01599-6
5. Nourollahpour SM, Cassinerio E, Modarres M, Zareiyan A, Hamzehgardeshi Z, Behboodi Moghadam Z. Reproductive health issues in female patients with beta-thalassaemia major: a narrative literature review. *J Obstet Gynaecol*. 2020;40(7):902–911.279. doi:10.1080/01443615.2019.1692802
6. Gulino F, Vitale S, Fauzia M, Cianci S, Pafumi C, Palumbo M. Beta-Thalassemia major and pregnancy. *Bratisl Lek List*. 2013;114(September):1–4. doi:10.4149/BLL
7. Hidayat W, Mustika I, Pribadi S, Zakiawati D, Agustina A. Profile of oral manifestations, oral hygiene, and nutritional status in pregnant women. *Padjadjaran J Dent*. 2019;31(I):215–219. doi:10.24198/pjd.vol31no3.23792
8. Figueiredo C, Rosalem C, Cantanhede A, Thomaz E, Cruz M. Systemic alterations and their oral manifestations in pregnant women. *Japan Soc Obstet Gynecol*. 2017;43(1):16–22. doi:10.1111/jog.13150
9. Chauhan SS, Pandey A, Raj A, Raj A, Nigam S. A classical case of pregnancy induced gingival enlargement: a case report. *J Evol Med Dent Sci*. 2014;3(45):11104–11108. doi:10.14260/jemds/2014/3449
10. Baiju C, Gupta G, Karuna J, Shagufta GUPTAN, Gupta ND. Gingival enlargement in thalassemia patient–A Conjectural Association. *Univ J Dent Sci*. 2020;6(3):74–77. doi:10.21276/ujds.2020.6.3.15
11. Akcalı A, Kahraman Çeneli S, Gümüş P, Buduneli N, Lappin DF, Özçaka Ö. The association between thalassemia major and periodontal health. *J Periodontol*. 2015;86(9):1047–1057. doi:10.1902/jop.2015.140639
12. Nabi AT, Muttu J, Chhaparwal A, et al. Implications of β-thalassemia on oral health status in patients: a cross-sectional study Aaysha. *J Fam Med Prim Care*. 2017;6(2):169–170. doi:10.4103/jfmpc.jfmpc
13. Muhammad W, Ishaq M, Khan MJ, Ahmad U, Waseem M. Iron chelation therapy needed for serum ferritin overloaded patients of beta thalassemia major. *Thalass Reports*. 2021;11(1):9779. doi:10.4081/thal.2021.9779

14. Nuraini P, Wahluyo S, Pradopo S, et al. Effects of Iron accumulation on dental caries, gingivitis, and candida albicans infection in children with beta thalassemia major: a narrative review. *Acta Med Philipp*. 2022;(47). doi:10.47895/amp.vi0.3994
15. Sahebjam Atabaki M, Moradi Haghgoo J, Khoshhal M, Arabi R, Khodadoostan A, Gholami L. Clinical effect of periodontal pocket irrigation with H2O2. *Avicenna J Dent Res*. 2011;3(1):55–61.
16. Food and Drug Administration. *Pharmacology/Toxicology Supervisory Memorandum*. Food and Drug Administration. 1–31. 2017.
17. Tsubura S, Uchiyama K, Yamada M, et al. The effect of mouth rinsing with stabilized chlorine dioxide on periodontitis. *Oral Surgery Oral Med Oral Radiol*. 2015;3(1):20–24. doi:10.12691/oral-3-1-5
18. Kerémi B, Márta K, Farkas K, et al. Effects of chlorine dioxide on oral hygiene – a systematic review and meta-analysis. *Curr Pharm Des*. 2020;26 (25):3015–3025. doi:10.2174/1381612826666200515134450
19. Kamrani P, Hedrick J, Marks JG, Zaenglein AL. Petroleum jelly: a comprehensive review of its history, uses, and safety. *J Am Acad Dermatol*. 2023;1–7:325. doi:10.1016/j.jaad.2023.06.010
20. Czarnowicki T, Malajian D, Khattri S, et al. Petrolatum: barrier repair and antimicrobial responses underlying this "inert" moisturizer. *J Allergy Clin Immunol*. 2016;137(4):1091–1102.e7. doi:10.1016/j.jaci.2015.08.013
21. Hammami C, Nasri W. Antibiotics in the treatment of periodontitis: a systematic review of the literature. *Int J Dent*. 2021;2021:1–8. doi:10.1155/2021/6846074
22. Akcalı A, Yıldız MS, Akcalı Z, Huck O, Friedmann A. Periodontal condition of patients with Thalassemia Major: a systematic review and meta-analysis. *Arch Oral Biol*. 2019;102:113–121. doi:10.1016/j.archoralbio.2019.04.004
23. Hanif A, Quraeshi S, Qidwai A, et al. Effect of non-surgical periodontal therapy on the clinical periodontal inflammatory parameters in β-thalassemia major (TM-β) patients with 336 gingivitis. *J Pharm Res Int*. 2022;19–27. doi:10.9734/jpri/2022/v34i42a36291