

Oral Manifestations of Hemolytic Anemia: A Case Report

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Abstract

Hemolytic anemia is a condition when there is a decreased number of erythrocyte in the circulation due to premature destruction. Mucosal pallor, jaundice, and paresthesia may appear as the oral manifestations of hemolytic anemia.

Case presentation: A 48-year-old man came to oral medicine clinic with complaint of discomfort and spontaneous bleeding from a bump on the left of his tongue. Bruises were noticed on arms and legs. Intraoral examinations showed pallor of the palatal and gingival mucosa, red black colored blood clot with spontaneous bleeding seen on the left lateral of his tongue and on the buccal mucosa. Complete blood count examination revealed blood disorders. Patient then was referred to the Internal Medicine Department who diagnosed him to have the warm type autoimmune hemolytic anemia with immune-mediated thrombocytopenia. Management of patient's systemic condition by Internal Medicine Department had given a significant progress of general health and oral manifestations

Conclusion: Dentist might be the first health professional who recognize oral conditions that usually reflect the early signs of systemic conditions. It is important for dentists to perform a complete examination to establish diagnosis and proper comprehensive treatment planning.

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Introduction

Red blood cells (RBCs) or erythrocytes by its involvement of hemoglobin perform the most vital function in tissue oxygenation of the human body. Adequate number of RBCs in a healthy person is about four to six million cells per millimeter cubic. Condition when there is a decreasing number of RBCs or an abnormality in hemoglobin is known as anemia. Dilatory of its detection may increase the risk of morbidity and mortality because anemia often occurs as an underlying condition that requires attention and medical treatment. The causes of anemia can be acquired and hereditary. Acquired anemia happens in iron deficiencies anemia, acquired

hemolytic anemia, acute blood loss, etc. While hereditary anemia happens in thalassemia, hemoglobinopathies and hereditary hemolytic anemias.¹

Hemolytic anemia is defined as an increased destruction of erythrocytes from the circulation before their normal life span of 120 days. The etiologies of hemolysis are categorized as acquired or hereditary. Acquired causes of hemolytic anemia include autoimmunity, microangiopathy, and infection.² Several signs and symptoms might appear in hemolytic anemia such as pallor in the nail bed and palpebral conjunctivitis. While pallor and jaundice of oral mucosa might be seen at the soft palate, tongue and sublingual tissue.³

Autoimmune hemolytic anemia (AIHA) occurs due to the presence of anti-erythrocyte autoantibodies and can be classified as either autoimmune, alloimmune and drug-induced, depending on the antigen that stimulates antibody of erythrocytes.² The overall incidence is being 1 in 80,000 to 100,000 of a given population/year in the Caucasians. Prevalence in

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Indonesia is still unknown. AIHA can affect infants but more than 70% of new cases are seen annually in patients above 40 years of age. The peak incidence being between 60 and 70 years of age and the frequency of the disorder is usually more in females than in males. The male to female ratio is 40:60.⁴

Large number of immunological and lymphoproliferative disorders can be associated with AIHA. Examples of immunological disorders that can be associated with are immune thrombocytopenia, systemic lupus erythematosus, rheumatoid arthritis, Sjögren's syndrome, primary biliary cirrhosis, hypothyroidism, inflammatory bowel disease, and primary hypogammaglobulinemia. Some patients have several associated diseases at the same time.⁴

Here we discuss a case of autoimmune hemolytic anemia with severe immune-mediated thrombocytopenia when its oral manifestations were becoming the major complaint. In this case, dentist was the first health professional who recognized the suspicious hematologic disorders.

Case Presentation

A 48-year-old male patient came to the Oral Medicine Division with a chief complaint of a spontaneous bleeding bump on his left lateral tongue for the last two weeks. The bump was painless, itchy, and small when first noticed and then increased in size. Other complaints that motivated him to seek for a more careful oral examination were extremely bad oral odor, difficulty when swallow and no improvement over the bump after having the previous prescribed mouthwash by physician. He had history of recurrent ulcerations mostly on the edges of tongue from chewing activity, but never lasts for more than one week. Long before the bump appeared, comfort mastication most often done in the right side. He also experienced fatigue, prolonged bleeding when wounded and had some bruises on his arms and legs which noticed after the tongue bump appeared. History of smoking one pack cigarettes per day, allergy of mint and full remission from tuberculosis in childhood was noted.

Extra oral examination showed no sign of lymphadenopathy. There were various sizes of purpuric lesions appeared on the perioral skin area. Pigmentations on the upper and lower lips were noticeable. Purpuric lesions also appeared

on his arms and legs one week after the presence of the hemorrhagic clots on tongue (Figure 1).

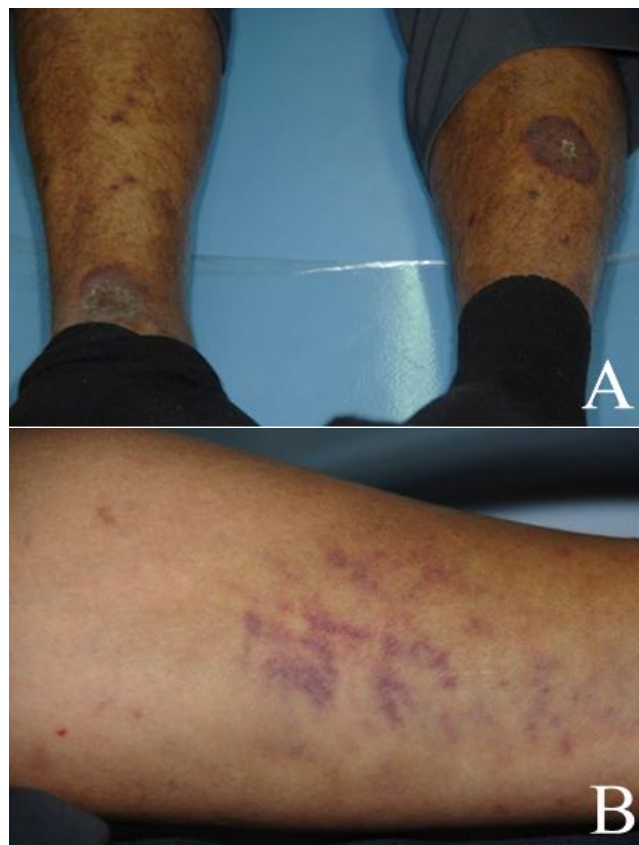


Figure 1. (A-B) Purpura on legs and arms.

Intraoral examination revealed the presence of multiple isolated hemorrhagic clots with variety of size. The largest hemorrhagic clot was seen on left lateral surface of the tongue. Overlying surface was rough and tender, the clot was isolated, no in duration, painless, red-black in color, size about 20 millimeters in diameter and profuse bleeding occurred on slight palpation. Similar kind of lesions present on the right side of lateral tongue and right posterior buccal mucosa but in smaller sizes (Figure 2). Gingiva was pale and blood clots seen at most area of the marginal gingiva. Extreme bad oral odor and mucosal pallor were recognized. Gingival inflammation resulted as plenty of subgingival and supragingival calculus found mainly on the left maxillary molars with presence of stain and debris on some surface areas of teeth. Poor oral hygiene could be concluded. History of tongue bite caused by sharp edges of necrosis left mandibular first molar and radix of right mandibular first molar was also noted.



Figure 2. (A-C) Hemorrhagic plaque on the lateral borders of the tongue and buccal mucosa.

From the chief complain, extra and intra oral examinations, the patient was suspected to have systemic condition related to blood disorder that manifested in the oral cavity. Patient then was referred to have laboratory examination for complete blood count and the blood glucose level. At this visit, patient and his family were given

explanations about possible factors causing his oral complaints and the need of further investigation by having laboratory examination. Meanwhile, no dental treatment could be performed on the patient. He was prescribed multivitamin containing Vitamin C, B1, B2, B6, B12, Zinc, and povidone iodine antiseptic mouthwash.

Complete blood count examination performed on the day after the first dental visit, the result showed an extremely low level of thrombocytes (6000/ μ L), decreased hemoglobin level (8.7g/dL), low level of erythrocytes (3.26 million/ μ L), high level of leukocytes (11900/ μ L), and a high glucose level (265mg/dL). Suspect of hematological disorder was considered. Patient then was referred to Internal Medicine Department.

On the next day before attending to Internal Medicine Department, he was delivered to emergency room because of worsen fatigue, diarrhea and bleeding. Emergency procedure spontaneously underwent the advance blood examinations. He was then hospitalized and had treatment with transfusions of packed red cells and thrombocytes. Basic on the result of hematological examinations, working diagnosis of warm type autoimmune hemolytic anemia with severe immune-mediated thrombocytopenia finally determined by Internal Medicine Department. In the first week hospitalization, treatment with intravenous 500mg tranexamic acid solutions and tablets of 10mg vitamin K were given for three times a day, followed with transfusion of platelet set units and intravenous 10mg/ml diphenhydramine solutions. Povidone iodine antiseptic mouthwash was continued for oral lesion management. A few days after hospitalized, medication using intravenous diphenhydramine solution was replaced with 10mg azathioprine tablets to be taken per oral for three times a day which then continued after he left the hospital, and intravenous 125mg methylprednisolone was given continuously once a day. This combination of treatments had given a good improvement either to the patient systemic condition and its oral manifestations.

The hemorrhagic isolated clot on tongue was completely disappear along with his better general condition, but invasive dental treatment was still not recommended by the Internal Medicine Department to be done. After three weeks hospitalization, thrombocytes level

increased to 70000/ μ L, hemoglobin was still low but increased to 10.5g/dL, while leukocytes level was still high (19024/ μ L). As prophylaxis treatment, patient was prescribed with 10mg vitamin K tablets, 50mg azathioprine tablets and 16mg methylprednisolone tablets, each drug was prescribed to be taken for three times a day. Patient was advised to have a routine visit to Internal Medicine Department once in a month for tapering down steroid dose treatment.

Discussion

Hematologic disorders in the form of both anemic and platelet disorders literally have manifestations in the oral cavity and orofacial region. Pallor of oral mucosal tissues often shows in all forms of anemia but may be difficult to appreciate.⁵ Persons with anemia may suffer from fatigue, breathless and loss of stamina. In this case, patient admitted that he experienced fatigue and loss of stamina but tends to ignore the signs because he practically had no significant difficulty in doing daily activities. Major complaint started when hemorrhagic plaques formed on his tongue which then gradually increased in sizes, followed with bad oral odor and difficulty when swallowing solid food. Patient also described the lesion as a 'fast growing bumps' because of its progression in short period of time. From intraoral examination mucosal pallor was obviously noticeable. Establishment of diagnosis was quite challenging as the clinical signs and symptoms might also be found in persons with the life threatening hematologic disorders such as leukemia.⁶⁻⁹ Similar hemorrhagic tongue lesions previously have been reported to occur in persons with very low thrombocyte counts.^{10,11} A careful anamnesis include history of recurrent ulcers on particular sites of the oral cavity then pursued suspicion into traumatic ulcer which initiated the formation of hemorrhagic plaques induced by hematologic disorders.

Anamnesis and oral examinations revealed the possibility of hematologic disorder that has manifestation in the oral cavity. This suspicion was also supported by the finding of purpuric lesions on the patient's extremities. Complete blood count screening examination was a necessary to identify the suspected systemic disease,¹² and the result showed marking of thrombocytopenia, anemia and

leukocytosis, that confirm the tendency of hematologic disorder. Further investigation done by Internal Medicine Department finally determined the diagnosis of autoimmune hemolytic anemia with severe immune thrombocytopenia.

Presentation of purpuric lesions on arms and legs as well as the hemorrhagic clots of the tongue may resulted from failure in forming plugs during hemostasis mechanism regarding to a reduction in thrombocyte number or function which is known in the term of thrombocytopenia. Thrombocytopenia defines when there are a decreased number of thrombocytes in the circulation. Normal amount of thrombocyte is 150.000 to 450.000/mm.³Thrombocytopenia might impact patient management and clinical outcome by the low platelet count, abnormal hemostasis and platelet dysfunction.¹³

The major concern on the first dental visit was giving information about the relationship between suspected systemic condition and the patient's oral complaints, following explanations about the importance of improving oral hygiene and how to prevent further trauma that could aggravate his oral soft tissue condition. He also given information that minor trauma to the oral mucosa during routine activities such as chewing, swallowing and tooth brushing may produce various types of hemorrhagic lesions, including ptechieae, purpura, ecchymosis, hemorrhagic bullae, and hematoma formation.⁵

By concerning its possible risk for the patient's health, no dental invasive treatment was done to eliminate patient's focus of infections which consisted of calculus removal and tooth extractions. Patient was advised to use antiseptic mouthwash instead of tooth brushing in order to prevent more gingival bleeding and to improve his oral hygiene.⁵ Antiseptic mouthwash containing povidone iodine was selected for its function against many different microorganisms include virus.^{14,15}

As the supportive therapy for his systemic conditions, multivitamin containing of Vitamin E, Vitamin C, B1, B2, B6, B12, pantothenic acid and zinc was prescribed to be taken once daily. Vitamin C improves neutrophil function and acts as an antioxidant as well as vitamin E. Vitamin B1 (thiamine) and B2 involved in energy metabolism reactions, while Vitamin B6 (pyridoxine) is involved in carbohydrate, fat, and protein metabolism, as well as other key

reactions such as converting tryptophan to niacin, heme biosynthesis, and neurotransmitter synthesis. Vitamin B5 (pantothenic acid) precursors of CoA protect cells and whole organs against peroxidative damage by increasing the content of cell glutathione. Multivitamin contains zinc was selected because zinc play a role in many body homeostatic mechanisms, including immune efficiency, enhances taste and appetite owing to its function to prevent changes in the epithelium of the tongue. Functions from these vitamins and mineral contribute in wound healing processes.¹⁶⁻¹⁸

Oral lesions may appear formerly as the monosymptom of hematological disorders manifestation. Dental professionals may have only limited time to overcome the risk of hematological disorders especially the life threatening ones. As the early diagnosis is highly important in this case, it becomes necessary for dentist to have full knowledge about systemic conditions and its sequence of management. The early detection may beneficial for health providers who work in a good collaboration to save patient's life.

Conclusions

Manifestations from the wide array of hematological disorders encountered in the internal medicine often appear in the oral cavity. Dentist might be the first health professional who recognize oral conditions that usually reflect the early signs of the systemic conditions. Performance of a complete history taking and thorough examination to establish diagnosis, along with proper comprehensive treatment planning becomes crucial as conditions resulted from systemic disorders can be a life threatening event.

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Declaration of Interest

The authors report no conflict of interest.

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