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Angular Cheilitis with Anemia as A Predisposing Factor: A Case Report

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Abstract

introduction: Angular cheilitis is a lesion in the corner of the lips caused by many factors, including nutritional deficiencies and systemic diseases. Angular cheilitis can be caused not only by trauma but also by systemic conditions such as anemia. The treatment of angular cheilitis depends on its causes.
Purpose: The treatment of angular cheilitis depends on its causes. *Purpose*: This article aims to describe angular cheilitis lesions and therapy.
Case report: A 17-year-old female patient came to Rumah Sakit Gigi dan Mulut (RSGM) Soelastri, Faculty of Dentistry, Universitas Muhammadiyah Surakarta, complaining of pain in the corners of her lips. The complaints were felt approximately one month ago. Lately, she often underwent dental treatments that made her open her mouth widely for too long. The patient has no habit of licking the corners of her lips but rarely eats vegetables and fruits. The patient often feels stressed due to heavy college burdens. An intraoral examination showed ulcerated lesions in the form of fissures with a reddish color located at the right and left (bilateral) corners of the lips, soft in consistency, and painful. The patient underwent a complete blood test and found that the MCV, MCH, and MCHC values decreased. The diagnosis of this case is angular cheilitis which is triggered by trauma and is predisposed by hypochromic microcytic anemia and stress.
conclusion: angular cheilitis can be treated by administering topical corticosteroid medications to reduce inflammation and educating the patient to eliminate predisposing factors, such as increasing iron intake and managing stress. The lesion completely healed after two weeks post-examination.

Introduction Section

The oral cavity is one of the essential organs for humans. This organ is a functional unit consisting of teeth, tongue, cheeks, gingiva, and saliva that are interdependent in carrying out their functions, namely mastication, speaking, and aesthetics (Setiadhi & Wihardja, 2019). The oral cavity is composed of soft tissues and hard tissues. The soft tissues in the oral cavity are labial mucosa, buccal mucosa, palate, gingiva, frenulum, and tongue (Setiadhi & Wihardja, 2019), while the hard tissues are teeth consisting of enamel, dentin, and cementum (Nasution, 2016) and alveolar bones (Nurniza et al., 2021).

The health of the oral cavity is significant to maintain so that its function can run properly. The soft tissues in the oral cavity line the entire surface of the bone and form walls that play a role in *defense*, mastication, swallowing, and speech (Hamdani et al., 2022). The condition of the soft tissues of the oral cavity is closely related to the systemic condition of the body. The oral cavity can display manifestations of systemic conditions and be an indicator of the body's overall health (Wight, 2017). These systemic conditions include autoimmune diseases, hematology, endocrine, or neoplastic changes. In addition, certain medications can also have an impact on the condition of the oral cavity (Kane, 2017).

Changes in systemic conditions can affect changes in the integrity of soft tissues in the oral cavity, one of which is characterized by the appearance of lesions such as angular cheilitis (Marinna & Yusri, 2022; Nurniza et al., 2021; Urse, 2014). Angular cheilitis is a lesion of the corners of the lips caused by many factors, including nutritional deficiencies and systemic diseases (Fajriani, 2017; Pandarathodiyil et al., 2021). Nutritional deficiencies, especially red blood cell-forming components such as vitamin B12, iron, and folic acid, can inhibit the regeneration process of epithelial cells of the oral cavity and increase the risk of ulceration. All systemic

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conditions that cause a decrease in the immune system (immunosuppressants) are at risk of causing lesions in the oral cavity (Díaz Rodríguez et al., 2022). Stressful conditions are also reported to lower a person's immunity and increase susceptibility to infection (Larasati, 2016; Mayasari & Pratiwi, 2009), including on the oral mucosa.

Case Report

The female patient, aged 17 years old, came to the Soelastri Dental and Oral Hospital (RSGM), Faculty of Dentistry, Muhammadiyah University of Surakarta. After screening which shows that the patient has no symptoms of fever, cold, or cough and has normal vital signs, the patient was then examined by the dentist. The patient complained of pain in the corners of the right and left lips. The complaint was felt by the patient approximately one month ago. She said that recently she often underwent dental treatment, which made her open her mouth widely for too long. The patient said the corners of her lips are sore, dry, and chapped. Complaints get worse when the patient eats hot and spicy food and feels more comfortable when eating cold food. The patient has never treated such complaints before. The patient claimed not to have any allergies to any drugs, food, or weather.

The anamnesis results also showed that the patient usually brushed her teeth twice daily after breakfast and before bed. The patient was not changing their toothpaste products to new brands and did not change her lip or face products with a new brand. The patient likes to eat sweet foods and chew ice cubes. The patient did not have the habit of licking the corners of her lips, but she admitted that she rarely ate vegetables and fruits and did not consume any vitamins or supplements. The patient explained that recently she often feels stressed and depressed due to the heavy college burden.

In the intraoral examination, it is found that there are ulcerated lesions in the form of fissures with a reddish color accompanied by peeling skin around them. These lesions located in the right and left (bilateral) corners of the lips are soft in consistency and also painful. The patient does not use dentures or orthodontic appliances, and no teeth are restored with certain materials. The clinical condition of the lesion can be seen in Figure 1.

Figure 1 clinical appearance of angular cheilitis lesions in the patient

Supporting examinations

In this case, the patient has carried out a supporting examination, *a complete blood count (CBC*), to determine the presence of systemic hematological factors against the appearance of angular cheilitis lesions in the oral cavity. This examination was chosen because the results of the patient's anamnesis and intraoral examination did not show any etiology, such as allergies, the use of orthodontic appliances, or a decrease in vertical dimensions. So a complete blood test was chosen to determine the presence of hematological factors that might

play a role in the appearance of angular cheilitis lesions suffered by the patient. The results of the patient's complete blood count can be seen in Table 1 below:

Table1. Results of the patient's complete blood test

Examination	Result	Reference Value	Unit
HAEMATOLOGY			
1. ROUTINE BLOOD			
WBC	6.7	4.0 – 10.0	$10^3/mm^3$
RBC	4.8	3.8 – 5.8	$10^6/mm^3$
Hb	8.4*	11.0 – 16.0	g/dl
Hct	28.6*	35 – 50	%
Plt	450	150 – 450	$10^3/mm^3$
MCV	57*	80 – 97	μm^3
MCH	15*	26.5 – 33.5	Pg
MCHC	26*	31 – 35	g/dl
RDW	16*	10 – 15	%
Lym	34	17 – 48	%
Mxd	5	4 – 11	%
Neu	61	43 – 76	%

The results of the patient's complete blood examination above show that the patient's hemoglobin (Hb) level is below normal values. This indicates that the patient has anemia. Anemia is a condition where the amount of hemoglobin is less than average and is usually influenced by age, sex, and geographical location (Henrika et al., 2018). Hemoglobin is a complex molecule in red blood cells that transports oxygen from the lungs to all body tissues (Marinna & Yusri, 2022). This oxygen will be used by all cells in the body to live and carry out their functions. If Hb levels decrease, as in anemic conditions, tissue oxygenation will decrease and reduce mucosal resistance, so it is prone to damage.

Another indicator is the MCV (Mean Corpuscular Volume*)* of the patient below the normal limit, which means there is a microcytic anemia condition. The MCH (Mean Corpuscular Hemoglobin) and MCHC (Mean Corpuscular Hemoglobin Concentration) values are also below the normal limit indicating the patient has hypochromic anemia. Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), and Mean Corpuscular Hemoglobin Concentration (MCHC) are indicators of the blood test results first introduced by Wintrobe in 1929 (GREEN, 1950)(GREEN, 1950). These three indicators are of great importance in determining the etiology of the anemia suffered by the patient. MCV is an indicator that shows the size or volume of red blood cells (erythrocytes).

A low MCV value in anemic patients means an iron deficiency called microcytic anemia. In contrast, an increase in MCV value means that there is a deficiency of vitamin B12 or folic acid, which is also called macrocytic anemia. MCH values indicate each red blood cell's average hemoglobin (Hb) weight. The high and low MCH will affect the color quantity of red blood cells, referred to as normochromic if the value is normal, hypochromic if the value is low, and hyperchromic if the value is too high. MCHC is an indicator to measure the average hemoglobin concentration in each red blood cell. A decrease in MCHC values means that there are iron deficiency conditions, microcytic anemia, and hypochromic anemia, while an increase in MCHC indicates the possibility of spherocytosis or hemolytic anemia due to molecular defects (Erwana, 2022; Sari & Ismail, 2016).

Case management

This subjective, objective, and supporting examinations conclude that the patient has angular cheilitis triggered by trauma and is predisposed by hypochromic microcytic anemia due to iron and vitamin B12 deficiency. This conclusion is in line with (Echarisma et al., 2021) that nutritional deficiencies can make patients susceptible to infection, where an infection that often occurs in the oral cavity is angular cheilitis.

The case management of angular cheilitis can be given topical corticosteroid medication to be applied to the lesions as anti-inflammatory, immunosuppressive, and mechanical protection, or mouthwash containing analgesics such as benzidamine to reduce pain (Marinna & Yusri, 2022). In this case, the patient refuses

medication, so case management emphasizes more on education. The patient was educated to increase the consumption of iron (Fe) sources such as vegetables, fruit, nuts, meat, or fish. It aims to increase the intake of iron which plays a role in erythropoiesis or the formation of red blood cells (Hidayati et al., 2017; Mardhani & Widiyaningsih, 2022) and increase the regeneration of epithelial cells as *a barrier*, including in the oral mucosa. The patient was also educated to relax and regulate stress because stress can lower cellular immunity and increase susceptibility to microbial infections (Mayasari & Pratiwi, 2009).

The patient was recalled approximately two weeks later. She said the pain had disappeared, and the corners of the lips were no longer rough and chapped. The patient admitted that she had increased vegetable consumption over the past two weeks. On intraoral examination, it was seen that the lesion had healed completely, and there were no signs of inflammation.

Discussion

Definition and description of the lesion

Angular cheilitis is an inflammatory lesion in the corner of the lips, precisely on the border of the muco-cutaneus, and can extend to the skin around the mouth (Pandarathodiyil et al., 2021) According to Soeprapto, (2017), angular cheilitis is a loss *of integrity* lesion, which is an ulcer. An ulcer is a lesion that histologically appears as the loss of the epithelial layer from the stratum corneum, stratum granulosum, stratum spinosum, to stratum basalis. Angular cheilitis lesion appears due to the body's inability to compensate for tissue damage due to infection with pathogenic microorganisms (Azizah et al., 2021). Clinically these lesions appear as ulcerated lesions, accompanied by fissures or crusts. Lesions can appear on one (unilateral) or two (bilateral) sides. Angular cheilitis can occur at any age, both men and women (Fajriani, 2017). In this case report, the lesion appeared as ulcerated lesions in fissures with a reddish color accompanied by peeling skin around them and pain. Lesions appear bilaterally in both corners of the lips.

Definition and description of the lesion

Fajriani, (2017) in his study explained that angular cheilitis could occur due to Candida albicans infection, trauma to the oral cavity, decreased nutrition, systemic diseases, and viral infections. According to Pandarathodiyil et al. (2021) in their study, the etiology of angular cheilitis can be distinguished into local and systemic etiologies as described in Table 2 below.

Etiology

Fajriani, (2017) in his study explained that angular cheilitis could occur due to Candida albicans infection, trauma to the oral cavity, decreased nutrition, systemic diseases, and viral infections. According to Pandarathodiyil et al. (2021) in their study, the etiology of angular cheilitis can be distinguished into local and systemic etiologies as described in Table 2 below.

Table2. Etiology of angular cheilitis

Local etiology	Example
Physical and anatomical factors	Reduced vertical dimensions of the jaw so that the corners of the lips are more often flooded with salivary fluid and become a place that supports microbial growth, prone to ulceration and infection.
Allergy factors	Allergy to nickel-containing materials such as braces, metal dentures, and retainers. Allergy to the ingredients contained in lipstick or other cosmetic products. Allergies to other products, such as toothpaste and chewing gum, can aggravate previously existing lesions because allergens will more easily penetrate the lesion.
Microbial infection factors	The condition of salivary flooded lip corners increases susceptibility to the overgrowth of microbes such as Candida albicans and Staphylococcus aureus.

Systemic etiology	Example
Nutritional factors	- Iron deficiency (Fe) Iron deficiency in the blood plasma causes the synthesis of cytochrome oxidase, catalase, and peroxidase enzymes to be disturbed. It causes inhibition in cell proliferation and *turnover*, including in the oral cavity's epithelial cells, so the epithelium becomes atrophied and more susceptible to ulceration and microbial infections. In addition, in anemia due to iron deficiency, there is a decrease in the amount of transferrin protein which acts as a fungistatic, so that fungal growth becomes excessive and causes infections such as angular cheilitis (Echarisma et al., 2021). - Vitamin B complex deficiency Vitamin B complex consisting of B2, B6, B3, B12, B9, and BW is a type of water-soluble vitamin that plays a role in cell metabolism. Vitamin B2 and B6 deficiency can manifest as angular cheilitis lesions, glossitis, sore throat, and swelling and erythema in the mucosa. Vitamin B12 (folic acid) is one of the essential components in forming red blood cells (erythropoiesis), so the lack of this vitamin can reduce the production of red blood cells so that anemia occurs. Anemia makes the mucosal barrier of the oral cavity weaken, and it is easy for angular cheilitis lesions to occur (Echarisma et al., 2021; Marinna & Yusri, 2022). - Eating disorders (anorexia, bulimia) Anorexia nervosa and bulimia nervosa are eating disorders that commonly appear in adolescents (Al Vianita et al., 2020). Anorexia is an excessive fear of weight gain, and bulimia is a state of a person overeating and then regurgitating (Dwintasari, 2018). (Dwintasari, 2018) Malnutrition conditions due to dietary disorders can also cause the appearance of lesions.
Systemic disease factors	Systemic conditions such as xerostomia or dry mouth caused by impaired salivary gland function, head-neck radiation therapy, chemotherapy, diabetes mellitus, or autoimmune diseases can cause the appearance of angular cheilitis lesions. Disturbances in salivary flow can cause dry mouth conditions and abnormalities in the oral cavity (Riolina et al., 2021). Xerostomia can also be caused by pharmacological agents such as antihistamine drugs, antidepressants, and antihypertensives. Systemic infection with the COVID-19 virus can also decrease immunity and increase the susceptibility of the oral mucosa to the appearance of lesions such as angular cheilitis. Díaz Rodríguez et al. (2022) report that one of the manifestations of the oral cavity present in COVID-19 patients is lesions of the tongue, palate, and commissure of the lips accompanied by angular cheilitis lesions. Riad et al. (2022) also reported manifestations of angular cheilitis lesions in 17 confirmed positive patients for COVID-19.
Psychological factors	**Example**
Stress factors	Stress is a state of anxiety about the demands faced by one (Larasati, 2016; Putri, 2021). The stress condition will trigger activation of the hypothalamic-pituitary-adrenal (HPA) axis to release the corticotropin-releasing hormone (CRH). The release of this hormone stimulates the secretion of the adrenocorticotropin hormone (ACTH) from the pituitary gland. ACTH will enter the bloodstream and go to the adrenal glands, then trigger the secretion of stress hormones, namely glucocorticoids and catecholamines. Both types of stress hormones act to provide a *fight-or-flight* response. Glucocorticoids increase the amount of energy substrate in different body parts to deal with environmental demands. Nevertheless, the activation of the HPA axis can suppress immune function, so there is an increased risk of infection.

In this case, anamnesis or subjective examination has been carried out on the patient where the patient says he is in a state of stress due to the heavy study load, as well as the condition of the patient who lives alone, which causes her not to have a balanced nutrition diet, the patient admits that she rarely consumes iron source foods such as vegetables, fruits, nuts, meat, and fish. Supporting examinations in the form of *complete blood counts (CBC)* showed a decrease in MCV, MCH, and MCHC values which showed that the patient had hypochromic microcytic anemia.

According to Erwana, (2022) in his book, the decrease in MCV values occurs in patients with iron deficiency anemia, pernicious anemia, and thalassemia. This condition is called microcytic anemia. In addition, MCH and MCHC values reduce in patients with iron deficiency conditions, microcytic anemia, anemia due to pyridoxine,

and thalassemia. This condition is called hypochromic anemia. This is in line with the subjective examination of the patient in this case, that the patient rarely consumes iron-source foods such as vegetables. So based on the above findings, it is concluded that the patient has hypochromic microcytic anemia.

Management of angular cheilitis lesions

The management of angular cheilitis lesions depends on the causes and clinical appearance of the lesions(Pandarathodiyil et al., 2021). If a decrease in vertical dimensions causes the lesions, fixing the condition such as using dentures is necessary. Patients who have the habit of licking the corners of their lips should be educated to avoid this habit. If an allergy to dental care products or cosmetics used by the patient is suspected, the use should be stopped and replaced with other products. Suppose the lesion is presumed to be due to allergies to metal materials contained in orthodontic devices or dental restoration materials. Replacing them with materials free of allergens, such as stainless steel, titanium, or ceramic, can be considered.

Anti-fungal medicine can be given if the lesion is suspected to arise due to the formation of an environment that supports the growth of Candida albicans microorganisms as the cause of lesions (Soeprapto, 2017), such as topical medicine nystatin, amphotericin B, ketoconazole, or miconazole nitrate. Topical corticosteroids can also be given as an anti-inflammatory, reduce pain in lesions, and increase mucosal re-epithelialization, i.e., triamcinolone acetonide 0.1% (Marinna & Yusri, 2022). In addition, it is imperative to maintain immunity and body health so that it is not susceptible to disease, as well as increase the intake of nutritious foods needed by the body (Fajriani, 2017; Soeprapto, 2017). Another study conducted by Azizah et al. (2021) stated that the first line of management of angular cheilitis lesions is with anti-fungal medicine accompanied by eliminating predisposing factors.

In this case, the patient refused to be given topical corticosteroid medication, so the treatment was emphasized more on education to increase the intake of iron-containing foods such as vegetables, fruit, nuts, meat, and fish. This education is based on the patient's complete blood examination results, which indicate that the patient has hypochromic microcytic anemia. Iron intake is expected to increase erythropoiesis so that the process of regeneration and re-epithelialization of the oral cavity mucosa goes well and accelerates the healing of lesions. The patient was also educated on improving stress management. Two weeks later, the patient said he had followed recommendations to increase iron intake, eat nutritious foods, and reduce stress. The complaints of pain in the corners of the lips have disappeared, and clinically it appears that the lesions have healed completely.

In this post-pandemic condition, everyone began to rise and move much more actively than three years ago before the pandemic. The latest data reported by the Google *COVID-19 Community Mobility Report* in 2022 shows that human mobility, especially in Indonesia, has increased by 20% in workplaces, increased by 23% in shopping areas, and increased by 29% to open environments such as parks and beaches (Google, 2022). Increased activity that is not accompanied by a healthy lifestyle and adequate rest can decrease the body's health and immunity (Amalia et al., 2020). This angular cheilitis lesion is just one of the many lesions in the oral cavity that systemic conditions can induce, one of which is decreased cellular immunity. Oral cavity lesions are often only considered as the result of local factors. However, the appearance of these lesions could become a sign of the lifestyle and nutritional intake that has been lived, as well as a reminder that we need to maintain the body's immunity by increasing nutritional intake and minimizing stress.

Conclusion

Angular cheilitis is a lesion in the corners of the lips caused by many factors, including systemic conditions. In this case, the patient has hypochromic microcytic anemia characterized by a decrease in MCV, MCH, and MCHC values on a complete blood test. This decrease in the volume and concentration of hemoglobin in erythrocytes can be caused by iron deficiency, which impacts the susceptibility of ulcerated oral mucose and microbial infections. Other conditions, such as stress and systemic diseases, can also lower immunity and increase mucosal susceptibility to infection. The above findings lead the authors to conclude that the patient has angular cheilitis

triggered by trauma and is predisposed by systemic conditions in the form of hypochromic microcytic anemia and stress. Treatment emphasizes more on education to improve iron source diet intake and stress management.

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