



## Drug Related Cheilitis Along with Developed Angular Cheilitis: Case Report

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### ARTICLE INFO

#### Article history:

Received 14 November 2023

Revised 15 March 2024

Accepted 15 March 2024

Available online July 2024

E-ISSN: [2615-854X](#)

P-ISSN: [1693-671X](#)

#### How to cite:

Ramadhan AF, Soegyanto AI, Rahmayanti F. Drug Related Cheilitis Along with Developed Angular Cheilitis: Case Report. Dentika Dental Journal 2024; 27(1): 00-00.

### ABSTRACT

Isotretinoin is used to treat severe acne, and despite the therapeutic benefits, it has many side effects, including cheilitis on lips. This case report reviewed the importance of assessing the medical and pharmacological histories during anamnesis in the management of drug-related and angular cheilitis. Case: A 22-year-old female patient presented with complaints of dry, cracked, bleeding, and pain on the upper and lower lips, which occurred 7 days ago. Previous similar complaints were reported, although not severe. The patient had habits of lip licking, low water intake, and an irregular menstrual cycle. There was a history of using Roaccutane (isotretinoin) for acne treatment. Extraoral examination showed dry, desquamated lips with crusts, while intraoral examination had no abnormalities. Case management: The patient was prescribed NaCl 0.9%, Vaseline album, and hydrocortisone cream 1% twice daily. However, during treatment, angular cheilitis developed, prompting the prescription of miconazole cream 2% twice daily. One month later, all of the patient's complaints were successfully treated with no subjective issues. Proper history taking and examinations were fundamental to making the right decisions and definite treatment plans.

**Keyword:** Drug-related Cheilitis, Angular Cheilitis, Isotretinoin

### ABSTRAK

Isotretinoin banyak digunakan untuk mengobati jerawat yang parah. Terlepas dari manfaatnya, isotretinoin memiliki banyak efek samping dan keilitis adalah salah satu efek samping Isotretinoin yang paling umum yang terjadi pada bibir. Laporan kasus ini meninjau pentingnya menggali riwayat medis dan farmakologis saat anamnesa dalam perawatan keilitis terkait obat dan angular cheilitis. Kasus: Pasien perempuan berusia 22 tahun datang dengan keluhan pada bibir atas dan bawah kering, berdarah, dan terasa nyeri sejak 7 hari yang lalu. Pasien memiliki riwayat keluhan bibir kering sebelumnya, tetapi tidak pernah separah sekarang. Pasien memiliki kebiasaan buruk menjilat bibir. Pasien mengkonsumsi air putih dalam jumlah sedikit. Pasien memiliki siklus menstruasi yang tidak teratur. Pasien memiliki riwayat mengonsumsi Roaccutane (isotretinoin) untuk mengobati jerawatnya. Pemeriksaan ekstraoral menunjukkan bibir atas dan bawah kering, deskuamasi, dan disertai krusta. Pada pemeriksaan intraoral tidak ditemukan kelainan. Manajemen kasus: Pasien diresepkan NaCl 0,9%, Vaseline album, dan krim hidrokortison 1% dua kali sehari. Tetapi di tengah pengobatan, muncul angular cheilitis dan diresepkan miconazole krim 2% dua kali sehari. Satu bulan kemudian, semua keluhan pasien sembuh dan tidak ada keluhan subjektif. Anamnesis yang lengkap dan pemeriksaan menyeluruh adalah kunci penting dan mendasar untuk membuat keputusan dan rencana perawatan yang tepat.

**Keyword:** Cheilitis terkait obat, Angular Cheilitis, Isotretinoin



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<http://doi.org/10.32734/dentika.v27i1.14369>

## 1. Introduction

Cheilitis refers to any signs of lips inflammation often associated with the habits of lip licking, hot weather conditions, or dehydration. Meanwhile, drug-related cheilitis is a rare reversible type that occurs due to allergy or a pharmacological effect [1]. The severity depends on various factors, such as the type of drug, dosage, and patient's response. Even though many drugs can cause cheilitis, aromatic retinoid compounds, such as etretinate and isotretinoin are among the most common factors, leading to dryness and cracking of lips [2]. Due to the various etiologies of cheilitis, it can be challenging to determine the precise type. Therefore, detailed history-taking and thorough examination are crucial for identification. This is a case report of a patient with a history of isotretinoin-induced cheilitis, with developed angular cheilitis.

## 2. Case Report

A 22-year-old female patient presented to the Oral Medicine Clinic of Universitas Indonesia Dental Hospital with complaints of dry, cracked, bleeding, and pain with a Visual Analogue Scale score of 7 out of 10 on the upper and lower lips, which occurred 7 days prior to presentation (Figure 1). The patient had a history of dry lips, although not severe. Despite applying Vaseline album 3-4 times per day, lips were still dry and often bled. These complaints were accompanied by spontaneous nosebleeds, which were rare occurrences previously, causing concern and anxiety. Furthermore, there were bilateral wounds on the corners of the lips. There was no history of systemic disease and allergies, but irregular menstrual cycle, which occurred every 2 to 3 months, lasting 6 to 7 days and becoming regular with routine exercise. The patient denied experiencing abdominal pain or bloody stools, and does not smoke or take alcohol. However, the patient admitted to bad habits of lip licking and minimal water consumption, averaging 1.5 L/day. A history of consuming Roaccutane (isotretinoin) 10 mg per day or 15 mg per 2 days was noted, prescribed by a dermatologist to treat acne, and discontinued 1.5 months prior to presentation. Acne had not recurred since the last Roaccutane intake, and 2 weeks before presentation, an orthodontist was visited for a fixed orthodontic appliance follow-up and scaling. Teeth were brushed twice a day, with no changes in toothpaste, and Listerine mouthwash was used every 3 days. Furthermore, proper meals were reported in the afternoon and evening, which included rice, vegetables, side dishes, and fruit, with milk consumed in the morning. As a dental co-assistant, the patient wore hazmat equipment during clinical hours, restricting water intake from 8 am to 1 pm, and reported feeling stressed due to a busy schedule.



Figure 1. Initial Clinical Picture

Extraoral examination showed dry, desquamated lips with crusts, and no abnormalities during the examination. Based on anamnesis and clinical results, a working diagnosis of drug-related cheilitis was made, with a differential diagnosis of exfoliative cheilitis. The patient was advised to maintain oral hygiene, discontinue mouthwash use, engage in routine exercise, consume proper meals thrice daily, increase water intake, and manage stress. Hydrocortisone 1% cream was prescribed to be applied twice daily, as well as NaCl 0.9% solution and Vaseline album to be applied as often as possible. A complete blood count examination was recommended to rule out the possibility of anemia or nutritional deficiencies. The laboratory results were in normal ranges except for a low lymphocytes count with an elevated erythrocyte sedimentation rate. One week after initiating treatment, healing of lips lesions was reported, but new lesions appeared and expanded in the corners of lips (Figure 2). A one-day service direct mycological swab produced positive yeast cells, leading to a diagnosis of angular cheilitis. Miconazole cream 2% was prescribed to be applied twice daily to the angular lips. The resolution of all complaints was reported 2 weeks later (Figure 3)

### 3. Figure Placement



Figure 2. Developed Angular Cheilitis



Figure 3. The last condition of the lips, all lesion was healed

Cheilitis is an inflammation of lips, and may constitute both the skin and oral mucosa. Physicians often face difficulty in determining the exact type of cheilitis, hence, appropriate diagnostic procedures are crucial to precisely characterize the condition based on features [1]. There are several etiologies and causes of cheilitis, making diagnosis a complex task. Angular cheilitis (AC) can be attributed to various causative and precipitating factors including infections (*Candida spp.* and *Staphylococcus spp.*), primary hypervitaminosis A, systemic immune suppression, local irritation, and moisture [3]. Drug-induced cheilitis refers to lip damage caused by drug consumption, primarily retinoids (isotretinoin, acitretin). Exfoliative cheilitis is characterized by persistent desquamation, mainly affecting the lower lips, accompanied by peeling, dryness, itching, or tingling. External etiologic factors like weather conditions, habits such as lip licking and biting, and excessive sun exposure also play significant roles. For instance, angular cheilitis is often associated with irritation, moisture, nutritional deficiencies, and skin infections in the corners of lips. Exfoliative cheilitis can be related to habits like mouth breathing, lip licking and biting, infections, and poor oral hygiene [4,5].

Several studies have grouped cheilitis into different types, with Oakley A, et al. classifying based on etiology. Lips inflammation types are classified into infection, toxin, allergy, medication, injury, or due to vitamin or mineral deficiency (iron or vitamin B deficiency). The use of certain drugs, both for therapeutic and recreational purposes, can induce AC. The common side effects observed in almost all patients taking isotretinoin included AC and cheilitis, often serving as early indicators of toxicity and patient compliance. These conditions typically constitute reversible cheilitis of a temporary nature. In addition, there is a tendency for secondary colonization by *Candida albicans* or *Staphylococcus aureus* after the use of isotretinoin, which may influence AC treatment. [4].

Based on the patient's history, complaints of dry, cracked, and bleeding lips were reported, with the current use of Roaccutane containing isotretinoin. Oral isotretinoin functions by potently inhibiting sebaceous gland activity through multiple pathways. Approximately 90% of patients experienced common and less severe side effects associated with oral isotretinoin, including dryness of the skin and mucous membranes. This was due to decreased sebum production and stratum corneum thickness, leading to changes in the skin barrier. Cheilitis is the most common mucocutaneous side effect affecting 90-100% of patients, with occurrence dependent on dosage, predictable, controllable, and reversible. Prevention measures include early use of moisturizers and lip lubricants from the outset of treatment [6]. Thorough anamnesis is important for every patient, as crucial information, such as drug and medical history, cannot be obtained without proper inquiry [7].

The patient had already applied Vaseline album to moisturize lips, but cheilitis persisted due to other external factors exacerbating the condition, such as bad habits of lip licking and minimal water consumption, which may also be influenced by irregular menstrual cycle. Lip licking, which brings saliva to lips, could result in irritation due to salivary digestive enzymes extracting moisture from lips and causing evaporation. Habits like sucking and biting the lower lip may result in sharply bordered perioral erythema [4]. The patient was promoted to discontinue the bad habit and continue using Vaseline album, as it can help maintain moisture and provide a protective layer to lips [8]. Low water intake can also contribute to dry lips. Recommendations for minimum intake vary, but generally range from 2–2.7L per day for adult females [9]. The patient admitted to having irregular menstrual cycle due to lack of exercise, potentially leading to hormonal imbalance, including estrogen-related issues [10,11]. Estrogen plays a role in preventing dryness of the skin or a mucosa by stimulating the secretion of oils and collagen, which help maintain skin density. A low level of estrogen can lead to reduced production of collagen and oil, affecting skin smoothness and moisture retention [12], hence further examination is necessary.

Based on the characteristics of cheilitis, the diagnosis was established as drug related cheilitis, with exfoliative cheilitis being excluded as a differential diagnosis. Topical corticosteroids are effective in conditions characterized by hyperproliferation, inflammation, and immunologic involvement. When prescribing topical steroids, it is important to consider the diagnosis, steroid potency, frequency of administration, treatment duration, delivery vehicle, and potential side effects. Hydrocortisone cream 1% was considered as the topical steroid of choice. Creams consisting of water suspended in oil have good lubricating qualities, can be absorbed into the skin, and are cosmetically appealing [13,14]. Hydrocortisone is a less potent topical corticosteroid and one of the safest agents for long-term use on large surface areas, including on the face and lips [15]. Supportive therapy with topical emollients is crucial in lip treatment, as it can alleviate symptoms, even after discontinuation of the causative agent, when possible.

One week after prescribing hydrocortisone cream, the patient reported that lips lesions had healed. However, new lesions appeared in the commissures, diagnosed as angular cheilitis, and is commonly associated with *Candida*, *Staphylococcus* or *Streptococcus* infections, isolated nutritional deficiencies, and particularly with deficiencies of iron or vitamin B12, as well as habits such as mouth breathing or lip licking [16,17]. The most potential factor was the low lymphocytes count and combination use of corticosteroid. Lymphocytes play a role in mediating Cell-Mediated Immunity (CMI), which is important for host defence against fungal infections, particularly at mucosal and epidermal surfaces [18]. Low lymphocyte count consequently influenced antifungal host defence, while repetitive behaviours like lip licking contributed to the severity of AC [19].

The patient was instructed to undergo a one-day direct mycological swab to rule out the presence of fungal infection or yeast, which was commonly suspected as the etiology of AC. Besides, direct mycological swab is a simple and cost-effective technique [20]. Treatment of AC depends on etiology, whether infectious or non-infectious. Since the most common risk factors constitute saliva, which can induce eczema and resultant maceration, protecting the labial commissures using a topical barrier application such as Vaseline is important [21]. Miconazole 2% cream topically has a history of providing the best response to treat AC due to inherent gram-positive bacteriostatic activity, making it a first-line treatment in some literature [19,22]. The patient reported all complaints had healed 2 weeks after treatment.

#### **4. Conclusion**

In conclusion, the case of dry lips or cheilitis was important, even though it appeared simple. There were several types of cheilitis, necessitating dentists to consider the possibility criteria, conduct proper history-taking and examinations to make right decisions, as well as formulate definite treatment plans for good results.

#### **5. Conflict of Interest**

The authors declare no conflicts of interest.

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