

Cheilitis – case study and literature review

Anna Rosińska-Więckowicz, Małgorzata Misterska, Leszek Bartoszak, Ryszard Żaba

Department of Dermatology, Poznan University of Medical Sciences, Poland
Head: Prof. Wojciech Silny MD, PhD

Post Dermatol Alergol 2011; XXVIII, 3: 231–239

Abstract

Inflammatory lesions of the lips are usually a cosmetic complaint, but may also be a relevant manifestation of systemic diseases. Cheilitis and angular cheilitis are usually considered as distinct entities as there are different underlying causes of the two conditions. However, they may also coexist with each other. Cheilitis may also coexist with or precede the onset of numerous systemic disorders. We present a patient with an 8-year history of cheilitis. Moreover, different possible underlying causes in the differential diagnosis and treatment possibilities are presented.

Key words: lip diseases, vermilion, granulomatous cheilitis.

Introduction

The definition of the vermilion as the transition area between the skin and the mucous membrane (*semi-mucosa*) was introduced for the first time by Jean Darier, a French dermatologist, in the 19th century. The lips are skin and muscle folds that surround the mouth. Muscular fibres are the marginal part of the orbicularis oris muscle, very well developed in the primates, in which it enables both food ingestion and articulation [1]. The lips are lined with the mucous membrane from the inside and with the epidermis from the outside, and are joined together in the angles of the mouth.

Anatomically the lips can be divided into three zones:

- 1) the external or front (skin) part, including the sulcus of the upper lip and ending on the vermilion border, covered with cornified stratified squamous epithelium and containing many skin appendages (sebaceous glands, sweat glands and hair follicles);
- 2) the central (transition) part or the vermilion – the border between the lip skin area and the mucous membrane with thin non-cornified stratified squamous epithelium with numerous vessels in the superficial plexus, which gives the typical tint; this part has no appendages and is moisturised by saliva secreted within the oral cavity;
- 3) the mucous part covered with non-cornified stratified squamous epithelium with many mucous and serous glands.

On the one hand cheilitis is a separate disease entity, and on the other it may precede systemic disorders

or coexist with them [1-3]. Although all abnormalities within the vermilion significantly decrease patients' life comfort, the problem is often underestimated in daily medical practice by gastroenterologists, stomatologists, allergologists and dermatologists. The term cheilitis stands for inflammation of the vermilion, and its aetiology may be very diverse. Initially the disease may manifest itself in lesions in the angles of the mouth (*cheilitis angularis, perleche*) or *de novo* cover the whole surface of the vermilion (*cheilitis*). On the other hand, the term *cheilosis* depicts non-inflammatory lip lesions [1-3].

Case report

A 22-year-old man was admitted to the Clinic of Dermatology of the Poznan University of Medical Sciences because of 8-year cheilitis and eczema-like lesions of the palmoplantar skin, observed for about 3 months. The patient has been working in engine repairs for a year and observed the association between the lesions on the vermilion and symptoms arising from the gastrointestinal tract. He has been under the care of the Gastroenterological Outpatient Clinic for about 8 years, where he was diagnosed with gastroesophageal reflux disease, irritable bowel syndrome and chronic gastric ulcer disease. Therefore the patient has been treated with mebeverine (135 mg twice daily), and periodically has received ranitidine or omeprazole. The family history for atopic diseases in the patient and his family was negative.

Address for correspondence: Anna Rosińska-Więckowicz MD, PhD, Department of Dermatology, Poznan University of Medical Sciences, 49 Przybyszewskiego, 60-330 Poznań, Poland, e-mail: rosinka.anna@gmail.com

Dermatological condition

The presence of oozing erosions in the angles of the mouth, in places covered with honey-yellow crust, was observed. Epithelial desquamation in the form of flakes, erythema, atrophy and single cracks visible within the vermilion were present. Lesions characteristic of juvenile acne were visible on the skin of the chin – papules, pustules and comedones. Additionally, slight epidermal desquamation with minor hyperkeratosis on the palmo-plantar skin was found (Fig. 1).

Diagnostics

The performed laboratory analyses showed: accelerated erythrocyte sedimentation rate (32 mm/h), elevated concentration of C-reactive protein (CRP – 11.32 mg/dl) and ALAT (53 IU/l) in blood serum. A laryngologist who consulted the patient diagnosed chronic suppurative inflammation of the palatine tonsils with indication for their removal. Due to the medical history of the patient's performed job, also patch tests with the European standard series of contact allergens (Chemotechnique Diagnostics, Sweden) were carried out. In addition, vermilion swabbing for bacteriological examination was carried out, which confirmed the presence of *Staphylococcus aureus* sensitive to doxycycline, erythromycin, clindamycin, trimethoprim/sulfamethoxazole, and also abundant aerobic and anaerobic microflora, physiologically present in the oral cavity. No antibodies against herpes simplex virus (anti-HSV1, HSV2 in the classes IgM and IgG) were found in blood serum. The concentration of vitamin B₁₂ and zinc in blood serum was normal. Ultrasound examination of the abdominal cavity and X-ray examination of the thorax showed no deviations from the norm. The conducted patch tests with group aeroallergens (Allergopharma, Germany) showed no allergy to the examined substances (grasses/cereals, grasses, trees I and II, weeds, moulds I

and II, hair, house dust mite). A skin specimen of the lower lip was collected for the histopathological examination, which found only epithelial oedema with dilated blood vessels under the epithelium together with the presence of single inflammatory cells. However, no lesions such as cellular atypia, inflammatory infiltrations, acantholysis, granulosis or bullae were diagnosed (Fig. 2).

Treatment

Systemic treatment was administered: cetirizine 10 mg twice daily for 7 days, then 10 mg once daily for 7 days, doxycycline 100 mg once daily for 10 days, clemastine 10 mg 1 pill before bedtime for 7 days. Local treatment included mupirocin ointment three times daily for 7 days. Additionally, the use of lip barrier balms was recommended, and before sun exposure – preparations for the vermilion containing UV filters. After the gastroenterological consultation, esomeprazole at the dose of 40 mg once daily was administered. As a result of the used treatment, total regression of the lesions within the vermilion was obtained.

Discussion

In most cases inflammation of the angles of the mouth and/or of the vermilion, thorough history taking and physical examination enable one to make a correct diagnosis. Since infectious agents are the most frequent cause of angular cheilitis, it is recommended to start the diagnostic procedure with swabbing the area or the denture part adherent to the mucous membrane of the oral cavity in patients wearing dentures for bacteriological examination. It is also recommended to assess the concentration of iron and vitamin B₁₂ in blood serum, and in small children – zinc concentration. However, it should be borne in mind that cheilitis may be the only symptom of serious systemic diseases.



Fig. 1. Desquamation of the epithelium of the vermilion in the form of small flakes, accumulated honey-yellow crusts and single rhagades

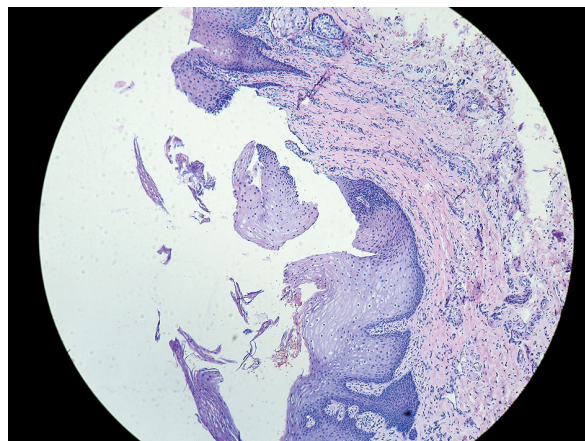


Fig. 2. Oedema of the epithelium with dilated blood vessels under the epithelium together with the presence of single inflammatory cells

Angular cheilitis and cheilitis

At the bottom of *cheilitis angularis* initially there is maceration of skin folds of the angles of the lips as a result of irritation caused by saliva enzymes, and only secondarily a fungal, bacterial, or – less frequently – viral superinfection occurs [4, 5]. The disease may be acute or chronic. Acute angular cheilitis (e.g. after dental procedures) more often is unilateral, while chronic lesions are usually bilateral [1-5]. The prevalence of angular cheilitis is the same in all age groups. The reasons for excessive saliva production may be different – and thus in newborns it is usually associated with dentition, in older children with habitual licking of the lips or lip dryness in the course of atopic dermatitis, whereas in elderly people ill-fitting dentures and greater slackness of skin around the lips are of the greatest importance [1-5].

However, it seems that the main causes of angular cheilitis are infectious agents, and the major part is attributed to yeast-like fungi from the genus *Candida* spp., and then to Gram-positive cocci *Staphylococcus* spp. and *Streptococcus* spp., while viral infections are rarely named [1, 6, 7]. Coexisting diabetes, anaemia or a proliferative process may also increase the risk of infections in the area.

The clinical picture of angular cheilitis includes erythematous and erythematous desquamative lesions, which lead to small cracks and oozing erosions. With time the erosions may become covered with honey-yellow crust, which indicates secondary bacterial superinfection, or with white coating suggesting *Candida* superinfection. With time the lesions may cover both the vermilion and the surrounding skin and spread along creases and fissures coming from the angles of the mouth. In some patients also eczema-like lesions on the skin of the cheeks and the chin are observed, resulting from a reaction to infection (bacterial antigens) or used drugs (e.g. local antibiotics) [4, 5]. The main factors predisposing to angular cheilitis are:

- dentures and orthodontic appliances,
- endocrinological disorders (diabetes, hypothyroidism),
- nutritional deficiencies (riboflavin – vitamin B₂, folic acid, cobalamin – vitamin B₁₂, iron, malabsorption syndromes, chronic inflammatory bowel diseases, cystic fibrosis),
- immunity disorders (HIV infection, organ transplantation, lymphoproliferative disorders, cancers),
- tobacco smoking,
- large tongue (Down syndrome),
- bulimia,
- dry mouth (e.g. Sjögren's syndrome),
- zinc deficiency (rarely).

While the most frequent causes of angular cheilitis are usually infectious agents, cheilitis is a more complex issue. Despite the fact that the most common cause is usually exposure to environmental factors (cold, UV radiation), cheilitis may be a symptom of systemic disorders.

The clinical picture of cheilitis is so distinctive that it usually does not require histopathological confirmation.

However, in the case of persistent lesions not responding to treatment, it is recommended to perform a biopsy. In the course of granulomatous cheilitis, oedema and dilation of lymph vessels and perivascular lymphocytic inflammatory infiltrations are observed, although also small dispersed non-caseating granulomas may be present [5, 8]. On the other hand, hypertrophy of the salivary glands with dilation of the secretory ducts, and also fibrosis and infiltration (lymphocytes, plasmocytes and histiocytes), located around the salivary glands, are noted in the course of glandular cheilitis [5, 8].

Potential causes of angular cheilitis and cheilitis are presented in Table 1.

Infections

Inflammatory infection lesions are most frequently found in the vermilion. The symptoms of oral herpes are most often located in the mouth area, and recurrent aggravation of the disease can be observed as a result of different stimuli (weakness, exhaustion, stress, exposure to UV). Contagious impetigo lesions (*impetigo contagiosa*) are also usually observed in the mouth and nose area because the mucous membrane of the nose and throat are a bacterial reservoir (*Streptococcus* spp., *Staphylococcus* spp.). The most common infectious agents of the mouth area are yeast-like fungi of the genus *Candida*. The fungi were found in a swab of the unchanged mucous membrane of the oral cavity in as many as 40% of patients [1, 2]. Colonization of the mucous membrane of the oral cavity by *Candida* spp. together with susceptibility to maceration by saliva accounts for the high percentage of *Candida* infections in this area [8].

Contact cheilitis

The cause of contact cheilitis may be irritation or allergic contact eczema [1]. The morphology of the lesions is usually characteristic of eczema and includes erythema, oedema, vesicles, erosions, exudate, crusts and cracks. The origin of contact cheilitis can usually be determined on the basis of the patient's history. The agent that most frequently irritates the mouth area is saliva, e.g. in the course of habitual licking of the lips (due to the irritative effect of digestive enzymes), and the subsequent factors include toothpastes, lip glosses and lipsticks, dentures, dental cavity filling, food and food preservatives. In some patients the lesions may be associated with the practised profession (e.g. glass manufacturing) or hobby (e.g. playing wind instruments). As part of the diagnostics of contact cheilitis, it is recommended to perform patch tests with the European standard series or series extended with dental or professional allergens [1]. It is also worth remembering phototoxic and photoallergic reactions related to both local application of cosmetics on the lips and administration of systemic drugs (non-steroidal anti-inflammatory drugs – NSAIDs, tetracyclines, sulfonamides,

Tab. 1. Differential diagnosis of lesions within the vermilion

Acute	Chronic
Physical factors: <ul style="list-style-type: none"> • Mechanical (injuries) • Wind • Temperature differences • UV radiation (including phototoxic reactions) 	Contact eczema: toothpastes, mouthwashes, lipsticks, phototoxic reactions
Infectious agents: <ul style="list-style-type: none"> • <i>Herpes simplex</i> • <i>Candida</i> spp. • <i>Streptococcus</i> spp. • <i>Staphylococcus</i> spp. • <i>Treponema pallidum</i> • HIV 	Atopic dermatitis
Erythema multiforme	Bullous diseases
Angio-oedema: <ul style="list-style-type: none"> • In the course of oral allergy syndrome – OAS • In the course of chronic urticaria • Drug-induced 	Lichen planus
Insect bites	Systemic lupus
	Compulsive behaviour: <ul style="list-style-type: none"> • Licking • Lip sucking, biting
	Effect of physical factors: <ul style="list-style-type: none"> • Mechanical (injuries) • Wind • Temperature differences • UV radiation (including Phototoxic reactions) • Irritation from cigarette smoke
	Drug-induced dermatitis: <ul style="list-style-type: none"> • Retinoids • Tetracyclines • Sulfonamides • Neuroleptics • NSAIDs
	Odontogenic (post)infectious
	Non-odontogenic (post)infectious: <ul style="list-style-type: none"> • Tuberculosis • Atypical mycobacterial infection • Leprosy • Syphilis
	Skin cancers: <ul style="list-style-type: none"> • Squamous cell carcinoma • Basal cell carcinoma
	Chronic sun-induced vermilion damage
	Granulomatous diseases: <ul style="list-style-type: none"> • Granulomatous cheilitis • Miescher's cheilitis • Melkersson-Rosenthal syndrome • Orofacial granulomatosis • Sarcoidosis • Leśniowski-Crohn's disease
	Gastroesophageal reflux disease
	Idiopathic: <ul style="list-style-type: none"> • Glandular cheilitis • Amyloidosis

retinoids, antiarrhythmic, antihypertensive, antifungal and neuroleptic drugs) [1-5].

Angio-oedema

Urticaria and angio-oedema are the most common allergic diseases – it is estimated that 20-40% of the global population at least once in a lifetime has experienced an episode of acute urticaria, while 1-4% suffers from the chronic form of the disease [9]. In the course of urticaria, oedema of the epidermis and superficial dermis layers is observed, while angio-oedema occurs in deeper layers of the dermis and the subcutaneous tissue. Most frequently angio-oedema is observed on the face – on the lips, eyelids and the mucous membrane of the oral cavity – and it usually persists for up to 72 h. The most common causes of the disease include non-steroidal anti-inflammatory drugs (mainly aspirin) and allergy cross-reactions to food colourings, preservatives and some food (peanuts, crustaceans), associated with them. Another cause is using angiotensin convertase inhibitors in the treatment of arterial hypertension. Allergic rhinitis patients may periodically suffer from recurrent angio-oedema of the lips after consumption of fresh vegetables (carrot, celery, parsnip) and fruit (apple, pear, peach, apricot) – the phenomenon is called oral allergy syndrome (OAS). Oral allergy syndrome is associated with the mechanism of contact urticaria in the course of cross-sensitivity to food allergens in allergy to aeroallergens (mainly birch and sagebrush pollen) [10].

Actinic cheilitis

Risk factors for actinic cheilitis include: male sex, age between 40 and 80 years, skin phototype I or II and long-term exposure to UV radiation associated with e.g. occupational activity (farmers, sailors, building workers) [1-5]. The lesions are usually papules or scales with a hyperkeratotic surface. Erythema, desquamation, erosions and crusts periodically occur in the mouth area. The lesions are usually more advanced on the lower lip, which is more exposed to UV radiation. Due to the long-term exposure to irritative factors (UV radiation, tobacco smoking, mechanical irritation), also leukoplakia – a precancerous stage – may develop. The irritative effect of nicotine and tobacco smoke is a risk factor for squamous cell carcinoma (SCC) on the basis of leukoplakia. Transition of leukoplakia into SCC may be manifested in the formation of a non-healing oozing ulcer within the whitened epithelium [11, 12].

Cancers

Cancers of the oral fissure are most often observed on the lower lip, which is more exposed to UV radiation and other irritative factors (tobacco smoke, alcohol, biting) due to the anatomical conditions. The most common cancer of the lower lip and the oral cavity is squamous cell carcinoma. Squamous cell carcinoma is usually observed in older

men, in whom it accounts for 4% of all cancers. In the last few years SCC has been more often diagnosed in younger patients, including smoking women [11, 12]. The clinical picture of SCC consists of non-healing and initially painless ulceration of various degree of tissue infiltration, and less frequently of exophytic tumour [11-13]. It should be remembered that mucous membranes are the second most frequent point of departure (after skin) for malignant melanoma. Naevi within the vermillion should be surgically removed due to the risk of irritation (e.g. by consumed food or biting) and long-term exposure to UV radiation, which may favour neoplastic transformation [11-13].

Lichen planus

The most typical lesions in the course of lichen planus include tree-like whitening of the mucous membrane epithelium of the cheeks along the line of occlusion, observed in about 50% of patients, while lesions on the tongue and vermillion are much less prevalent. In the erosion form of lichen planus, painful erosions and deep ulceration on the vermillion and the mucous membrane of the oral cavity with a tendency to cicatrization are noted [14]. In the context of lichen planus, one should also remember the possible development of lichen-like lesions on the lips and the mucous membrane of the cheeks resulting from administration of some drugs (gold salts, antimalarial, sedative, neuroleptic drugs) (Fig. 3) [15].

Erythema multiforme

Erythema multiforme (EM) is a disease of acute course, characterized by the presence of well-separated erythemas, sometimes with the presence of bullae on the surface that affect the mucous membrane of the oral cavity and/or the sexual organs. Erythema multiforme is associated with herpes simplex virus infection (HSV-1 and HSV-2) and with response to some drugs (NSAIDs, sulfonamides, barbiturates, neuroleptics, antidepressants). Lesions on the mucous membrane of the oral cavity include bullae and erosions,

while lesions on the lips are usually accumulated haemorrhagic crusts. The lesions subside in the course of EM without a trace, although they may be recurrent. It has been proved that in the case of recurrent EM, many-months treatment with acyclovir may lengthen the periods between the disease recurrences or even stop the dissemination of the lesions [16]. The erythema multiforme group includes Lyell's syndrome, associated with drug-induced reaction and characterized by over 30% of the body surface area (including the mucous membrane of the oral cavity, sexual organs, conjunctivae and corneas) being covered with bullae and erosions, high fever, serious general condition of the patients and high risk of death, and also Stevens-Johnson syndrome, whose aetiopathogenesis includes both drugs and viral infections. In this syndrome, bullous lesions cover less than 10% of the body surface area, and mainly erosions and accumulated haemorrhagic crusts, sometimes with accompanying eye and nail complications, are observed in the clinical picture (Fig. 4).

Atopic dermatitis

Cheilitis may be the only symptom of atopic dermatitis (AD). Cheilitis is one of the 23 minor criteria for the diagnosis of AD according to Hanifin and Rajka, and isolated chronic or recurrent lesions on the lips may precede the occurrence of this dermatosis [17, 18]. Because of skin dryness observed in the course of AD, the patients often habitually lick their lips, which paradoxically intensifies the inflammatory state in this area due to the irritative effect of the digestive enzymes contained in saliva. Therefore not only emollients for everyday skin care but also barrier balms for lips should be recommended to AD patients.

Granulomatous cheilitis

A chronic inflammatory state in the lip area may lead to granulomas. The disease usually develops in young adult patients and the clinical symptoms usually include sudden diffuse or nodular oedema of the upper lip, low-



Fig. 3. Erosive lichen planus



Fig. 4. Lyell's syndrome

er lip or the cheeks, while other areas are less frequently affected (the forehead, eyelids, hairy head skin) [19]. What may be characteristic in making the diagnosis is that the oedema is not tender while the lip may be painful. During the episodes of oedema, the near lymph nodes may be enlarged and the patient may report malaise. This group of granulomatous diseases includes Miescher-Melkersson-Rosenthal syndrome, Miescher's cheilitis and Leśniowski-Crohn's disease [5, 19].

Miescher-Melkersson-Rosenthal syndrome

Miescher's cheilitis is diagnosed when a granulomatous inflammatory state is observed only on the lips, which may be a part of Melkersson-Rosenthal syndrome. When inflammatory lesions appear in other areas of the oral cavity (the tongue, gums) and of the face (cheeks, eyelids) or other elements of the triad of symptoms are observed, (Miescher)-Melkersson-Rosenthal syndrome is diagnosed. Apart from granulomatous cheilitis lesions, the syndrome also includes episodic, non-tender and painless oedemas with subsequent persistent thickening of one or both lips, lesions on the tongue (fissured tongue – *lingua plicata* – in about 20-40% of patients) and facial nerve paralysis (30% of patients) [20, 21]. Additionally, enlargement of regional lymph nodes is observed in about 50% of patients. However, it should be emphasized that simultaneous presence of the triad of symptoms of Miescher-Melkersson-Rosenthal syndrome is rare – usually the subsequent elements of the syndrome appear gradually during many years of a patient's observation. The lips are soft and firm with palpable nodular structure in the palpation examination. The granulomatous disease process may also affect the eyelids, cheeks, tongue, gums and hard palate, which hinders food consumption or correct articulation (Fig. 5) [19-22].

Inflammatory bowel diseases

Granulomatous cheilitis may precede other granulomatous diseases, such as Leśniowski-Crohn's disease.



Fig. 5. Miescher-Melkersson-Rosenthal syndrome

The aetiology of Leśniowski-Crohn's disease is unknown. Its course includes inflammatory infiltration of the entire thickness of the bowel wall with formation of non-caseating granulomas and fistulae. It is more often observed in men from developed countries, and the highest incidence is noted between the 2nd and 3rd and the 6th and 7th decade of life [22-24]. Lesions in the oral cavity are found in about 9% of Leśniowski-Crohn's disease patients, and their presence is a risk factor for parenteral symptoms of the disease, which include arthritis (often sacroiliitis), clubbed fingers, pyoderma gangrenosum and erythema nodosum. The symptoms of Leśniowski-Crohn's disease in the oral cavity are: diffuse oedema of the mucous membrane of the lips, gums and cheeks, aphthous ulcers, pseudopolyps and angular cheilitis [22-24].

The aetiology of ulcerative colitis (*colitis ulcerosa* – CU) also remains unknown. The inflammatory state in its course is limited only to the mucous and sub-mucous membrane of the large intestine. Lesions in the oral cavity are rare; they usually occur as aggravation of the basic disease. Aphthous ulcers of the oral cavity and angular cheilitis are observed in about 5-10% of CU patients [25, 26].

Glandular cheilitis

Glandular cheilitis (GC) is a disease of unknown aetiology, where thick saliva is secreted from the swollen minor salivary glands, and then cakes in the form of accumulated crusts. Inflammatory hyperplasia of the salivary glands of the lower lip most often occurs in older men, usually of Caucasian origin. It is believed that the long-term effect of irritative physical factors (wind, sand, UV radiation, chemical compounds, tobacco smoke) contributes to formation of the lesions, and the greatest importance is attributed to long-term exposure to UV radiation. In the course of GC, lip enlargement to a various extent with visible reddened and dilated openings of the minor salivary glands in the vermilion is observed. The palpation examination reveals nodular structure of the lips with visible thick mucopurulent discharge secreted from the swollen minor salivary glands when pressured. Glandular cheilitis is considered as a precancerous stage. So far there has been described a range of cases of transition of GC into SCC – a carcinoma which also more frequently occurs on the lower lip as a result of the effect of similar irritative factors [5, 13, 27, 28]. There are also cases of HIV-infected patients in whom SCC developed during several months after the diagnosis of GC [29, 30].

Vitamin B₁₂ and iron deficiencies

Vitamin B₁₂ deficiencies are expected in vegans, anorexics and alcoholics, whereas iron deficiency is most commonly observed in women of reproductive age, which is usually associated with blood loss during menstruation, and less frequently with adopting e.g. a strict diet. In the

elderly vitamin B₁₂ deficiency may result from unbalanced diet, and iron deficiency e.g. from chronic bleeding from the gastrointestinal tract in the course of cancer diseases of the large intestine. Iron deficiency may manifest itself in recurrent angular cheilitis, pale vermilion or atrophic lesions in the mucous membrane of the oral cavity. On the other hand, vitamin B₁₂ deficiency is related to the symptoms of inflammation of the tongue (smoothing of the tongue surface resulting from atrophy of the tongue papillae) and of the mucous membrane of the stomach and oral cavity; initially the lesions on the tongue are hypertrophic, bright red and painful, with time becoming atrophic and smooth-surfaced (so-called bald tongue) [5, 30]. The lesions on the mucous membrane of the oral cavity may be accompanied by neurological symptoms in the form of sensory disorders. However, it is worth emphasizing that vitamin B₁₂ deficiency rarely occurs in young healthy people [5, 31].

Acrodermatitis enteropathica

This is a rare disorder associated with a genetic defect of the production, structure and function of the factor binding and transporting zinc to cells. The clinical symptoms affect the skin and its appendages, the mucous membrane, the gastrointestinal tract and the organ of vision. Skin lesions in the form of erythematous exudative lesions and small vesicles are usually observed in newborns and small children after weaning. Eruptions are usually located in the area of natural body openings (the eyes, nose, lips, ears, nappy area), the cheeks and distal limb segments (fingers). The diagnostics of *acrodermatitis enteropathica* consists in assessment of zinc concentration in blood serum (the normal range is 70-150 µg/dl) and supplementation with zinc sulphate: in newborns – 2.5-10 mg/kg b.w./day, older children – 35-150 mg, maintenance dose of 1-3 mg/kg b.w./day [32, 33].

Syphilis

The clinical picture of syphilis depends on the duration of the disease. The primary symptom of the first stage of syphilis (primary syphilis) is usually a painless oval ulceration with cartilaginous base, healing within 2-6 weeks without a trace or leaving a disappearing scar, located on the lips or in the oral cavity. Secondary syphilis manifests itself in papules located on the lips. Their surface may macerate and disintegrate and with time become covered with crusts – the clinical picture may resemble impetigo (so-called impetigo papules) [34].

HIV infection

Similarly as in the course of syphilis, HIV infection may be associated with a wide range of dermatological symptoms on the lips and the surrounding skin. The most common disorders observed in the course of HIV infection include severe recurrent herpes simplex virus infections not responding to treatment, molluscum contagiosum

virus infections (including lesions on the tongue and the mucous membrane of the oral cavity, rarely observed in immunocompetent persons), human papilloma virus infections (genital warts in the angles of the mouth, in the area of the gums, palatine arches, uvula), recurrent impetigo-type lesions resistant to standard treatment or folliculitis [35-37].

Compulsive behaviour

This concerns habitual, often unconscious or compulsory licking, biting or sucking of the lips, more often observed in women. Recurrent injury causes skin maceration, a chronic inflammatory state and secondary bacterial or yeast superinfection. The most common clinical picture in the course of compulsive behaviour is desquamative cheilitis. The clinical symptoms include increased hyperkeratosis and desquamation of the vermilion, which in turn is associated with lip dryness and “the need” for a patient to lick lips. Hence a peculiar vicious circle of symptoms is created, which is difficult to break only with the use of local treatment and care preparations – psychotherapy is often necessary. Due to the aetiology of desquamative cheilitis, classic treatment with corticosteroids for local application is ineffective. In the case of recurrent and desquamative cheilitis lesions not responding to treatment, one should remember that the nature of the disease is self-mutilation and the disease may be associated with mental disorders [1, 28, 38].

Treatment

Effective treatment of cheilitis presents a challenge to specialists of many fields of medicine. In the acute phase of cheilitis in the first stage an attempt should be made to eliminate potential physical factors that may aggravate the disease course and to use local neutral moisturising preparations containing UV filters (lip balms, lipsticks, protective pastes) or so-called barrier balms/creams or preparations facilitating healing of damaged skin, containing zinc, copper, manganese, sucralfate, madecassoside or allantoin [2, 3].

Erosive lesions and deep cracks may require cauterization e.g. with 10% silver nitrate [2, 3]. In the case of a strong inflammatory reaction, local administration of weak or medium-acting glucocorticosteroids should be considered. Hence one should remember the possibility of symptoms of perioral dermatitis (*dermatitis perioralis*) resulting from too long or too frequent treatment with glucocorticosteroids or administration of too strong preparations [1-4]. Creams or ointments containing calcineurin inhibitors (tacrolimus, pimecrolimus) are an alternative to locally applied glucocorticosteroids, especially in AD patients in the case of necessary long-term therapy or treatment of recurrent lesions [1, 2]. In order to decrease oedema and itching, systemic administration of antihistamine drugs should be considered [28].

In the case of impetiginization or detection of pathogenic bacterial flora, a local broad-spectrum antibiotic (mupirocin cream or ointment three times a day, fusidic acid cream or ointment three times a day) should be used. When no therapeutic effect is observed, systemic treatment according to the antibiogram may be administered. White coating that covers erosions requires administration of local anti-fungal drugs (ketoconazole cream twice daily, miconazole cream twice daily, nystatin suspension for painting the oral cavity 2-3 times daily). In the case of no expected therapeutic effect, it is recommended to swab for mycological examination and then introduce local or systemic treatment, optimally according to a mycogram (ketoconazole, fluconazole, itraconazole) [1-4]. One of the methods of granulomatous cheilitis treatment is lip glucocorticosteroid injections (triamcinolone acetate) [39]. Very good results in the treatment of glandular cheilitis were obtained after performing vermilionectomy (removal of the vermilion border) [27, 40].

Some authors state that the best treatment results are achieved by combining surgical debridement, local glucocorticosteroid injection and systemic administration of tetracyclines [1]. Systemic treatment with metronidazole gave good results in the case of Leśniowski-Crohn's disease patients [41].

Cancer lesions or precancerous states can be treated with destruction with liquid nitrogen (in the case of superficial lesions) or with surgical excision (in the case of infiltrative lesions) [40]. For the last few years, 5% imiquimod cream has been successfully used in the treatment of precancerous lesions [40]. What is more, application of lasers combined with photosensitizing agents (photodynamic therapy) is also one of the newer therapeutic possibilities in modern dermatology [40, 42, 43].

Conclusions

In the case of the patient presented by the authors, the onset of recurrent cheilitis lesions coincided with the diagnosis of diseases of the gastrointestinal tract (gastroesophageal reflux disease, irritable bowel syndrome and chronic gastric ulcer disease). Obviously, chronic cheilitis may precede or coexist with diseases of the gastrointestinal tract. However, recently it has been reported that cheilitis may be a manifestation of gastroesophageal reflux disease [44-47]. Reflux of the gastric contents to the oesophagus causes a decrease in pH of the oral cavity below 5.5 – such a low acidic reaction of saliva may result in chronic irritation of the lips. In this case using barrier balms for the lips is especially recommendable. It has been proved that during treatment with proton pump inhibitors, inflammatory symptoms on the lips gradually subside, which was observed also in the case of our patient.

References

- Rogers R, Bekic M. Diseases of the lips. *Sem Cut Med Surg* 1997; 16: 328-6.
- Gonsalves W, Chi A, Neville B. Common oral lesions: part I. Superficial mucosal lesions. *Am Fam Physician* 2007; 75: 501-7.
- Siegel M. Strategies for management of commonly encountered oral mucosal lesions. *J Calif Dent Assoc* 1999; 27: 210-18.
- Braun-Falco O, Plewig G, Wolff H, Burgdorf W. *Dermatologia*. Czelej, Lublin 2003; 1093.
- Schulman J, Beach M, Rivera-Hidalgo F. The prevalence of oral mucosal lesions in US adults: data from the Third National Health and Nutrition Examination Survey 1988-1994. *J Am Dent Assoc* 2004; 135: 1279-86.
- Cannon R, Chaniffin W. Oral colonization by *Candida albicans*. *Crit Rev Oral Biol Med* 1999; 10: 359-83.
- Lamey P, Lewis M. Oral medicine in practice: angular cheilitis. *Br Dent J* 1989; 176: 15-8.
- Huber M. A review of premalignant oral conditions. *Tex Dent J* 2006; 123: 502-9.
- Rosińska A, Łopińska P, Karpisiewicz M, Piotrowska K. Prawdopodobne przyczyny pokrzywki przewlekłej u chorych hospitalizowanych w Klinice Dermatologii Akademii Medycznej w Poznaniu w latach 1997-2003. *Post Dermatol Alergol* 2004; 21: 128-35.
- Ballmer-Weber B. Cutaneous symptoms after ingestion of pollen-associated foodstuffs. *Hautarzt* 2006; 57: 108-15.
- Cataldo E, Duko C. Solar cheilitis. *J Dermatol Surg Oncol* 1981; 7: 989-95.
- Stanley R, Roenigk R. Actinic cheilitis – treatment with the carbon dioxide laser. *Mayo Clinic Proc* 1988; 63: 230-5.
- Castineiras I, Del Pozo J, Mazaira M, et al. Actinic cheilitis: evolution to squamous cell carcinoma after carbon dioxide laser vaporization. A study of 43 cases. *J Dermatol Treat* 2010; 21: 49-53.
- Chuang T, Stitle L, Brashear R, et al. Hepatitis C virus and lichen planus: a case control study of 340 patients. *J Am Acad Dermatol* 1999; 41: 787-9.
- Torrente-Castels E, Figueredo R, Berini-Aytes L, et al. Clinical features of oral lichen planus. A retrospective study of 65 cases. *Med Oral Patol Oral Cir Bucal* 2010; 14: 25-9.
- Munoz-Corcuera M, Esparza-Gomez G, Gonzales-Moles M, et al. Oral ulcers: clinical aspects. A tool for dermatologists. Part I. Acute ulcers. *Clin Exp Dermatol* 2009; 34: 289-94.
- Hanifin J, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol Suppl (Stockh)* 1980; 92: 44-7.
- Gliński W, Kruszewski J, Silny W, et al. Postępowanie diagnostyczno-profilaktyczno-lecznicze w atopowym zapaleniu skóry. Konsensus grupy roboczej specjalistów krajowych ds. dermatologii i wenerologii oraz alergologii. *Post Dermatol Alergol* 2004; 6: 265-77.
- Van der Wall R, Schulten E, van de Scheur M, et al. Cheilitis granulomatosa. *J Eur Acad Dermatol Venereol* 2001; 15: 519-23.
- Miescher G. Über essentielle granulomatose makrocheilie (cheilitis granulomatosa). *Dermatologica* 1945; 91: 57-85.
- Allen C, Camisa C, Hamzeh S, et al. Cheilitis granulomatosa: report of six cases and review of the literature. *J Am Acad Dermatol* 1990; 23: 444-50.
- Scully C, Cochran K, Russel R, et al. Crohn's disease of the mouth: an indicator of intestinal involvement. *Gut* 1982; 23: 198-201.

23. Stricker T, Braegger C. Images in clinical medicine. Oral manifestations of Crohn's disease. *N Eng J Med* 2000; 342: 1644.
24. Plauth M, Jenss H, Meyle J. Oral manifestations of Crohn's disease. An analysis of 79 cases. *J Clin Gastroenterol* 1991; 13: 29-37.
25. Handlers J. Oral manifestations of gastrointestinal disease. *J Calif Dent Assoc* 1999; 27: 311-7.
26. Zervou F, Gikas A, Merika E, et al. Oral lesions in patients with inflammatory bowel disease. *Ann Gastroenterol* 2004; 17: 395-401.
27. Nico M, Nakano de Melo J, Lourenco S. Cheilitis glandularis: a clinicopathological study in 22 patients. *J Am Acad Dermatol* 2010; 62: 233-8.
28. Eisenberg E. Cheilitis Glandularis. Available at: www.emedicine.com. 2010.
29. Butt F, Chindia M, Rana S, et al. Cheilitis glandularis progressing to squamous cell carcinoma in an HIV-infected patients – a case report. *East Afr Med J* 2007; 84: 595-8.
30. Leao J, Ferreira A, Martins S, et al. Cheilitis glandularis: an unusual presentation in a patient with HIV infection. *Oral Surg Oral Med Oral Pathol Oral Radiol Oral Endod* 2003; 95: 142-4.
31. Rosińska A, Nistrata Z, Cichy W. Wpływ składników pokarmowych na stan fizyko-chemiczny skóry. *Przegl Dermatol* 2006; 93: 325-32.
32. Ackland M, Michalczyk A. Zinc deficiency and its inherited disorders – a review. *Genes Nutr* 2006; 1: 41-9.
33. Maverakis E, Fung M, Lynch P, et al. Acrodermatitis enteropathica and an overview of zinc metabolism. *Am Acad Dermatol* 2007; 56: 116-24.
34. Chodyncka B, Serwina, Klepacki A. Kiła. In: *Choroby przenoszone drogą płciową*. Mroczkowski T (ed.). Czelej, Lublin 2006; 245-330.
35. Scully C. Oral manifestations of HIV infection and their management. I. More common lesions. *Oral Surg Oral Med Oral Pathol* 1991; 71: 158-66.
36. Mirowski G, Hilton J, Greenspan D, et al. Association of cutaneous and oral diseases in HIV-infected men. *Oral Dis* 1998; 4: 16-21.
37. Erdal E, Zalewska A, Schwartz RA. Cutaneous manifestations of HIV disease. Available at: www.emedicine.com. 2009.
38. Reade P, Sim R. Exfoliative cheilitis: a factitious disorder. *J Oral Maxillofac Surg* 1986; 15: 313-17.
39. Bacci C, Valente M. Successful treatment of cheilitis granulomatosa with intralesional injection of triamcinolone. *J Eur Acad Dermatol Venereol* 2010; 24: 363-4.
40. Shah A, Doherty S, Rosen T. Actinic cheilitis: a treatment review. *Int J Dermatol* 2010; 49: 1225-34.
41. Kano Y, Shiohara T, Yagita A, et al. Treatment of recalcitrant cheilitis granulomatosa with metronidazole. *J Am Acad Dermatol* 1992; 27: 629-30.
42. Rossi R, Assad GB, Buggiani G, Lotti T. Photodynamic therapy: treatment of choice for actinic cheilitis? *Dermatol Ther* 2008; 21: 412-5.
43. Sotiriou E, Apalla Z, Koussidou-Erremonti T, Ioannides D. Actinic cheilitis treated with one cycle of 5-aminolaevulinic acid-based photodynamic therapy: report of 10 cases. *Br J Dermatol* 2008; 159: 261-2.
44. Mathelier-Fusade P. Cheilitis: a new manifestation of gastro-oesophageal reflux. *Ann Dermatol Venerol* 2009; 136: 887-9.
45. Barlett D, Evans D, Anggiansah A, et al. A study of the association between gastro-oesophageal reflux and palatal dental erosion. *Br Dent J* 1996; 181: 125-31.
46. Arkuszewska C, Stowik-Rylska M, Sysa-Jędrzejowska A, et al. Zespół Melkerssona-Rosenthala mylnie rozpoznawany jako nawracający obrzęk Quinckego. *Post Dermatol Alergol* 2007; 24: 202-5.
47. Sobjanek M, Żelazny I, Włodarkiewicz A, et al. Zespół Melkerssona-Rosenthala. Opis przypadku i przegląd piśmiennictwa. *Post Dermatol Alergol* 2008; 25: 43-7.