Facial and perioral primary impetigo: a clinical study

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Impetigo is the most common skin infection in children. The face, especially the perioral region, is one of the most frequently involved areas. Impetigo is a disease that interests the pediatric dentist, as it poses significant problems in its differential diagnosis from other conditions. Sixteen otherwise healthy children were examined suffering from facial and perioral impetigo. The typical clinical appearance was scattered, painless, slightly pruritic erosions covered by "honey-colored" crusts. In 4 children impetigo was localized in the facial and perioral area, whereas in all other cases lesions were diffused in perioral area and several regions throughout the body. Four children exhibited neck lymphadenopathy and one had mild fever. The treatment of impetigo included the application of topical measures with the systemic antibiotic chemotherapy.
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INTRODUCTION

Impetigo comprises the most common skin infection (dermatosis) in children. It is of bacterial etiology, caused by *Staphylococcus aureus* and *Streptococcus pyogenes (GAS)*, in combination or individually.[1] The bacteria can cause superficial infections of the epidermis characterized by vesicles and/or ulcers, followed by crusted erosions. The disease is contagious and the means of spread are mainly the contact with infected playmates and contaminated objects, such as toys. The infection may arise as primary infection by means of minor superficial breaks in the skin or as secondary infection superimposing preexisting dermatoses (impetiginization or secondary infection) or certain systemic diseases (i.e. diabetes mellitus).[2,3] Abrasions, neglected minor trauma etc., can provide the portal of entry and prior antibiotic therapy instigates the development of impetigo.[2,4] Immunodeficiency also plays a key role in the manifestation of impetigo.[5,6] Thus, impetigo has been observed in children with underlying impaired immunity as HIV-infection (AIDS) or kidney transplantation.[5-7]

The face (commonly the perioral region) is one of the most frequently involved areas. The reason for this fact is the colonization of the perioral skin and nares by *S. aureus* and *GAS*, which is promoted by warm ambient temperature, high humidity, poor hygiene, crowded living conditions.[2]

The incidence of impetigo culminates during the warm, humid summer months[8] and in overcrowded areas with poor socioeconomic status.[9]

It is speculated that impetigo is a disease that interests mainly pediatric dentist as well as the specialists in oral medicine, as poses significant problems in its differential diagnosis from other conditions.

The purpose of the present study is to describe the facial and perioral lesions pertinent to impetigo in otherwise healthy children.

PATIENTS AND METHODS

In a one-year period (January 2003 to February 2004), we tried to locate children suffering from facial and perioral impetigo. During this period, we examined 16 consecutive patients (7 boys and 9 girls). None of the patients had any other concurrent or underlying disease and the impetigo was characterized as primary infection.

Clinical information of the patient and follow-up

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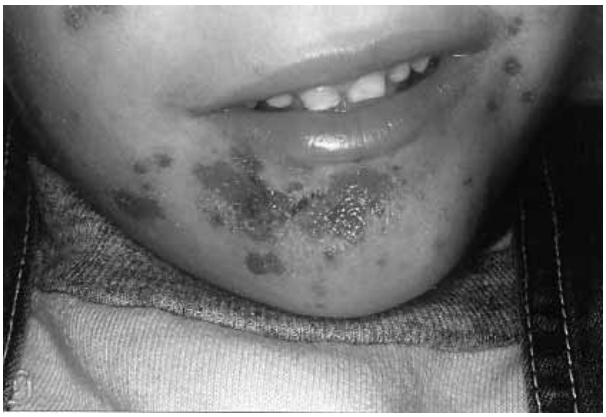

Figure 1. The typical clinical appearance of impetigo. Scattered painless, slightly pruritic erosions covered by "honey-colored" crusts.

were obtained by a specialist in oral medicine with collaboration of a dermatologist. In the first examination, diagnosis was established (based on the medical history and the clinical manifestations) and the children underwent the appropriate treatment. The follow-up continued until the disease totally resolved.

RESULTS

Patient characteristics

The study population comprised of 16 otherwise healthy children (9 females and 7 males). The mean age of patients was 4.5 years with a range from 2.5 to 11 years.

Presenting symptoms

The typical clinical appearance was scattered painless, slightly pruritic erosions covered by "honey-colored" crusts (Figure 1). In some cases (the early diagnosed) disseminated erythematous regions intermingled with the typical erosions covered by crusts (Figure 2). As far as the lately diagnosed cases are concerned, the lesions were characterized by the presence of scaling (Figure 3). In terms of location, in 4 cases impetigo was exclusively confined in the facial and perioral region. The remainder had an invariable distribution-along with the facial region- throughout the patients' body, such as the nuchal-postauricular region, the thorax, the buttocks and the extremities. In all cases the majority of lesions located in the facial and perioral region.

All patients were free of systemic symptoms, except for one case in which the patient was febrile (38°C) from the first day of symptoms onset. The fever had 3-day duration and the temperature involuted before the start of treatment. At the time of diagnosis 4 cases (3 female and I male) exhibited neck lymphadenopathy. The nodes were moveable, painful in palpation and had firm consistency. These findings were consistent with an inflammatory process. History revealed that the disease commenced 2 to 5 days before diagnosis was established and the mean duration of the disease was 9 days.

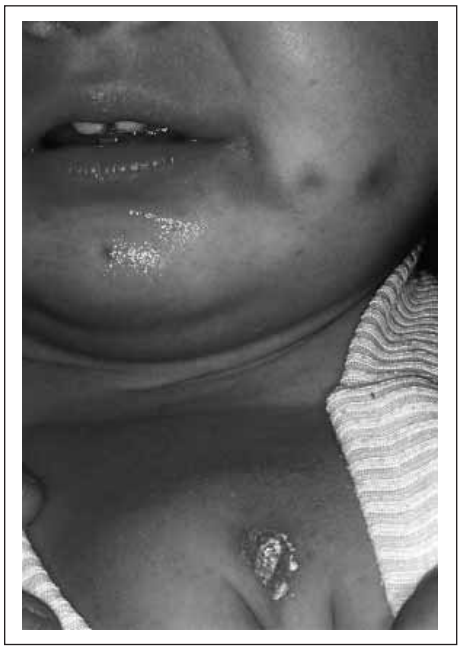

Figure 2. In some cases there are disseminated erythematous regions intermingled with the typical erosions covered by crusts.

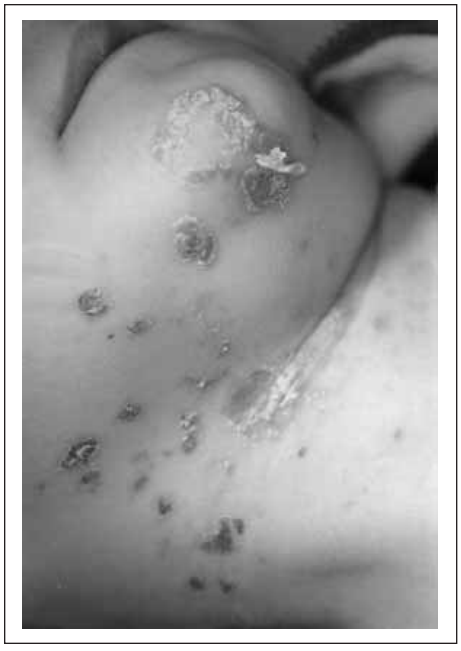

Figure 3. In neglected cases the lesions were characterized by the presence of scaling.

Treatment

The treatment of impetigo included the application of topical measures, such as removal of the crusts and cleansing of the wound and application of topical cream mupirocin 2% w/w (twice a day, for 5 days) along

with the systemic antibiotic chemotherapy. Indeed, we administered clarithromycin per vs (the dosage was commensurate to the age of patient). The tried therapy was proved effective, as we manage to eliminate impetigo in all cases. The lesions completely resolved 3-6 days after treatment.

DISCUSSION

Several clinical variants of the disease have been reported,[2,3,10-12] which have as common denominator the bullous and nonbullous (impetigo contagiosa) forms of impetigo.

Bullous impetigo (staphylococcal impetigo) most frequently affects the neonates,[3] but may occur in young adults.[2] Typically it occurs on the face, but it may affect any body surface.[10] There may be a few lesions localized in one area; nevertheless, in some cases the lesions may be so numerous and widespread that resemble poison ivy.[10] One or more vesicles enlarge rapidly to form flaccid bullae, in which the contents turn from clear to cloudy. Subsequently, the center of the thin-roofed bulla collapses, but the peripheral area may retain fluid for many days. A subtle, flat, "honey-colored" crust may appear in the hub and, if removed a bright red, inflamed, moist base that oozes serum will be encountered. The peripheral lesion may dry without forming a crust, leaving a typical collarete of scale.[3] In some neglected cases the lesions may extend radially forming narrow blisters which reach 2 to 8cm and may remain for months. Hyperpigmentation in blacks is the only complication involved with the healing process.[10]

Nonbullous impetigo is the most prevalent type of impetigo and admittedly the most common childhood skin infection.[11] It generally originates as a single 2-4mm erythematous macule, which soon becomes vesicular or pustular.[3] The vesicles are thin-roofed and easily rupture, leaving erosions, which in turn are covered by characteristic-but not pathognomonic 2 "honey-colored" crusts. There is a surrounding erythema. Satellite lesions may appear beyond the periphery. [10]

Pruritus and regional lymphadenopathy are not rare[1], especially in the nonbullous form.[10]

Etiopathogenetically, bullous impetigo is attributed to *Staphylococcus aureus* (*S. aureus*). Koning *et al*.[13] point out that nasal carriage of *S. aureus* is an important predisposing factor for the development of bullous impetigo. Hanakawa *et al*.[14,15] found that exfoliative toxins A and B (ETA, ETB) specifically disassemble desmoglein I (Dsg-1), a desmosomal cadherin that mediates cell adhesion. Furthermore, they state that ETA and ETB are serine proteases that specifically bind to and cleave a calcium-dependent conformation of Dsg l at a unique site after a glutamic acid residue. ETA and ETB's presumptive active site contains the catalytic triad of serine 195, histidine 57 and aspartic acid 102,[14] whereas, Sakurai *et al*.[16] believe that Tyrosine-157 and Tyrosine-159 residues of ETB are essential for its toxicity and antigenicity.

The specific location of the bullae in the subcorneal cell layer is explained by the "desmoglein compensation hypothesis." This hypothesis states that in areas of epithelium where both Dsg-1 and Dsg-3 are expressed, a spontaneous blister will not occur after Dsg-I is hydrolyzed, because Dsg-3 compensates. Nevertheless, if only Dsg l is present, a blister will occur. In mucosae and deep layers of epidermis both Dsg-l and Dsg-3 are represented, whereas only Dsg I was found in the superficial layers of epidermis. This fact elucidates the clinical presentation of bullous impetigo.

On the other hand, nonbullous impetigo is ascribed to group A beta-hemolytic streptococcus *(GAS)*,[3] albeit *S. aureus* has been implicated in this concrete disorder more frequently (staphylococcal exotoxins ETA and ETB were isolated from nonbullous specimen).[13,17] Moreover, it is postulated that when *GAS* is dominant in number, thick-walled pustules with an erythematous base are the early manifestations.[18] Among *GAS* strains, the *emm* pattern D strains are more likely to cause impetigo, whereas the *emm* patterns A, B and C are more likely to cause pharyngitis.[19,20]

It is well known that the nares consist a nidus for both *GAS* and *S. aureus* and the corneum stratum is a potent physical barrier. Whenever an epithelial lysis of the cornea! layers occurs, *GAS* gains access to epidermal keratinocytes. Darmstadt *et al*.[21,22] opine that *GAS* adheres preferentially to receptors predominantly present on terminally differentiated keratinocytes. Svensson *et al*.[23] point out that the early phase of the *GAS* infection is instituted by secretion of a molecule with cysteine protease activity (namely SpeB) and is subsequently established and disseminated (at the exponential phase of growth) by means of streptokinase and plasminogen activation molecule (PAM). There is plausible evidence that inflammatory exudate, PMNs and cytokines TNF-alpha provide the nutritious medium for the bacterial proliferation and expansion of impetigo.[23]

On the contrary, Darmstadt *et al*.[24] suggest that TNF-alpha and IL-Ia impede streptococcal adherence and diminish its ability to form a nidus of infection in the skin.

Complications concerning impetigo are hives, kidney disease and scarlet fever.[8] Osteomyelitis, arthritis, pneumonia, as well as meningitis may complicate bullous impetigo.[3,10] In nonbullous impetigo the most severe complication is acute glomerulonephritis, which affects up to 5% of the patients. The serotypes of streptococcus isolated in acute glomerulonephritis are 1,4,12,25 and 49.[25] In children, the infection normally subsides without sequelae, whereas the effects may be long term in adults.[3] Ardiles *et al*.[26] detected anticardiotipin antibodies in the serum of patients with nonbullous impetigo, but free of renal involvement. This finding was initially linked to the risk of thrombosis;

Table 1. Diseases to be ruled out in differential diagnosis of impetigo

Bullous	Non-bullous
Pemphigus vulgaris	Herpes simplex
Bullous pemphigoid	aricella (Shingles)
Thermal burns	Atopic dermatitis
Stevens-Johnson syndrome	Contact dermatitis
Bullous erythema multiforme	Dermatophytosis
Necrotizing fasciitis	Candidiasis
Epidermolysis bullosa	Scabies
	Pediculosis
	Discoid lupus erythematosus
	Angular cheilitis

nonetheless, it was unrelated to glomerular disease.

The differential diagnosis of impetigo involves the diseases tabulated in Table 1. The outlook of impetigo is unpredictable. It may resolve spontaneously without scarring or become chronic and widespread.[10] As far as the treatment is concerned, Brown *et al*.[3] recommend that before antimicrobial therapy is initiated, bacterial cultures from cutaneous lesions should be taken. Local wound care, including cleansing, removal of the crusts and application of wet dressings can be helpful.[27] Topical antimicrobials are indicated in localized cases without complications. Mucopurin 2% ointment is considered a reliable and effective regimen in eliminating both *S. aureus* (methicillin-resistant strains included) and *GAS*. The usual therapeutic scheme is 3 times daily application to the affected skin and to nares for 7-10 days.[2] Topical fusidic acid cream is also an effective treatment for impetigo with few side-effects, equivalent to mupirocin.28 Nishijim *et al.* [29] found that there were no strains of *S. aureus* isolated from impetigo, between 1994 and 2000, that were resistant to fusidic acid. Topical hydrogen peroxide cream is an alternative to fusidic acid for the treatment of nonbullous impetigo.[30] Tea lotion and cream are another alternative proposed for treatment of nonbullous impetigo.[31]

In terms of systemic administration of antimicrobials we should point out that they should cover Gram-positive bacteria and they are treatment of choice for widespread or refractory infections and infections complicated by systemic symptoms.[10] Penicillins resistant to acid and beta-lactamase such as isoxasolyl penicillins (dicloxacillin, cloxacillin etc) must be used. The newer macrolides, azithromycin and clarithromycin are also effective. Other alternative antimicrobials for the treatment of methicillin-resistant strains of *S. aureus*, include clindamycin, minocycline, or trimethoprim/sulphamethoxazol.[3] Nishijim *et al*.[29] found one strain *S. aureus* resistant to minocycline and ofloxacin, respectively, after 2000.

It is generally accepted that if the initial antimicrobial does not provoke a clinical response within 7 days of initiation of the treatment, noncompliance or antimicrobial resistance should be suspected, and a second sample of exudate should be sent for culture and sensitivity test.[3]

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