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Impetigo

Review article

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صدق الله العظيم

[المجادلة: 11]

Abstract

Impetigo is the most common bacterial skin infection in children between the ages of 2 and 5. There are two main types: non-bulbous (70% of cases) and bullous (30% of cases). Non-bullous impetigo was caused by Staphylococcus aureus or Streptococcus pyogenes and was characterized by honey-colored skin on the face and limbs. Impetigo primarily affects the skin a secondary infection and insect bites, eczema, or herpes lesions. Bullous impetigo caused only by S. aureus causes large, relaxed blisters and was more likely to affect the interstitial area. Both types usually resolve within a few weeks without scarring, and complications were rare, the most serious of which was streptococcal glomerulonephritis. Treatment includes topical antibiotics such as mupirocin, retapamulin, and fusidic acid. Oral antibiotic therapy can be used for impetigo with large blisters, or when topical therapy was not practical. Amoxicillin / clavulanate, dicloxacillin, cephalexin, clindamycin, doxicillin, minocycline, trimetoprim / sulfamethoxazole, and macrolides are optional, but penicillin is not .

Keywords: Impetigo; Staphylococcus aureus; Streptococcus pyogenes.

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Abbreviation

EDIN: Epidermal Cell Differentiation Inhibitor

ETA: Exfoliative Toxin A.

ETB: Exfoliative Toxin B.

GAS: Group A Streptococcus

MRSA: Methicillin Resistant Staphylococcus aureus.

MSSA: Methicillin Sensitive Staphylococcus aureus.

MSCRAMM: Microbial Surface Component Recognizing Adhesive Matrix Molecules.

PMN: Polymorphonuclear Cells.

PSGN: Poststreptococcal Glomerulonephritis.

RBC: Red Blood Cell.

Introduction

Impetigo is a common acute superficial bacterial skin infection (pyoderma) which is highly contagious. It is characterized by pustules and honey-colored crusted erosions ("school sores"). Impetigo involves the epidermis and is seen mostly in preschool children. It is caused by two microorganisms: S. aureus and GAS, other bacterial infections that involve deeper parts of the skin are erysipelas and cellulitis. Erysipelas involves the upper dermis and is most commonly caused by B-hemolytic streptococci. Cellulitis involves the deeper dermis and subcutaneous fat and is most commonly implicated by S. aureus and GAS. It can be divided into nonpurulent and purulent cellulitis, and treatment is based on extent of infection and risk factors. Abscesses involve the dermis and deeper skin tissues as a result of pus formation [1].

Impetigo is observed most frequently among children 2-5 years of age and is transmitted through direct contact ٭ Risk factors for impetigo include poor hygiene، low economic status, crowding and underlying scabies . Important consideration is carriage of GAS and S. aureus which predisposes to subsequent impetigo, Over 140 million people are suffering from impetigo at each time point, over 100 million are children in the past impetigo was caused by either S. aureus or group A β-hemolytic streptococci. Currently، however, the most frequently isolated pathogen in cases of impetigo is S. aureus [2].

The first type of impetigo is impetigo contagiosa، known as non-bullous impetigo and this is one of the most common skin infection in children, differential diagnoses for this type are atopic dermatitis، candidiasis, contact dermatitis and other, the second type of impetigo, bullous impetigo, is caused exclusively by S. aureus. Differential diagnosis for this type is bullous erythema multiforme, bullous lupus erythematosus, bullous pemphigoid etc [3].

Treatment options for impetigo can be divided into topical and systemic. Among topical, mupirocin and fusidic acid are most commonly used, systemic antibiotic is usually reserved for more severe cases, in which topical therapy is impractical, such as cases of bullous impetigo or widespread lesions [1].

Epidemiology

Over 140 million people are suffering from impetigo at any time point; 100 million are children, in the United Kingdom, the annual incidence of impetigo is 3 percent in 2018 among children up to the age of four and 1.6 percent among children aged five to fifteen years .

Although incidence estimations do exist, they are all based on a limited literature review of impetigo in the context of larger studies and no update has recently been done, furthermore, the most available data arrives from records of hospital departments, which may under represent the true population prevalence of skin diseases , another cross sectional study which took place (n ،265 =relative prevalence 5.3%, among 50,237 outpatients (showed a pattern of male predominance in childhood، adulthood and overall (OR 2.0) [3].

Impetigo is a highly contagious infection, direct contact being the main mode of transmission. Patients with impetigo can easily inoculate themselves and spread the infection to people in close contact after excoriating an infected area. This fact may lead to a rapid dissemination of infection, mostly in grade schools, kindergartens، nurseries and day care centers. It is known today that children usually become infected through contact with other children; however, fomites are another important source of infection. Adults may develop impetigo from contact with children or by fomites as seen when sharing grooming devices, in barber shops, in beauty parlors etc, the incidence of impetigo is greatest during the summer time due to the close contact among children، interestingly, in tropical regions GAS causes impetigo، while in temperate areas it leads to pharyngitis [5].

Microorganisms associated with Impetigo

Impetigo is mainly caused by Staphylococcus aureus and sometimes by Streptococcus pyogenes. Both bullous and non-blistery are primarily caused by Staphylococcus aureus, and streptococci are often involved in non-blistery morphology. Looking at all age groups, the incidence is the same for men and women [6].

GAS

GAS, is a gram positive bacterium, whose reservoirs are the human mucosal membranes and skin surface، causes an array of infections involving the respiratory tract and soft tissues, ranging in severity from mild to severe. Moreover, it initiates two nonsuppurative sequels: Acute rheumatic fever and PSGN, the capsule, made from hyaluronic acid, functions as an accessory virulence factor. It prevents phagocytosis by PMN and macrophages of the host. A great variation exists with regard to the level of encapsulation, the capsule possessed by GAS is similar chemically to the one found in the connective tissue of humans, hence, it is a poor immunogen, and no antibodies production has been demonstrated in humans against this structure, the major somatic virulence factor of GAS is protein M. This protein is known to confer resistance to phagocytosis by PMNs. It also gives GAS the ability to multiply quickly in fresh human blood and to initiate diseases, recent reports have demonstrated that pili are involved in the formation of biofilms and in the adherence of GAS to human tonsils, keratinocytes, lung and throat epithelial cells, which distinguishes it as a major adhesion of the organism [7].

GAS possesses numerous extracellular products during its growth both in vivo and in vitro (such as hemolysin)، however, only a limited number have been well characterized. Two types of hemolysin have been described in the literature. The first hemolysin is streptolysin O. This molecule can be inhibited in a reversible manner by oxygen and irreversibly by cholesterol, apart from being toxic to RBC, it is toxic to other cells and some cell fractions, such as PMNs and platelets. The production of streptolysin O occurs in almost all strains of GAS, as well as in many organisms classified in groups C and G and it is antigenic in origin. The measurement of antibodies targeted to streptolysin O in the human sera can indicate recent streptococcal infection. The second hemolysin to be described is streptolysin S, obtained by strains that grow in the presence of serum, biopsies taken from pyodermal lesions often reveal GAS [8].

To a much smaller extent, there is involvement of serogroups C and G. GAS associated with impetigo is different from those which are connected to pharyngitis and tonsillitis. Skin strains belong to different M serotypes than the classic throat strains. Various tests, seeking streptococcal antibodies play no part in the diagnosis of impetigo; however, they can support the evidence of recent streptococcal infection in patients with suspicious PSGN. The response of anti-streptolysin O to GAS in patients with impetigo is relatively weak, probably due to inhibition of streptolysin O by skin lipids, such as cholesterol [9].

Staphylococcus aureus

Members belonging to staphylococcus genus are gram-positive cocci, with a diameter ranging between 0.5to 1.5 μm, and occur singly and in pairs, tetrads، short chains and irregular grapelike clusters. Staphylococci are not motile, not spore forming and are usually positive to catalase, S. aureus is a highly successful opportunistic pathocrobiological gen. It frequently colonizes the mucosal surfaces and the skin. It is found in 30% of the healthy human population within the anterior nares. S. aureus causes a wide variety of diseases. Apart from infections where it is physically present, S. aureus can cause “distant” diseases, through the secretion of various toxins, those toxins may either be produced in a direct way by the bacteria on the surface which it colonizes or in an indirect manner through the colonization of food or beverages, the ability of the bacterium to cause many different diseases is related to its capacity to adapt and survive in a great variety of environments, skin infections, together with respiratory tract ones، are the most common infections caused by this pathogen [10].

Infections of the respiratory tract are mostly nosocomial، whereas those of the skin are usually community acquired. Pneumonia caused by S. aureus usually develops in hospitalized patients with an underlying condition، such as immune deficiencies or infections caused by different viruses. This bacterium may also cause a variety of other, sometimes severe as well as life-threatening diseases; among them are infective endocarditis، osteomyelitis, SSSS and toxic shock syndrome, initiation of various skin infections is done through ETA and ETB which are active serine proteases produced by some strains of S. aureus. While ETA is encoded on a prophage, ETB is encoded on a large penicillinase type plasmid. ETA and ETB lead to epidermal cleavage، through the effect on desmogelin-1 which is a desmosomal cadherin. This cleavage is directly responsible for the clinical manifestation of the blistering skin disease: Pemphigus

neonatorum and/or generalized staphylococcal scalded skin syndrome in neonates, and bullous impetigo in young children and adults [11].

Although similar dermatologic effects exist, strains producing ETB are assumed to be more virulent. Reports have shown that the activity of ETB can be enhanced by EDIN, which facilitates the formation of disseminated foci and serves a risk factor for deep-seated staphylococcal tissue infections following bacteremia, in order to make a diagnosis based on phenotypic characteristics, and to reveal new, yet unknown mechanisms which confer antibiotic resistance, it is crucial to obtain a culture. Colonies grown should be Gram stained and subcultured and further tested for their genus، species, as well as antibiotic susceptibility, out of the clinical isolates of S. aureus, over 90% have elaborated a capsule made of polysaccharides, the capsule was found to exist among 11 serotypes, %75 of clinical infections are attributed to capsule type 5and type 8. These two are composed of different sugars، among them are fucose and mannose, both these capsules have antiphagocytic properties and lead to an increase in virulence in several animal models. Animal models of sepsis have shown that antibodies against these capsular types are protective. Although the vaccine showed some promise in an initial Phase 3 trial in ESRD patients on hemodialysis, it was found to be ineffective in a second Phase 3 trial, leading to its development being halted [12].

Various surface adhesions are carried by S. aureus. These permit the adherence to different host matrix proteins. Those microbial surface components which react with the adherence matrix molecules are reassembled under the acronym MSCRAMM. Most of these molecules are bound to the peptidoglycan component of the cell wall. A conserved mechanism which permits the anchoring of the adhesive molecule exists in gram positive bacteria. This mechanism involves a membrane bound enzyme, called sortase, which has the ability to recognize a conserved amino acid motif (LPXTG) at the carboxyl terminal end of wall attached proteins. Sortase binds the threonine residues of LPXTG in a covalent way to a free acceptor in the peptidoglycan side chain, usually glycine in the case of S. aureus, among the MSCRAMM, clinical significance is attributed to clumping factor B, which assists in the colonization of the nasal epithelium, clumping factor A and fibronectin binding proteins A and B which play a role in the development of endocarditis as well as in ventricular assisted device-related infections. It is important to note that S. aureus harbors many MSCRAMMs at their surface, hence, inactivation of

only one molecule may not be noticed as its function can be complemented by others [13].

In a study conducted on 60 patients with impetigo، only one patient grew GAS, six grew S. aureus and GAS and the rest had S. aureus. It is important to note that problems may be encountered when interpreting the results of skin culture and wound, as they are not sterile، and the detection of a common colonizing organism، for example S. aureus, may point to a contamination [14].

Men are affected more often in adults.

Most common in children over the age of 25, but can occur at any age. The peak frequency is summer and autumn. Bullous impetigo is common in infants. children under the age of 2 account for 90% of cases of bullous impetigo. Host factors such as skin barrier integrity at acidic pH, presence of sebum secretion (fatty acids, especially oleic acid), lysozyme and defensin production, and proper nutritional status play important roles in resistance to infection . Softening, water, previous skin lesions, obesity, corticosteroid or chemotherapy treatment, leukemia cell disorders such as leukemia and chronic granulomatosis, diabetes, malnutrition, and other congenital or acquired Immunodeficiency such as AIDS is a predisposing factor. Most bacteria grow best at neutral pH and temperatures of 37° C [15].

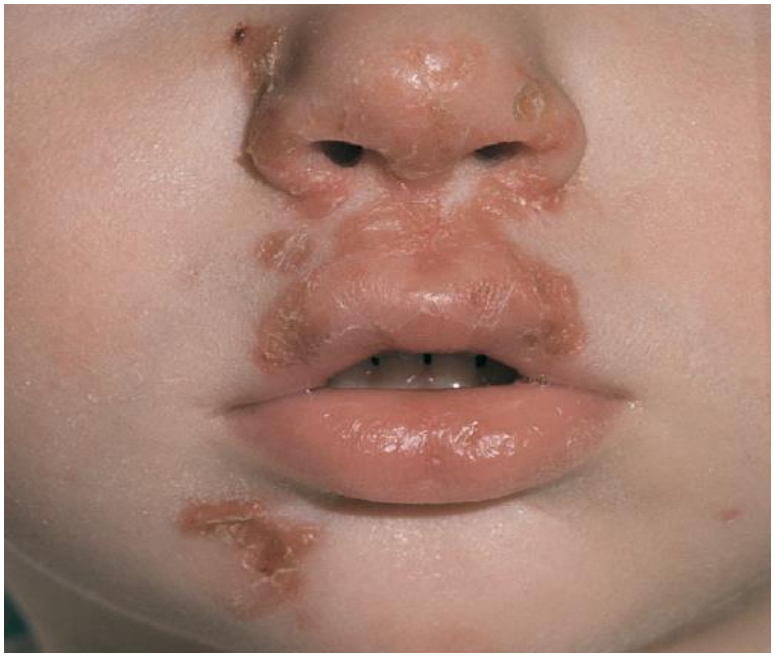

Figure 1. *Impetigo: MSSA Crusted erythematous erosions becoming confluent on the nose, cheek, lips, and chin in a child with nasal carriage of S. aureus.*

Clinical Presentation of Impetigo

Impetigo is a highly contagious infection with direct contact being the main mode of transmission ،a previously mentioned, children are the main ones to present with impetigo. Further populations that commonly suffer from impetigo are the homeless and patients who received organ transplants. An investigation of renal transplant recipients has found that impetigo was prominent in the first year following the transplant، with a peak being in the third month, and it did not affect a considerable number of recipients after the first year following the transplantation[16].

The most common locations for the lesions are head and neck (65.4%), followed by upper extremity(%19.6) and trunk and lower extremities (7.5% each), there are two forms of impetigo, non-vesicular (also known as impetigo) and bullous. Non-bullous impetigo: The most common form and can be further classified as a primary or more general secondary (general) form. Primary impetigo is a direct bacterial invasion of intact, healthy skin. Secondary (common) impetigo is a bacterial infection of the damaged skin caused by trauma, eczema, insect bites, scabies or herpes outbreaks, and other diseases, diabetes or other underlying systemic diseases also increase susceptibility, impetigo begins as a patchy papular lesion that transforms into thin-walled vesicles that burst rapidly, with superficial, sometimes itchy or painful erosions covered with classic honey-colored skin, leave behind. If left untreated, the course of infection may take 2-3 weeks, when the crust dries, the rest will heal without scars. The exposed skin of the face (nostrils, perioral area, etc.) and limbs are the most commonly affected areas. Local lymphadenitis may occur, but systemic symptoms are unlikely. Non-bullous impetigo is usually caused by Staphylococcus aureus, but S. Streptococcus pyogenes can also be involved in particularly warm and moist climates. Bullous impetigo: Caused only by Staphylococcus aureus and is characterized by large, fragile, flaccid blisters that can rupture and leak yellow fluid. It usually disappears within a few weeks without leaving a scar. After the bladder ruptures, a pathological scaly collar develops around it, leaving a light brown skin on the remaining erosions [17].

These larger bubbles are formed due to the exfoliating toxin produced by the Staphylococcus aureus strain that causes the loss of cell adhesion in the epidermis. Bullous impetigo is usually found in the trunk, armpits, limbs, and interstitial (diaper) areas. This is the main cause of ulcerative rashes on the buttocks of infants. Systemic symptoms are rare, but include fever, diarrhea, and weakness, relationship between impetigo and its COVID19: Long-term use of the mask not only exacerbates existing facial dermatitis (acne, rosacea or perioral dermatitis), but also mechanical and occupational dermatitis (irritation) of acne caused by the mask material and prolonged contact. It also increases the incidence of both sexual and allergic contact eczema) caused by the wearer. The increased warmth and moisture of the facial skin due to exhaled air and sweating prevented the skin's moisture and caused an occlusive effect that stimulated the sebaceous ducts with changes in the skin's microflora. It leads to the activation of S. aureus, for example using sebum to cause individual infections from the standpoint of proper skin hygiene. To avoid excessive washing, use a mild detergent close to the skin's natural pH (pH 5) and add a non-comedogenic moisturizer [18].

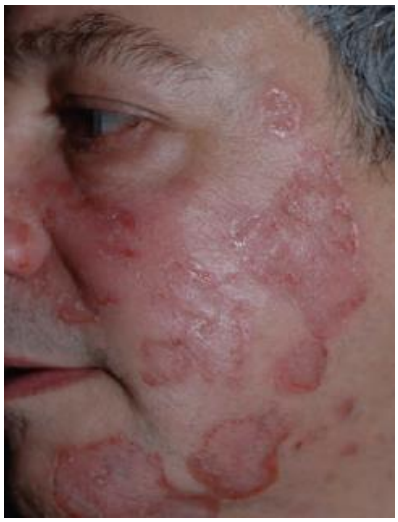

Fig.2*: Impetigo: MRSA*

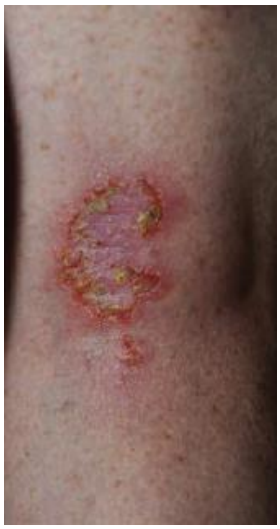

Fig.3 *: Secondary infection of Hailey–Hailey disease: MRSA*

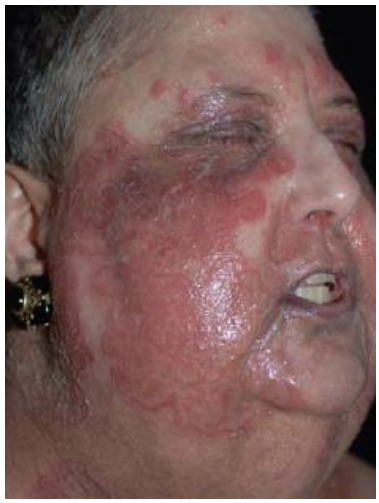

Fig.4: *Secondary infection of pemphigus foliaceus: MRSA*

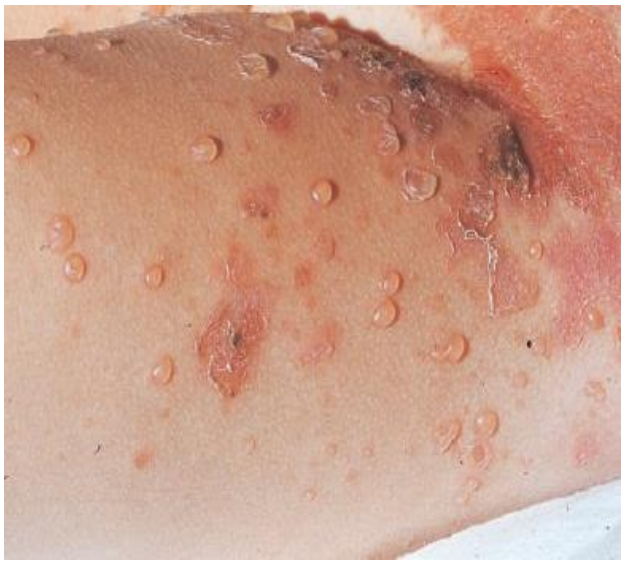

Fig.5: Bullous impetigo. *Scattered, discrete, intact, and ruptured thin-walled blisters on the inguinal area and adjacent thigh of a child; lesions in the groin have ruptured, resulting in superficial erosions.*

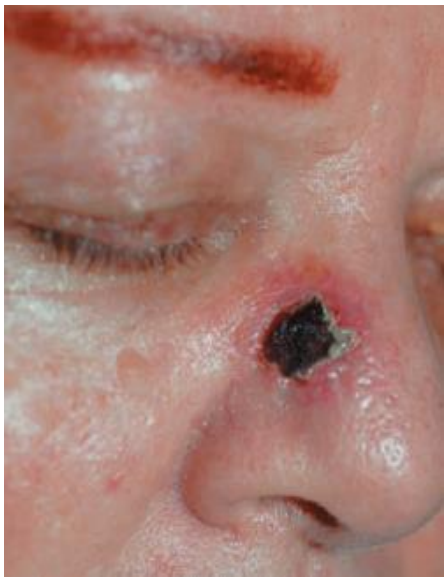

Fig. 6: Ecthyma MSSA. *Thickly crusted erosion/ulcer on the nose had been present for 6 weeks, arising at the site of a small wound. The crust was adherent and the site bled with debridement.*

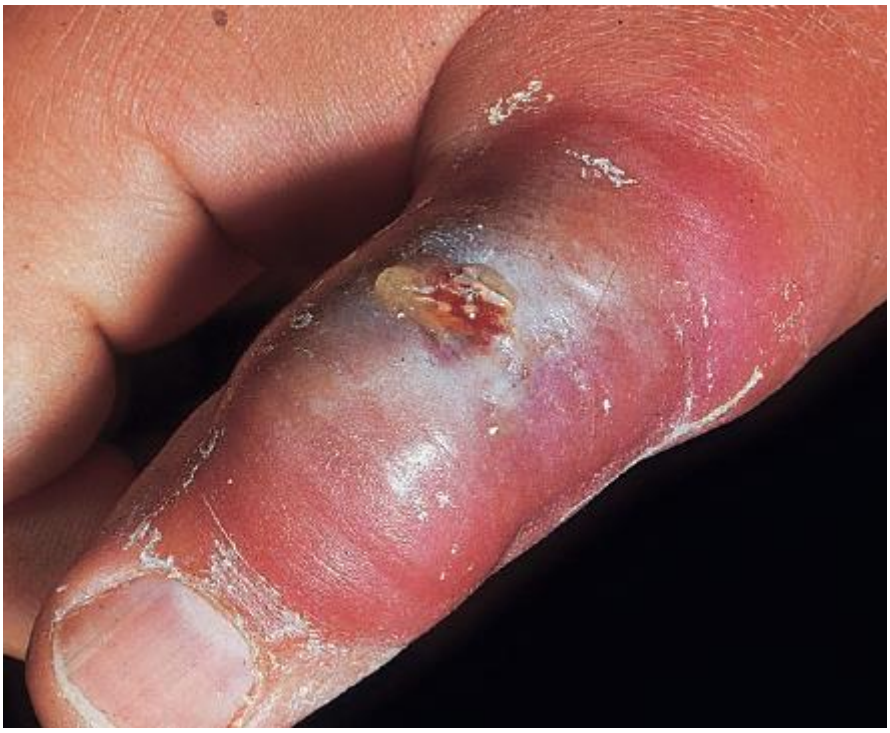

Fig.7: Bullous impetigo with blistering dactylitis: S. aureus*. A large, single bulla with surrounding erythema and edema on the thumb of a child; the bulla has ruptured and clear serum exudes.*

Diagnosis

Diagnosis of non-vesicular and bullous impetigo is almost always clinical. The differential diagnosis includes many other blisters and rash conditions. Skin swabs cannot distinguish between bacterial infections and colonization, in patients who fail first-line treatment, pus or bullous fluid cultures, rather than intact skin, may help identify pathogens and are susceptible to antibiotics. Serological testing of streptococcal antibodies is useful in diagnosing streptococcal acute glomerulonephritis, but not in impetigo [19].

Impetigo contagiosa typically presents with a single، two to four mm erythematous macule, which quickly becomes vesicular or pustular. Due to their delicacy، the vesicles can easily rupture, leaving an exudate with a characteristic "honey-colored" yellow crust over the superficial erosion. Several individual or coalesced macules and patches erupt due to the direct extension of the primary lesion, which quickly follows. The macules and patches may be eroded or crusted, when GAS is in high number, pustules with a thick wall and with an erythematous base are an early manifestation, the nares and the perioral region are the surfaces that are subjected to environmental trauma and are involved most often. Very often, a linear distribution may be observed when the patient's fingernails have scratched the skin. Most often the patients only show skin lesions; however، mild lymphadenopathy is a systemic symptom which is frequently encountered، an important complication of impetigo contagiosa is acute PSGN, which affects up to 5% of the patients, few strains of streptococcus are known to commonly affect kidney; among them are serotypes 1, 4, 12, 25 and 49

Appropriate treatment with antimicrobials is generally believed to have no effect on the risk of PSGN (Table 1) .

Bullous impetigo, the second type of disease presentation، is caused exclusively by S. aureus, it is characterized by fragile, large, flaccid bullae that can rupture and ooze yellow fluid. It often resolves within a period of two to three weeks without scarring, this form of impetigo most frequently affects the neonates, and S. aureus can be isolated from the skin lesions, at first, the large and fragile bullae can develop on the trunk and extremities, and it may also affect the anogenital area and buttocks of infants, being one of the most common causes of ulceration in these regions, most frequently, only remnants of the bullae are seen، and they are observed as oval or annular superficial erosions with typical collaret of scale at the periphery of the bulla [20].

An epidermal separation often occurs due to an exotoxin produced by the pathogen, often made by phage group 2 , S. aureus ETA and ETB, which show extreme specificity in causing loss of cell adhesion in the superficial epidermis, brings about the formation of blisters by splitting the granular cell layer of the epidermis (Table 2) [21].

Table 1: Differential diagnoses of impetigo contagiosa.

Diagnosis	Distinguishing features
Atopic dermatitis	Chronic or relapsing pruritic lesions and abnormally dry skin; there is marked lichenification on the flexural areas which distinguishes it from impetigo
Candidiasis	Erythematous papules or red, moist plaques; unlike impetigo, this disease is usually confined to the mucosal surfaces and intertriginous areas
Contact dermatitis	Pruritic areas with weeping on sensitized skin that comes in contact with haptens (e.g.- poison ivy)
Dermatophytosis	Lesions may be scaly and red with slightly raised "active border" or classic ringworm; or may be vesicular, especially on feet
Discoid lupus erythematosus	Well-defined plaques with adherent scale that penetrate into hair follicles
Ecthyma	Crusted lesions that cover an ulceration, unlike impetigo in which there is an erosion only. The ulceration may persist for weeks and may heal with scarring as the infection extends to the dermis
Herpes simplex virus	Vesicles on an erythematous base that rupture to become erosions covered by crusts, usually on the lips and skin
Insect bites	Papules usually seen at site of bite, which may be painful; there may be an associated urticaria, which is not typical for impetigo
Pemphigus foliaceus	Crusts with occasional vesicles, usually starting on the face in a butterfly distribution or on the scalp, chest and upper back as areas of erythema, scaling, crusting, or occasional bullae
Scabies	Lesions consist of burrows and small, discrete vesicles, often in finger webs; nocturnal pruritus is characteristic
Sweet's syndrome	Abrupt onset of tender or painful plaques or nodules with occasional vesicles and pustules
Varicella	Thin-walled vesicles on an erythematous base that start on trunk and spread to face and extremities; vesicles break and crusts form. Unlike impetigo, in varicella the lesions are in different stages

Table 2: Differential diagnoses of bullous impetigo.

Diagnosis	Distinguishing features
Bullous erythema multiforme	Vesicles or bullae arise from a portion of red plaques, 1 to 5 cm in diameter, on the extensor surfaces of extremities, an unusual location for impetigo
Bullous lupus erythematosus	Widespread vesiculobullous eruption that may be pruritic; tends to favor the upper part of the trunk and proximal upper extremities
Bullous pemphigoid	Vesicles and bullae appear rapidly on widespread pruritic, urticarial plaques may appear, unlike in impetigo
Herpes simplex virus	Grouped vesicles on an erythematous base that rupture to become erosions covered by crusts, usually on the lips and skin; may have prodromal symptoms which are not usually observed in impetigo
Insect bites	Bullae seen with pruritic papules grouped in areas in which bites occur
Pemphigus vulgaris	Non-pruritic bullae, varying in size from one to several centimeters, appear gradually and become generalized; erosions last for weeks before healing with hyperpigmentation, but no scarring occurs
Stevens-Johnson syndrome	Vesiculobullous disease of the skin, mouth, eyes, and genitalia; ulcerative stomatitis with hemorrhagic crusting is the most characteristic feature. Ulcerative stomatitis is not seen in impetigo
Thermal burns	History of burn with blistering in second-degree burns
Toxic epidermal necrolysis	Steven-Johnson-like mucous membrane disease followed by diffuse generalized detachment of the epidermis. Much more severe than impetigo
Varicella	Thin-walled vesicles on an erythematous base that start on trunk and spread to face and extremities; vesicles break and crust forms; lesions of different stages are present at the same time in a given body area as new crops develop

Course

Untreated, lesions of impetigo may become more extensive and progress ecthyma. With adequate treatment، prompt resolution. Lesions can progress to deeper skin and soft-tissue infections, non-suppurative complications of GAS infection include guttate psoriasis, scarlet fever, and glomerulonephritis. Ecthyma may heal with scarring. Recurrent S. aureus or GAS infections can occur because of failure to eradicate pathogen or by recolonization. Undiagnosed MRSA infection does not respond to usual oral antibiotics given for methicillin-sensitive S. aureus [22].

Management

Patients with impetigo should keep the lesions clean and wash with soap and warm water to remove secretions and crusts, topical antibiotics are the best treatment for most cases of impetigo. There is strong evidence that topical antibiotics are superior, or at least equivalent, to oral antibiotics in the treatment of localized impetigo, in addition, oral antibiotics have more side effects than topical antibiotics. For localized, uncomplicated, bullous impetigo, topical therapy is the only treatment of choice [23].

Before topical antibiotic therapy, the crust should be removed with soap and water. Mupirocin and fusidic acid are the first choices. Fusidic acid is very effective against Staphylococcus aureus, has good penetration into the skin surface, and has a high concentration at the infected site. It is also effective against Streptococcus and Propionibacterium acnes. Gramnegative bacilli are resistant to fusidic acid. Resistance, in vitro and in vivo, to fusidic acid has been verified but at low levels. As it belongs to the fusidanes group, it has a very different chemical structure from that of other classes of antibiotics, such as betalactams, aminoglycosides and macrolides, thereby reducing the possibility of crossresistance. The incidence of allergic reactions is low and cross allergy has not seen [24].

Mupirocin (Pseudomonas acid A) is the main metabolite of Pseudomonas fluorescence fermentation, its chemical structure has nothing to do with antibacterial agents and due to its unique mechanism of action, it is not cross-resistant to other antibiotics. Mupirocin functions by inhibiting bacterial protein synthesis through binding to the isoleucine tRNA synthetase enzyme, preventing the uptake of isoleucine into the protein chain, very effective against Staphylococcus aureus, Streptococcus pyogenes, and all other streptococcal species except Group D. Bordetella pertussis and Moraxella catarrhalis. It has no effect on the bacteria of normal skin flora and does not change the natural defense of the skin. The bactericidal effect of mupirocin is increased by the acidic pH of the skin. It can eradicate Staphylococcus aureus on the skin, Bacterial resistance is low, about 0.3% for S. aureus stock. MRSA resistance to mupirocin has already been described. Side effects have been reported in 3% of patients, with itching and irritation at the site of application being the most common. Since the ultraviolet rays absorbed by the product do not pass through the ozone layer, light reactions are unlikely to occur [25].

Oral or parenteral preparations are not available because systemic absorption is minimal and the absorbed material is rapidly converted to almost inactive metabolites. Especially in patients with renal failure, it is not recommended for use in patients with widespread or burns due to the risk of nephrotoxicity and absorption of the carrier polyethylene glycol. In the United States, formulations of mupirocin ointment that do not contain polyethylene glycol already exist. It is believed to be safe and effective for patients over 2 months, systemic antibiotics, when deeper structures (subcutaneous tissue, fascia) are involved, fever, lymphadenopathy, pharyngitis, peripheral oral infections, scalp infections, and / or It is indicated for 5 or more lesions, the range of selected antibiotics should include staphylococci and crusts for both bullous impetigo and crusted impetigo. Therefore, benzathine penicillin or penicillinase-sensitive penicillin is not indicated for the treatment of impetigo [26].

Penicillin resistant to penicillinase (oxacillin, cloxacillin, dicloxacillin) can be used. First-generation cephalosporins such as cephalexin and cefadroxil can be used because no difference was seen in the meta-analysis. Cheaper erythromycin may be the best antibiotic for the most disadvantaged. The potential resistance to Staphylococcus aureus, which occurs at different frequencies depending on the population surveyed, should be taken into account [22]. Other macrolides such as clarithromycin, roxithromycin, and azithromycin are more costly, but have the advantages of fewer gastrointestinal side effects and more comfortable doses. Staphylococcal strains that are resistant to erythromycin are also resistant to clarithromycin, roxithromycin, and azithromycin. Amoxicillin associated with clavulanic acid is a combination of penicillin and a beta-lactamase inhibitor (clavulanic acid), which can adequately cover streptococci and staphylococci. Clindamycin, sulfamethoxazole / trimethoprim, minocycline, tetracycline, and fluoroquinolones are the best antibiotics for MRSA [24].

About 20% of cases resolve spontaneously. Scarring is rare, but some patients can develop pigment changes. Some patients may develop exodermis. When treated, it will heal within 10 days. Newborns can develop meningitis. A rare complication is acute streptococcal glomerulonephritis, which occurs 23 weeks after skin infection [25].

Complications

Treatment improves most patients, but some patients may experience renal failure. This is more likely to occur if the infection is due to streptococcus. Renal dysfunction occurs 714 days after infection. Temporary hematuria and proteinuria can last for weeks or months. Other complications include septic arthritis, scarlet fever, sepsis, and staphylococcal scalded skin syndrome [27].

Conclusion

Impetigo is a highly contagious bacterial skin infection، caused by GAS and S. aureus, both which have various factors assisting in skin adhesion. It is seen especially in children at the summer time, due to the close proximity between kids which leads to rapid spreading.

The clinical presentation of the bullous form of impetigo، which starts with erythematous macules and progresses to vesicles, is due to ETA and ETB, harbored by S. aurues. The areas involved mostly are the nares and perioral regions.

This review emphasized the most important differentials for each form of impetigo (the bullous and the non-bullous one).The usage of topical treatment for impetigo, mainly with mupirocin and fusidic acid is still prevalent today.

Systemic therapy is needed, as in cases of the bullous form or widespread lesions, various options exist, with an average treatment of 10 days. Various studies testing new treatments haven’t proven adequate efficacy, and larger studies will need to take place.

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