Causes and Management of Cellulitis

Khalifa May’ouf Albuainain,1 Abduljabbar Abdullah Aljuwayd,1 Ahmed Abdullah Almarzouq,2 Zainab Ali A. Abu AlSaud,3 Nofou Abdullah Mazia’d Alkhattaf4, Eman Ahmed Alabdrabalrasol1, Neda Ahmed Zamzamy5, Abbas Hassan Al-Lashit6, Mahdi Hussain Al-Saad7

1 Imam Abdulrahman bin Faisal University, 2 Medical University of Gdansk, 3 Dammam Primary Health Care, 4 Al Yamamah Hospital, 5 Maternity and Children Hospital Makkah, 6 Hamdard University, 7 King Faisal University

INTRODUCTION

The definition is cellulitis is a diffuse, deep, acute inflammation of the skin including the dermis and subcutaneous tissue. It often follows an acute or chronic trauma, and is an important cause of hospital admissions. About 10% of infections-related hospital admissions in the US annually are due to cellulitis. The most common cause of cellulitis is group A streptococci.

ABSTRACT

Background: Cellulitis is a diffuse, deep, acute inflammation of the skin including the dermis and subcutaneous tissue. It often follows an acute or chronic trauma, and is an important cause of hospital admissions. About 10% of infections-related hospital admissions in the US annually are due to cellulitis. The most common cause of cellulitis is group A streptococci.

Aim: of this review was to study the common causes of cellulitis, and understanding the approach to its management. Methodology: We conducted this review using a comprehensive search of MEDLINE, PubMed, and EMBASE, January 1983, through February 2017. The following search terms were used: cellulitis, soft tissue infection, etiology of cellulitis, investigation of cellulitis, management of cellulitis, resistant cellulitis

Conclusion: Cellulitis is a common cause of infection-related hospital admissions worldwide. Mild cases can resolve with empiric antibiotic treatment, whereas moderate or severe diseases are harder to treat and are associated with higher recurrence rates. Recurrence rates can be minimized by treating predisposing factors like obesity, lymphedema, and skin injuries.

Keywords: cellulitis, soft tissue infection, streptococcal skin infection, MRSA skin infection

INTRODUCTION

The definition is cellulitis is a diffuse, deep, acute inflammation of the skin including the dermis and subcutaneous tissue. It often follows an acute or chronic trauma, and is an important cause of hospital admissions. In fact, it was estimated that about 10% of infections-related hospital admission in the US, and up to 14 million outpatients’ visits annually were due to cellulitis [1]. On the other hand, the over-diagnosis of cellulitis is also considered an important health issue as it may cause the delay of proper management and treatment of the disease. A reason for this is that physicians do not usually consult dermatologist until standard therapy fails. However, changing of this behavior will lead to early proper diagnosis and management which will reflect as a significant improvement in care [2].

METHODOLOGY

• Data Sources and Search terms
We conducted this review using a comprehensive search of MEDLINE, PubMed, and EMBASE, January 1983, through February 2017. The following search terms were used: cellulitis, soft tissue infection, etiology of cellulitis, investigation of cellulitis, management of cellulitis, resistant cellulitis

• Data Extraction
Two reviewers have independently reviewed the studies, abstracted data, and disagreements were resolved by consensus. Studies were evaluated for quality and a review protocol was followed throughout.

Pathology

Cellulitis occurs when an infectious organisms invades the dermis of the skin (usually through a break). This disruption of the skin can result from several causes including fungal infections (like onychomycosis, and tinea pedis), venous leg ulcers, pressure ulcers, and web spaces. The natural presence of low temperature, low pH and skin flora play an important role in reducing pathogenic colonization on the skin surface [3].

Under the microscope, cellulitis is characterized by lymphatic dilation, dermal edema, along with diffuse, heavy neutrophil infiltration around blood vessels. Histiocytes, lymphocytes, and granulation tissue may be observed in late cases [4].

When performing biopsy or needle aspiration, cultures are usually negative or yield a low concentration of bacteria. This leads to the assumption that the initial inflammatory process can be induced by a relatively small number of bacteria. Another possible explanation is that the number of viable bacteria is reduced significantly by the actions of an intact immune system. Therefore, bacterial load does
not provide a reliable definition of cellulitis, and the presence of inflammatory mediators with bacterial toxins is a more reliable \[5\].

**Etiology**

In adults with intact immune system, the most common cause of cellulitis is group A streptococci (*Streptococcus pyogenes*). Another important but less common organism is *Staphylococcus aureus*.

However, the exact incidence and prevalence of each causative organisms is still an area of debate, due to the challenging nature of accurate diagnosis, and the fact that most cellulitis cases are treated without determining the causative agent. Therefore, most cases of cellulitis are empirically treated \[6\].

The recent raising concern has been about the emergence of bacteria that is resistant to antibiotics treatment, like methicillin-resistant *S aureus* (MRSA). Infections with MRSA has increased recently causing an increase in the need of the use of vancomycin, clindamycin, doxycycline and other anti-MRSA antibiotics \[7\]. However, the empiric addition of anti-MRSA antibiotics in the treatment of uncomplicated cellulitis did not cause improvement in outcomes. On the other hand, gram-negative bacteria are usually not involved in cellulitis \[8\].

Therefore, the most appropriate initial empiric treatment is a narrow-spectrum antibiotic that targets methicillin-sensitive *S aureus* and *Streptococcus*.

An infection with *S aureus* is more likely to be the cause in cases of suppurative inflammation and the presence of purulent drainage, pustules, or abscesses. A study on patients with purulent or complicated cellulitis found that about 59% of patients had an infection with MRSA, 17% had methicillin-sensitive *S aureus*, and only 2.6% had β-hemolytic streptococci. It is not possible to clinically distinguish between methicillin-sensitive *S aureus* and MRSA.

Therefore, high-risk patients with suggesting clinical presentation should be considered for MRSA treatment. Predisposing factors that increase the risk of acquiring MRSA include prisoners, homosexuals, athletes, long-term care facilities residents, previous MRSA exposure, intravenous drug abuse, and military recruits \[9\].

**Clinical Presentation**

The typical presentation of cellulitis is an acute, unilateral, spreading skin infection with poorly demarcated erythema, and typical signs of inflammation including pain, erythema, heat, and swelling. Other signs include edematous lymphatics of the skin that can lead to the appearance of the orange peel sign, formation of bulla, and/or inflammation of proximal lymph vessels causing lymphangitis. Tender lymphadenopathy may also complicate severe cases of cellulitis. Most cases of cellulitis are on the lower limb. Cellulitis on the upper limb is usually associated with intravenous drug abuse. Fever can be present or absent depending on the case \[10\].

**Differential Diagnosis**

Cellulitis should be distinguished from erysipelas that is sharply-demarcated superficial inflammation of the skin. Some authors suggest that erysipelas is a subtype of cellulitis, due to the mutual etiologies between the two diseases. In our review, we will consider both to belong to the same entity when discussing predisposing factors, diagnosis, and management \[4\].

Another rare but potentially fatal skin condition is necrotizing fasciitis. It presents with a rapidly progressive subcutaneous and fascia infection, with destruction of the tissue. Necrotizing fasciitis can initially look similar to cellulitis. However, it can be distinguished with the presence of edema, necrosis, bullae, numbness, crepitus, and/or pain out of proportion. Immediate diagnosis of necrotizing fasciitis is crucial as proper early treatment will significantly improve outcomes \[11\].

Collection of pus within the skin (abscess) can be distinguished from cellulitis by performing a proper physical examination. Ultrasound can be used when examination is not conclusive. Most abscesses are caused by *S aureus* infection, and are managed by drainage and incision. Some patients may have coexisting cellulitis and abscess, which will result in failure of treatment if not both managed properly \[12\].

**Investigations**

Diagnosis of cellulitis depends mainly on thorough physical examination. Further laboratory investigations and imaging are not usually needed, unless there is a severe infection. In these cases, ultrasound or CT scan can be used to investigate the presence of deeper infections \[11\].

**Treatment**

Mild non-purulent cellulitis with the absence of systemic symptoms are usually empirically treated with dicloxacillin, cephalaxin,
amoxicillin/clavulanate, or other antistreptococcal antibiotics. Clindamycin can be used in patients with penicillin allergy. High rate of treatment failure should be expected when there are systemic manifestations like fever. Moderate cellulitis is defined as a non-purulent cellulitis that has only one of the following: heart rate more than 90/min, temperature more than 38°C or less than 36°C, white blood cell count more than 12 000 cells/mm³ or less than 4000 cells/mm³, or respiratory rate more than 20/min. Moderate cellulitis can be treated with oral antibiotics. Patients with two or more of the previous criteria, and patients who fail to resolve with oral treatment, will be considered to receive intravenous treatment with ceftriaxone, cefazolin penicillin G, or clindamycin. In any cellulitis case, antibiotics coverage must be defined in special cases.

Intravenous vancomycin with imipenem, piperacillin/tazobactam, or meropenem should also be considered in non-purulent cellulitis that presents with hypotension, high fever, immunocompromise, or sepsis.

When patients present with severe cellulitis, agents targeting MRSA (like vancomycin) should be considered. Penetrating trauma, or active intravenous drugs abuse are also indications of anti-MRSA treatment. Patients who cannot tolerate intravenous vancomycin can receive oral linezolid. In immunocompromised patients, broad-spectrum antibiotics should be used.

Other novel antibiotics options that can potentially cover MRSA include tedizolid, oritavancin, telavancin, and dalbavancin. However, these drugs are still new with no sufficient information regarding its efficacy and safety. Therefore, they are only considered in special cases.

Surgical assessment and interventional approaches should be considered whenever there is tissue necrosis. In these cases, culture of tissue should follow surgical excision. The appearance of any sign of shock is an indication of penicillin G and clindamycin to prevent streptococcal toxic shock syndrome.

In any cellulitis case, antibiotics coverage must be narrowed when culture results are available. Pseudocellulitis must be taken into consideration when symptoms fail to resolve within the first 48 hours following initiation of treatment. Other causes of treatment failure include infection with an atypical or resistant organism, fungal, parasitic, or viral co-infection. In these cases, biopsy and aspiration must be done to determine the underlying cause.

Treatment Failures
Up to 16% of acute cellulitis cases may fail to resolve following initial treatment. Among risk factors for treatment failure include wrong selection of antibiotics, and obesity. Treatment failure can be associated with severe complications. Pseudocellulitis is considered when cellulitis fails to respond to all modalities of treatment including conventional therapy and atypical causes.

CONCLUSION
Cellulitis is a common cause of infection-related hospital admissions worldwide. Mild cases can resolve with empiric antibiotic treatment, whereas moderate or severe diseases are harder to treat and are associated with higher recurrence rates. Recurrence rates can be minimized by treating predisposing factors like obesity, lymphedema, and skin injuries. Cases that fail to respond to treatment should draw the attention to other possible etiologies like pseudocellulitis. Further research is still needed to define ideal management guidelines.

REFERENCES
Causes and Management of Cellulitis


