Update on Cutaneous Manifestations of Infectious Diseases

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- MRSA
- Staphylococcus
- Monkey pox
- Mycobacteria
- Fungal
- Chikungunya

BACTERIAL INFECTIONS

Community-acquired, methicillin-resistant Staphylococcus aureus (CA-MRSA) has emerged as the most important new bacterial pathogen for dermatologists because of its tendency to present with furunculosis and abscesses.\(^1\) Large outbreaks often occur in daycare centers and among members of athletic teams, and CA-MRSA has moved into hospitals and become a major cause of hospital-acquired sepsis.\(^2\) CA-MRSA infections can be particularly severe in children, where life-threatening pneumonitis, lytic bone lesions, and other systemic complications can occur.\(^3,4\) Multi-drug-resistant strains are emerging and the widespread use of drugs, such as tetracycline, in animal feed may contribute to the emergence of resistance.\(^5\)

The majority of CA-MRSA abscesses will respond to drainage.\(^6,7,8\) A systemic antibiotic should be used when there is evidence of sepsis or invasion into adjacent tissues, and decolonization is reasonable when there is evidence of spread to other members of a family or other close contacts. Any attempt at decolonization must address both the skin and the nares because intervention aimed only at the nares often fail.\(^9\) Bleach baths (two tablespoons of bleach per quarter tub), chlorhexidine, and triclosan remain effective for decolonization of moist intertriginous and eczematous skin. Mupirocin, retapamulin, triple antibiotic, and tea tree oil cream have all been used for nasal carriage, as have oral regimens of rifampin plus minocycline. Emerging clindamycin resistance makes nasal decolonization with this agent problematic in many areas.\(^10,11\)

Most patients who require antibiotic therapy can be managed cost effectively with trimethoprim-sulfamethoxasole or a tetracycline. As noted earlier, emerging clindamycin resistance makes this antibiotic a more problematic choice. Inducible clindamycin resistance is particularly common among children with cystic fibrosis.\(^12\)

Refractory and complicated skin infections often need newer antibiotics, including parenteral agents. According to the US Food and Drug Administration and the Centers
for Disease Control, complicated skin infections are those that involve deeper soft tissue, require surgical intervention beyond simple incision and drainage, occur concurrently with systemic involvement; occur in the presence of a significant underlying disease state that complicates the response to treatment; occur in an anatomic site where the risk for anaerobic or gram-negative pathogen involvement is higher (eg, rectal area); occur from injury sustained in a wet environment where unusual pathogens are more likely; or occur as a result of a bite injury. Physical signs and symptoms suggesting more serious infection include rapid progression, pain out of proportion to physical findings, anesthesia, bullae, hemorrhage, slough or gas in tissue.

The treatment of complicated skin infections will generally require surgery in addition to an antibiotic. In this setting, antibiotic selection should generally be based on the results of culture and sensitivity, although in injuries resulting from bites, empiric therapy directed against *Pasteurella* species is appropriate. Drugs, such as oral amoxicillin/clavulanate, intravenous ampicillin/sulbactam, or ertapenem, are often used in this setting. Other organisms may occur in bite injuries, including *Staphylococcus aureus*, *Bacteroides* species, and *Capnocytophaga canimorsus*.

Therapeutic failure is being reported more commonly with vancomycin, and may relate intracellular survival of bacteria. This resistance can often be overcome by the addition of rifampin. Fluoroquinolones provide inconsistent coverage against staphylococci, including CA-MRSA, They remain appropriate for pseudomonas infections. Linezolid can be effective, even in wounds with compromised blood flow.

Linezolid is an oxazolidinone. One of its outstanding characteristics is that is has almost 100% oral bioavailability. It has proved to be more reliable than vancomycin in the treatment of serious staphylococcal infections. Daptomycin is a cyclic lipopeptide. It acts through disruption of bacterial membrane electrical potentials. Daptomycin has been used effectively in serious skin infections including CA-MRSA infections. It may be effective in some MRSA isolates with heteroresistance to vancomycin. The drug can be dosed once daily. It is cleared renally, and is generally well tolerated, although there are some reports of myopathy and potential for adverse interactions with HMG-CoA reductase inhibitors. Resistance has been reported, and in vitro sensitivity testing may not always predict clinical outcome. Tigecycline is an intravenous glycyclcline 9-tert-butyl-glycylamido derivative of minocycline. It has proved particularly useful for the treatment of infections involving MRSA and enteric organisms. Unfortunately, it has minimal activity against *Pseudomonas aeruginosa* and *Proteus spp.*., but it may be effective in the treatment of serious infections caused by *Acinetobacter baumannii*, when few choices are available.

Quinupristin-dalfopristin, a parental streptogramin, has been used effectively in some critically ill patients who have MRSA infections that failed to respond to vancomycin. Unfortunately, 31% of MRSA isolates are resistant in some areas. Telavancin, a multivalent lipoglycopeptide derivative of vancomycin, demonstrates rapid bactericidal activity against CA-MRSA. It has a long serum half-life, allowing once daily administration. Dalbavancin, a semisynthetic glycopeptide derivative of teicoplanin, has an even longer half-life allowing for weekly administration. In a randomized, controlled, double-blind trial, once-weekly dalbavancin was as effective as twice-daily linezolid. MRSA accounted for 51% of the cultured pathogens. Carbapenems, such as panipenem, meropenem, and ertapenem, demonstrate broad-spectrum activity and synergism with vancomycin. Their spectrum is too broad for most skin infections. Ceftobiprole medocaril is a parenteral cephalosporin active against MRSA. In some studies, it compared favorably to vancomycin. Small-colony variants of staphylococci may not be as susceptible to the drug.
*Vibrio vulnificus* is often found in brackish water and causes serious infection in patients who have cirrhosis who sustain injuries in aquatic environments or consume raw oysters. Marine *Vibrio* infection should be suspected in anyone with liver disease and cellulitis, hypotension, or sepsis.

*Acinetobacter baumannii* is an important emerging pathogen, causing severe systemic and soft-tissue infections, mostly in hospitalized patients. Some strains are resistant to almost all available antibiotics, but tend to be susceptible to carbapenems.

**MYCOBACTERIAL INFECTIONS**

Tuberculosis and nontuberculous mycobacterial infections have emerged as important pathogens in patients who have iatrogenic immunosuppression, including therapy with biologic agents, in particular anti-TNF therapy. Disseminated *Mycobacterium avium* complex infection, often associated with HIV infection, has also been reported in patients treated with infliximab.

Severe skin infections with nontuberculous mycobacteria have been reported in association with nail salon foot baths or following mesotherapy. Patients typically present with abscesses, deep draining sinus tracts, or furuncles. *Mycobacterium chelonae* infections have been reported after liposuction. Disseminated nontuberculous mycobacterial infection in Thai patients without HIV often demonstrate coinfection with other opportunistic pathogens, suggesting the possibility of a new transmissible AIDS like agent.

Tuberculosis has also reemerged as an important disease, partly in relation to the HIV epidemic, and partly because of the widespread use of anti-TNF agents. Skin tests may fail to detect infection and patients who have signs or symptoms of infection may need imaging studies, interferon gamma release assays, or DNA hybridization studies.

Clarithromycin has emerged as the best empiric choice for cutaneous nontuberculous mycobacterial infections. Other agents that are often effective for *M. marinum* include minocycline or a combination of rifampin and ethambutol.

*M. abscessus* infections generally need surgical and multidrug antimicrobial therapy with clarithromycin or azithromycin combined with amikacin.

**FUNGAL INFECTIONS**

Zygomycosis (mucormycosis) is an increasing important pathogen because of its high morbidity and the rising prevalence of diabetes, the major risk factor for infection. The diagnosis is typically based on a biopsy specimen. The organism is vasculotropic and vasculodestructive and is visible in histologic sections as wide, brightly eosinophilic ribbons with hollow centers. Posaconazole is active against Zygomycetes and has improved the outlook for these infections.

Fusarium is replacing *Candida* and *Aspergillus* as fungal pathogens in immunocompromised hosts because of better prophylaxis that has decreased the incidence of the other two pathogens. Fusarium isolated from patients who are non-neutropenic and nonimmunosuppressed is rarely a pathogen, but in the setting of chemotherapy-induced neutropenia, the infection is often fatal. As in *Candida* sepsis, fever and myalgia are typical presenting findings. Skin lesions typically present as leathery, black eschars with scalloped erythematous and edematous borders. The organism may be recovered from a skin biopsy or from blood cultures. Fusariosis may also present with arthritis, onychomycosis, keratitis, or endophthalmitis. The prognosis is poor despite amphotericin B therapy unless the neutropenia resolves. Newer agents, such as voriconazole, show activity against fusariosis.
**Penicillium marneffei** is an opportunistic dimorphic fungal pathogen endemic to Southeast Asia. It is being seen in patients who have AIDS who have traveled to endemic regions. Histopathologically, the organism closely resembles histoplasmosis. Amphotericin B and itraconazole are active against *P. marneffei.*

*Exserohilum*, a dematiaceous fungus, has emerged as a cause of cutaneous, corneal, and sinus infection, especially in the southern United States. Aggressive debridement is critical, as the organism responds poorly to amphotericin B. The addition of a triazole antifungal may be of benefit.

**VIRAL INFECTIONS**

Monkeypox emerged as an important pathogen in the Midwestern United States in 2003. The index case was a 3-year-old girl who developed fever and cellulitis after having been bitten by a prairie dog. The outbreak was traced to a single shipment of exotic animals from Ghana. Clinical manifestations are similar to those of smallpox. After an incubation period of 5 to 21 days, the patient experiences headaches, fever, chills, sweating, and lymphadenopathy. This prodrome is followed in a couple of days by a vesiculopustular eruption. Individual lesions evolve from umbilicated pustules to hemorrhagic crusts. In contrast to smallpox, lesions are in various stages of evolution.

Just as monkeypox was important because of its clinical similarities to smallpox, Chikungunya virus is important because of its clinical similarities to Dengue. Several outbreaks occurred recently in popular Indian Ocean resort islands. Travelers brought the infection home with them, and it has become established in countries like Italy where vectors already existed. Transmission is by way of Aedes aegypti mosquitoes that had spread to Italy from the United States. It is only a matter of time before the virus becomes endemic in parts of the United States. Infection typically presents with fever, arthralgia, myalgia, and rash. Atypical features, such as bullous lesions and genital ulceration, have been reported. Other systemic features may include cardiovascular, neurologic, or respiratory involvement. The overall mortality is approximately 10% and increases with age.

We have become a global village and diseases now spread easily from remote corners of the world. New medications, such as the biologics, offer dramatic results for our patients, but may be complicated by unusual infections. The dermatologist is on the front lines with these infections, as they typically present with cutaneous lesions.

**REFERENCES**

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