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Community-Acquired MRSA

Developed by Jordanna Roesler, Dr. Wingfield Rehmus, Dr. Jennifer Tam, and Dr. Laura Sauvé for PedsCases.com.
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Introduction:

Hello and welcome to "community acquired methicillin-resistant *Staphylococcus aureus*", a podcast made for PedsCases.com. My name is Jordanna Roesler and I am a third-year medical student at the University of British Columbia. This podcast was developed under the guidance of Dr. Wingfield Rehmus, a pediatric dermatologist at BC Children's Hospital and the University of British Columbia, Dr. Jennifer Tam, a pediatric infectious disease specialist at BC Children's Hospital and the University of British Columbia, and Dr. Laura Sauvé, a pediatric infectious disease specialist at BC Children's Hospital and the University of British Columbia, and the chair of the CPS Infectious Diseases committee.

In this podcast, we will discuss community acquired methicillin-resistant *Staphylococcus aureus* skin infections, an emerging issue in the pediatric population.

Learning Objectives:

After listening to this podcast, the learner should be able to:

1) Describe the common clinical presentations of community acquired methicillin-resistant *Staphylococcus aureus* skin infections, which will be referred to as "community acquired MRSA".
2) Identify some common skin and soft tissue infections and risk factors associated with community acquired MRSA.
3) Discuss the importance of antimicrobial resistance and stewardship.
4) Describe commonly used treatment options for community acquired MRSA in infants and children as outlined by the Canadian Pediatric Society.

Case:

Let's begin with a clinical case. You are a third-year medical student at a busy pediatric clinic and your preceptor asks you to see Rachel, a 12-year-old girl brought in by her

mother. Rachel's mother is concerned about a purulent lesion on Rachel's right lower limb, which she says looks like a "spider bite". Upon further questioning, Rachel's mother tells you that their family had just come back from a picnic when she noticed the mark on Rachel's right lower leg. Rachel's mother is very worried that Rachel may have been bitten by a spider and about the possibility of an infection. Rachel describes her lesion as red, very painful, and "icky".

You recall that sometimes lesions caused by antibiotic resistant *Staph. aureus* are misdiagnosed as spider bites (Dominguez, 2004). Let's discuss the clinical presentation and differential diagnosis for *Staph. aureus* infections so we can work through Rachel's case.

Clinical Presentation and Differential Diagnosis:

Recall that *Staph. aureus* are gram-positive, aerobic bacteria that are cocci-shaped and arranged in clusters. While skin and soft tissue infections are more common, *Staph. aureus* can also cause more serious illnesses such as pneumonia, bacteremia, and osteomyelitis (Robinson and Salvadori, 2011). Today we will focus on the various clinical presentations of skin and soft tissue infections caused by *Staph. aureus*.

Staph. aureus is a common cause of many skin and soft tissue infections, and both methicillin-susceptible *Staph. aureus* (or, MSSA) and *methicillin-resistant Staph. aureus* (MRSA) should be considered when a child presents with a skin and soft tissue infection (Robinson and Salvadori, 2011).

Dermatology Morphology: Terminology

Let's take a minute to go over some important terms used in dermatology to describe skin lesions that are seen in staph aureus infections to help guide us with our differential diagnosis.

- Papule: a raised, scaly, or crusted area of involved skin less than 1cm in diameter
- Plaque: a raised, scaly, or crusted area of involved skin greater than 1cm in diameter
- Vesicle: a fluid-filled blister less than 1cm in diameter
- Bulla: a fluid-filled blister greater than 1cm in diameter
- Pustule: a collection of pus in the skin
- Nodule: a solid or cystic palpable lesion greater than 1cm in diameter, located in the dermis or subcutaneous tissue
- Abscess: a deep or large collection of pus

Staph Aureus – Common Skin and Soft Tissue Infections:

The types of skin and soft tissue infections caused by *Staph. aureus* are broad. Let's discuss the common ones.

Impetigo:
Impetigo is a commonly occurring skin infection in children that spreads easily with close contact. Some risk factors for developing impetigo include challenges with maintaining personal hygiene as well as over-crowded living conditions (Cole and Gazewood, 2007).

Impetigo can be bullous or non-bullous (Darmstadt and Lane, 1994). Non-bullous impetigo is a superficial infection of the epidermis that is often described as a "honey-crusted" lesion (Cole and Gazewood, 2007). Typical areas for non-bullous impetigo include the face and limbs.

In comparison, bullous impetigo consists of vesicles and/or bullae that contain clear or yellow fluid. When bullae rupture, a rim of scale is left behind and the surface is often crusted. A common location for bullous impetigo is the trunk. Bullous impetigo occurs due to *Staph. aureus* exfoliative toxin, which affects the adhesion of the cells in the superficial epidermis, leading to the formation of bullae (Amagai et al., 2000).

The majority of cases of non-bullous impetigo and all cases of bullous impetigo are caused by *Staph. aureus* (Darmstadt and Lane, 1994). Group A beta hemolytic streptococci is responsible for the minority of non-bullous impetigo that are not caused by *Staph. aureus* (Darmstadt and Lane, 1994).

Both bullous and non-bullous impetigo can be diagnosed clinically if the presentation is typical. However, a gram stain and culture can also be used to confirm the diagnosis. For treatment, both topical and oral options are available depending on the extent of the infection. Typically, a beta-lactamase-resistant oral antibiotic is used for patients with greater skin involvement (Darmstadt and Lane, 1994). For patients with limited impetigo, mupirocin and fusidic acid are first line topical treatments that are often used (Edge and Argáez, 2017).

If the infection is due to MRSA, then other antibiotics may be necessary depending on the sensitivity profile of the organism. Some agents that might be used include trimethoprim/sulfamethoxazole (TMP-SMX), doxycycline, or clindamycin (Hartman-Adams, Banvard, and Juckett, 2014).

Cellulitis:
Cellulitis is an infection that extends to the dermis and subcutaneous tissue and is erythematous, firm, and painful (Stulberg, Penrod, and Blatny, 2002). Patients with cellulitis may also have systemic symptoms including malaise, fever, and chills. It can be caused by either Staph or Strep, so both bacteria need to be considered when you are choosing empiric antibiotic coverage. You should always consider if a child is known to have MRSA or have close contacts with MRSA when prescribing treatment.

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Bacterial Folliculitis:
Folliculitis is another common skin manifestation that occurs when a follicular or peri-follicular area becomes inflamed (Gjede and Graber, 2014). This level of inflammation can be either superficial or deep. Oftentimes, folliculitis is the result of a bacterial infection, and can occur due to either MRSA or MSSA. The typical presentation of bacterial folliculitis consists of follicular pustules and papules, which may be pruritic and/or painful (Stulberg, Penrod, and Blatny, 2002). If the inflammation is deep, then nodules may be appreciated.

Common sites of infection include areas of skin that have hair, such as the chest, upper back, shoulders, face, and scalp.

Abscesses

Furuncles and Carbuncles:
Furuncles and carbuncles are abscesses associated with hair follicles. Furuncles are commonly referred to as “boils”. They are indurated lesions that involve the hair follicle and can have central necrosis. Systemic symptoms are not commonly found in a patient with a single furuncle. Furuncles may occur more commonly on the abdomen, buttocks, thighs, and legs.

Carbuncles can be thought of as a network of furuncles (Stulberg, Penrod, and Blatny, 2002). Carbuncles are larger and deeper than furuncles and are connected subcutaneously. A patient presenting with carbuncles may also have systemic symptoms present, such as fever and fatigue. Like furuncles, carbuncles commonly occur on the abdomen, buttocks, thighs, and legs.

Bacterial Abscesses:
A larger abscess may occur when a furuncle or carbuncle is left untreated. In comparison to those hair follicle infections, abscesses can also occur when bacteria enter the skin through a cut, scrape, or puncture. The infection spreads deeper, and a pocket of pus forms. These abscesses are often tender, painful, swollen, and erythematous.

Abscesses are typically managed with incision and drainage (Gorwitz, 2008). However, depending on the child’s age and extent of infection, antibiotics may also be given in conjunction with drainage. For example, if the child is immunocompromised, systemically unwell, or has significant cellulitis, a course of antibiotics would be given after incision and drainage.

Additional management includes wearing loose fitting clothing, showering and/or bathing after sports or exercise, and not sharing personal items like towels, sports equipment, or razors.

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If untreated, these deeper infections put patients at risk for development of potentially life-threatening systemic infections through lymphatic or hematogenous spread (Gorwitz, 2008). These infections include osteomyelitis, necrotizing fasciitis, arthritis, endocarditis, pneumonia, and sepsis (Gorwitz, 2008).

Case Continued:

After thinking about common skin and soft tissue infections, you walk into the room, and see a well appearing child who is talking happily with her mother. You wash your hands, introduce yourself, and begin to ask some questions. Let's go through an approach to taking Rachel's history.

History:

Now that we've established a framework for our differential diagnosis, let's discuss how we'll approach the history and examination.

Some important questions we would want to consider include asking about the onset and progression of the lesion. For example:

- When was it first noticed?
- Did it occur acutely or gradually?
- Has it changed in appearance over time?
- Has a similar lesion occurred in the past?
- Was there any apparent trigger? (for example, after exposure to another child with known infection, travel, outdoor activity, sports).

It is also important to ask questions about the location and distribution of the lesion:

- Where is it located?
- Has it spread anywhere?
- Are there any other lesions or rashes?

Also ask about any associated features, such as:

- Is it itchy?
- Does it hurt?
- Is there any discharge, bleeding, or blistering?
- Is there any fever?
- Has there been any recent, unintentional weight loss?
- Is there any fatigue?
- Is there any arthralgia?

Ask about alleviating and aggravating factors, including:

- Does anything make it better?
- Does anything make it worse?

- Have any treatments been used, such as over the counter medications or home remedies? If so, did they seem to help, worsen, or result in no change?

While all of those questions can be applied to a history for any new lesions, it is also important to inquire about exposures and risk factors pertaining to community acquired MRSA:

- Is the patient or any of the patient's close contacts known to be colonized with MRSA?
- Has the patient been sick recently or has there been frequent use of antibiotics?
- Has there been any contact with any sick individuals?
- Has maintaining hygiene been a challenge? Has there been any sharing of personal items, such as towels or sports equipment? Has there been a lack of showering, especially after exercise or sports?
- Has there been any skin trauma?

It is also important to make sure we take a complete pediatric history, which would cover:

- The patient's past medical history, including medical conditions, surgeries, and hospitalizations
- Medications and the indications for each
- History of immunizations
- Allergies and reactions to allergies
- A family history
- A social history
- A review of systems, including any signs of an undiagnosed immunocompromised condition, such as recurrent infections or a history of serious infections
- The patient's feelings, ideas, impact on function, and expectations (FIFE)

Case Continued:

Now that we know what to ask, lets use these skills for Rachel's case.
Rachel can't quite pinpoint when she first noticed the lesion, but mentions that she might have previously noticed a smaller, tender "bump" where her current lesion is located.

You ask Rachel and her mother about any recent travel, water exposure, skin trauma, or animal bites, which are all negative. She has not had any frequent exposure to antibiotics or contact with any sick individuals.

Rachel lives at home with her mother and younger brother and attends public school. No one else in Rachel's family has noted any skin lesions or illness. Rachel tells you that she loves to swim and also runs track and field with her friends from school. She

also reports that she does not have any issues with maintaining hygiene and does not share towels or other sports equipment with her friends.

Upon further review, you confirm that Rachel does not have any current or previous medical conditions, recent or past hospitalizations, surgeries, or illnesses and is up to date with her immunizations.

Physical Examination

Now that we have our history, let's discuss what to look for on physical exam, and review the terminology used to describe our findings.

First, it is important to obtain a set of vitals to assess for signs of systemic involvement, such as fever, tachycardia, or hypotension. Remember to complete a general inspection and make note if the child looks unwell. When assessing the lesion, be sure to characterize its size, shape, colour, and associated features. For example, is there associated pain, blood, purulence , or surrounding cellulitis?

Recall that a papule is a raised, scaly, or a raised, scaly, or crusted area of involved skin less than 1cm in diameter and that a plaque is a raised, scaly, or crusted area of involved skin greater than 1cm in diameter. A vesicle is a fluid-filled blisters less than 1cm in diameter, while a bulla is a fluid-filled blister greater than 1cm in diameter. A pustule is a collection of pus in the skin, while a nodule is a solid or cystic palpable lesion greater than 1cm in diameter, located in the dermis or subcutaneous tissue. Finally, an abscess is a deep or large collection of pus.

In addition to general appearance and a skin examination, always complete a head to toe examination. It is important to ensure that there are no other lesions you have missed, and to check for any other sequelae of serious MRSA infection such as sepsis, shock, or pneumonia with a thorough cardiac, respiratory, and abdominal examination. It is also important to complete a joint examination as osteomyelitis and septic arthritis can be seen in MRSA infections.

Upon physical examination, you get another set of vital signs and note that Rachel does not have any signs of systemic involvement such as a fever, tachycardia, or hypotension. Rachel also denies feeling fatigued, dizzy, or having had any chills.

You take a look at Rachel's lesion and note a 1.0 cm erythematous, indurated nodule with central necrosis without any signs of surrounding cellulitis. You think that based on your physical examination that Rachel likely has a skin abscess. Before you go to see your preceptor, you take a moment to think about your assessment and management plan, as well as information you can provide Rachel and her mom to prevent this from re-occurring.

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Epidemiology and Risk Factors:

Some of the risk factors for developing a skin abscess due to community acquired MRSA include challenges in maintaining hygiene, such as not having adequate access to a bath or shower, sharing towels with others, and not showering after sports or exercise. Over-crowded living conditions and skin-to-skin contact are also risk factors for infection. Other risk factors include a history of recent skin trauma, such as cuts or scrapes, and frequent exposure to antibiotics (Irvine, 2012).

While you couldn't identify any of the above risk factors in Rachel's case, you recall that MRSA can still be present in many patients without any risk factors (Irvine, 2012).

Background on Community Acquired MRSA:

Community acquired MRSA is widespread, and can affect neonates, children, and adults. While many skin and soft tissue infections are caused by MSSA, MRSA should always be considered in children presenting with a skin and soft tissue infection (Robinson and Salvadori, 2011). Transmission occurs through contact with a contaminated surface or contact with an individual infected with MRSA (Irvine, 2012). Increased rates have been reported in children who attend daycare, athletes, recent courses of other antibiotics, and underlying skin conditions like atopic dermatitis; however, infection due to community acquired MRSA can occur without any risk factors (Robinson, 2011 and Balma-Mena et al., 2011). Some studies have suggested that Indigenous children in several countries including Canada, the United States, New Zealand and Australia, have higher rates of MRSA; this is mostly likely due to social determinants of health – such as crowded housing, poverty and lack of access to safe water. There can also be higher rates in settings where children are crowded and / or sharing personal items – such as sports teams or daycares (Irvine, 2012).

The spectrum of presentation is wide, ranging from asymptomatic skin and soft tissue infections, to life-threatening invasive infection. Typically, community acquired MRSA presents as a skin and soft tissue infection.

Diagnosis, Management, and Treatment:

Diagnosis

If your history and physical exam has allowed you to diagnose a specific type of skin infection, a diagnostic sample should be sent if possible. If incision and drainage is done, a sample should be sent to the microbiology lab to identify the bacteria and susceptibility profile. It is optimal to send a sample of purulence to the lab, as a swab alone has a lower yield than aspirated purulence. If you can't aspirate purulence, then you can swab the skin; however, keep in mind that a swab of intact skin is unlikely to be helpful.

A gram stain and culture with susceptibility testing is the only way that MRSA can be distinguished from methicillin-susceptible *Staph. aureus* (also known as MSSA) and

other viral or bacterial causes (Heilpern, 2007). The results of the culture will also guide your treatment choices (Miller et al., 2007).

Case

Let's return to our case. You decide to swab the purulent aspect of the abscess and send it for cultures. You then incise and drain the abscess.

Your preceptor mentions that if Rachel had been systemically ill then more investigations, like a blood culture, may have been completed. You discuss that other reasons for ordering a blood culture include immunodeficiency and neutropenia. Otherwise, children with uncomplicated skin and soft tissue infections generally do not require blood cultures (Trenchs et al., 2015)

You ask Rachel's mom to follow up with the clinic if there isn't any improvement within 48 hours or if Rachel becomes systemically ill. You also remind Rachel and her mom to not share any personal items such as towels and sports equipment.

Later, the culture returns positive for gram positive cocci in clusters and susceptibility testing confirms the diagnosis of community acquired MRSA.

Antimicrobial Resistance:

Community acquired MRSA is resistant to all beta-lactam antibiotics, therefore cephalosporins, such as cephalexin, and penicillins, including cloxacillin, should not be used (Irvine, 2012). The choice of non-beta-lactam antibiotic depends on the local antibiogram and susceptibility patterns. Some more specific antibiotic choices to consider will be described shortly. Unfortunately, resistance to many of the commonly prescribed antibiotics such as mupirocin, fluoroquinolones, tetracyclines, and clindamycin is on the rise, leading to issues of increasing antimicrobial resistance (Styers, et al., 2006). Therefore, it is important to promote antibiotic stewardship and adhere to health authority guidelines outlining the responsible use of antimicrobials to help reduce the rate and risk of increasing resistance.

Antibiotic Stewardship Principles (Le Saux, 2014):

Some antibiotic principles in the context of MRSA include:

- Avoid antibiotics when possible
- Use the narrowest possible antibiotic in a given situation
- Do not prescribe antibiotic courses unnecessarily
- If an abscess is drained, send a specimen for culture and susceptibility to guide management, and narrow treatment based on your culture whenever possible

Management and Treatment of CA-MRSA Skin Abscesses: (Robinson and Salvadori, 2011)

Let's discuss the management and treatment of community acquired MRSA skin abscesses as outlined by the Canadian Pediatric Society, also known as CPS. The CPS

has provided statements and a treatment table outlining the management options of community acquired MRSA skin abscesses in infants and children. While drainage of community acquired MRSA skin abscesses is usually sufficient for previously healthy children who are older than three months of age with an uncomplicated skin abscess, certain cases may require antibiotics. These cases include:

Infants younger than 1 month:

- For infants younger than 1 month of age that are unwell, they should be admitted, and started on IV antibiotics, typically vancomycin.
- Infants younger than 1 month of age may be managed as an outpatient if the infant has dependable caregivers, an abscess smaller than 1 cm, no signs of systemic illness or fever, and no underlying medical conditions or illnesses. In these cases, the antibiotic of choice is usually clindamycin.

Infants between 1 to 3 months of age:

- For infants between 1 to 3 months of age, empiric antibiotics are given orally while cultures are pending. If there is no sign of systemic illness or fever, then trimethoprim/sulfamethoxazole (TMP-SMX) is given until cultures are confirmed. Infants with signs of sepsis will need admission for management, including intravenous antibiotics.

Children 3 months or older:

- Children 3 months or older who are otherwise healthy without a fever or those who have a low-grade fever, no other signs of systemic illness, and no surrounding cellulitis are typically observed following abscess drainage. However, if there are no signs of improvement in 48 hours or if the culture returns positive for a pathogen other than MRSA, antibiotics should be started.
- Children 3 months or older with no signs of systemic illness and who are afebrile or have low-grade fever, but have a significant amount of cellulitis require antibiotics. Oral cephalexin and trimethoprim/sulfamethoxazole (TMP-SMX) should be started to provide coverage for both Group A streptococcal infection and Staph aureus while cultures are pending.
- Children who are 3 months or older who are systemically unwell or have a significant amount of surrounding cellulitis should be started on empiric oral or parenteral antibiotics while cultures are pending.
- In the case of children with underlying medical issues, empiric oral antibiotics should be started while cultures are pending.

Antibiotics:

Antibiotics used to treat community acquired MRSA should be chosen based on the severity of infection or disease, patient factors, the route of administration, and cost in order to promote positive patient outcomes (Nemerovski and Klein, 2008).

Generally, Trimethoprim/sulfamethoxazole (TMP-SMX) is well tolerated, covering both MSSA and community acquired MRSA. Therefore, it is often used in the case of an uncomplicated abscess warranting antibiotics (Robinson and Salvadori, 2011).

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TMP/SMX is generally not used in neonates due to the concern that sulfamethoxazole may displace bilirubin from albumin and lead to hyperbilirubinemia and kernicterus (Wadsworth and Suh, 1988).

Clindamycin is another option if susceptible; however, more community acquired MRSA isolates have shown to be resistant, and clindamycin may increase the risk of *Clostridium difficile* colitis (Robinson and Salvadori, 2011). Also, the liquid formulation is unpalatable, so it may not be well tolerated in young children that cannot swallow tablets.

Doxycycline is another antibiotic that treats MRSA, but it is used less often in the pediatric population due to previous concerns regarding tooth discoloration, and it is only available in pill form. Linezolid is another oral antibiotic that could be used; however, it is cost-prohibitive and therefore not recommended in cases of uncomplicated skin abscesses (Robinson and Salvadori, 2011).

Take Home Messages:

1. Risk factors for community acquired MRSA include frequent use of antibiotics, challenges in maintaining personal hygiene, overcrowded living conditions, sharing personal items, recent skin trauma, atopic dermatitis, and skin-skin contact. Remember though, many children with community acquired MRSA may not have any risk factors.
2. Community acquired MRSA can lead to systemic illness such as septic arthritis, pneumonia, osteomyelitis, necrotizing fasciitis, and sepsis.
3. A swab and culture are needed to definitively diagnose a lesion suspected to have been caused by community acquired MRSA.
4. Drainage alone (with no antibiotics) is preferred for community acquired MRSA skin abscesses in children older than 3 months of age without significant cellulitis. However, antibiotics may be used in addition to drainage in infants under three months of age, and in children with underlying medical conditions, systemic symptoms, or extensive cellulitis.
5. Antimicrobial resistance is an ongoing health issue, and it is important to promote antibiotic stewardship to help reduce the rate and risk of antimicrobial resistance.

Learning Objectives:

After listening to this podcast, the learner should be able to:

1) Describe the common clinical presentations of community acquired methicillin-resistant *Staphylococcus aureus* skin infections, which will be referred to as “community acquired MRSA”.
2) Identify some common skin and soft tissue infections and risk factors associated with community acquired MRSA.
3) Discuss the importance of antimicrobial resistance and stewardship.

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4) Describe commonly used treatment options for community acquired MRSA in infants and children as outlined by the Canadian Pediatric Society.

Conclusion:

Rachel and her mom follow up with you and let you know that Rachel is feeling much better. She mentions that she will continue to practice handwashing and maintain personal hygiene after sports and exercise.

That concludes this episode of PedsCases, thanks for listening!

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