Superficial Fungal Infections  
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Week 14

Educational Objectives:

1. Describe the different cutaneous infections associated with intertrigo
2. Review the differential diagnosis and treatment of tinea capitis
3. Understand the etiology and treatment of dandruff and seborrheic dermatitis

Editor’s Note:

Preceptors- As with any derm topic, a picture is worth a thousand words. You may want to have a color atlas of clinical dermatology handy (marked to the relevant pages) to pass around while you discuss the following cases.

CASE ONE:

A 55-year-old female presents to your office complaining of a rash underneath her breasts for the last two weeks. “I always have a mild rash in that area, since I sweat a lot. I use baby powder on a daily basis, but recently it has gotten very red and raw. It was itchy initially, but now it is more like a burning pain.” Her PMH includes morbid obesity with a BMI of 43 and IDDM.

Your exam is significant for a maculopapular, intensely erythematous, sharply demarcated rash in both inframammary folds. Some areas appear macerated and you notice erythematous pustules and papules in the periphery of the rash. Your preceptor describes these as “satellite lesions.”

Questions:

1. What is your diagnosis? Discuss the infectious and noninfectious causes of this condition.

Your patient has intertrigo, which is a clinical description of an inflammatory skin reaction that occurs on opposing skin surfaces of body folds. It is primarily caused by skin on skin friction in areas that harbor moisture or have poor air circulation. Typical locations include the inner thighs, the inframammary region, axillae, skin folds of a pannus, the perineal area, the intergluteal cleft, and between toes and fingers. Intertrigo is frequently seen in overweight patients, diabetics, babies, and in patients with medical devices which predispose the skin to moisture (e.g., artificial limbs).
Intertrigo initially presents as an erythematous macular rash. As the inflammation progresses, erosions, fissures or maceration develop. Oozing and crusting can be seen as well. The differential diagnosis for simple intertrigo includes allergic or irritant contact dermatitis, atopic dermatitis, seborrheic dermatitis, and less common disorders like psoriasis or pemphigus. Preceptors please refer to Table 1 of the reference article (Janniger, 2005).

Superinfections with bacteria and fungi are very common. When a particular superinfection is identified, the diagnosis is then based on that infectious etiology. The fungus most commonly associated with intertrigo is Candida which causes cutaneous candidiasis. The associated rash has an erythematous base and is usually sharply demarcated; small vesiculopustules in the periphery are typical and are called “satellite lesions.” With increased friction, the skin can erode and lead to a more confluent rash.

Interdigital intertrigo is commonly superinfected by dermatophytes like Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum. Intertrigo in this area is often accompanied by a burning sensation and maceration (Janniger, 2005).

Among the organisms that can be isolated from intertrigonal areas are Malassezia yeast species. Whether Malassezia-complicated intertrigo is a distinct entity or a type of seborrheic dermatitis is unclear (Janniger, 2005).

Erythrasma presents as a well demarcated faint red-brown macular rash. It mimics epidermal fungal infections and can cause burning and itching. Corynebacterium minutissimum is the responsible bacteria and can complicate intertrigo at times. Other bacteria that may cause superinfection of intertrigo include Staph aureus, group A beta hemolytic Streptococcus, Pseudomonas aeruginosa, and Proteus species.

2. **What diagnostic tests are available to determine if this patient has infection?**

   **What treatment options are available?**

   The diagnosis of intertrigo is a clinical diagnosis. As stated, superinfections are common. The characteristic appearance of the rash often indicates the type of infection and guides the clinical diagnosis. If fungal infections are suspected, a KOH preparation of a swab or skin scrapings can aid in differentiating dermatophytes from Candida. Candida appears as pseudohyphae on microscopic examination, whereas dermatophytes form hyphae. Hyphae are cylindrical filamentous structures with parallel side walls. Pseudohyphae are long elongated structures with daughter cells budding from larger parent yeast cells. These daughter buds can elongate. As a result, there is a septum formation within a tubular structure. This septum, as well as the presence of daughter buds help differentiate pseudohyphae from hyphae. Wood’s lamp examination is easy to perform in the office setting and can identify Pseudomonas or Corynebacterium minutissimum (Erythrasma) infections. Erythrasma has a coral-red fluorescence
and Pseudomonas infections fluoresce green under the Wood’s light. A culture can identify the specific organism, but is rarely needed. This patient’s intertrigo is described as painful, erythematous and confluent with satellite lesions, which is characteristic for a Candida albicans superinfection.

Cutaneous superficial Candida infections are preferably treated with topical antifungals:

- **Topical azole antifungal agents** include ketoconazole (Extina, Nizoral, Xolegel), sertaconazole (Ertazo) and miconazole (Lotrimin AF powder or spray, Micatin). These are broad-spectrum antifungals that are active against Candida albicans and both dermatophytes and Malassezia yeast. Some azoles, especially sertaconazole and ketoconazole have anti-inflammatory and antibacterial properties as well.
- **Allylamine antifungals** that are available topically include terbinafine (Lamisil) and naftifine (Naftin).
- **Ciclopirox Olamine** (Loprox) is the only hydroxypyridone topical antifungal available. It is a broad-spectrum antifungal that is active against Candida species, dermatophytes and Malassezia furfur. Its mechanism of action differs from other antifungal agents. Its effects may be additive when applied in combination with an azole or allylamine antifungal agent. This agent is also reported to have some anti-inflammatory antibacterial properties.
- **Topical Nystatin** has activity against Candida but is not effective against dermatophytes. Topical corticosteroids are usually not used in conjunction with an antifungal agent. Some antifungals exhibit anti-inflammatory activity (ketoconazole, sertaconazole, ciclopirox) reducing symptoms like burning, itching and pain.

Since we are confident that this patient has a Candida infection, using a Nystatin powder or cream would be effective. Treating with a broad-spectrum antifungal like an azole antifungal to capture dermatophytes or Malassezia species is also a reasonable approach. Treatment is twice daily until symptom resolution. Further moisture and friction should be minimized in the affected area. The patient should be advised to wear non-synthetic clothing to prevent sweating.
CASE TWO:

A 25-year-old healthy male presents to you, complaining of hair loss. He has noticed a bald spot on the crown of his scalp. His mother told him that it looked scaly. He has used a selenium sulfide shampoo OTC for the last month without any improvement. He lives alone and works in an animal shelter. Scalp examination reveals a 4 cm round hyperkeratotic plaque of alopecia with broken off hairs. The area of alopecia has white–gray scales that are easily dislodged. You notice enlarged occipital lymph nodes on neck examination. The remainder of his examination is normal.

3. Discuss the differential diagnosis for the patient’s scalp condition.

The differential diagnosis for this patient includes tinea capitis, seborrheic dermatitis (dandruff), psoriasis of the scalp, impetigo, secondary syphilis, alopecia areata, and trichotillomania.

The description of the scalp lesion is typical for tinea capitis of the “gray patch type”. Occipital adenopathy is often associated with tinea capitis. Dandruff affects the scalp diffusely and does not cause alopecia. Psoriasis can cause alopecia, however there are usually multiple scalp lesions, as well as psoriatic plaques on the rest of the body. Impetigo is a bacterial infection characterized by a thicker, honey colored crust. There is often oozing from the scalp lesion when the crust is removed. Secondary syphilis can cause a “moth eaten alopecia” with multiple patches of hair loss. Other signs and symptoms of secondary syphilis are often present. Trichotillomania is the compulsive urge to pull one’s own hair. The resulting hair loss is usually in areas that are easy to reach, scaling of the scalp is not associated with trichotillomania.

Tinea capitis is caused by the dermatophytes of the Microsporum and Trichophyton species. It is predominantly a disease of pre-adolescent children, in adults it occurs most commonly in rural setting or in immunosuppressed patients. Transmission occurs usually from person to person or from animal to person. Asymptomatic human and animal carriage is common. Pets or stray cats and dogs can harbor Microsporum canis and transmit it to humans. The clinical presentation of tinea capitis can be very variable depending on the type of infection:

- **Gray patch tinea capitis** presents with partial alopecia, often circular and well demarcated. Broken off hairs are typical and there is minimal inflammation in this type. The associated scales are fine. This type is often caused by Microsporidium species that cause an ectothrix infection, which affects the surface of the hair shaft. Microsporum canis is contracted from cats and dogs and can cause this type of tinea in adults.
• **Black dot tinea capitis** is an endothrix infection, affecting the inside of the hair shaft. This type is caused by Trichophyton species. Broken off hairs near the surface appear as “dots”. This is the most common type in the US and affects mostly children but can be seen in adults, especially in the elderly, as well.

• **Moth eaten tinea capitis** presents as patchy alopecia.

• **Diffuse scale tinea capitis** resembles dandruff.

• **Pustular tinea capitis** is characterized by follicular pustules. Severe forms can lead to a kerion.

• **Kerion.** This type is characterized by inflamed nodules and plaques. The lesion is very painful and often drains pus. Remaining hairs are loose and can be pulled out without causing pain. Kerion often occur in immunocompromised adults.

**CASE TWO CONTINUED:**

You suspect tinea capitis. Microscopic examination of a KOH-scalp scraping preparation shows branching hyphae, which confirms your diagnosis. (The diagnosis can be challenging as KOH preparations can yield false negative results if the specimen is collected from an area that does not contain the fungus or if the specimen is thick-layered and thus obscures the view. Microscopy is operator dependent and the diagnosis requires a trained eye.) You also pluck several hairs from the region and send them out for a fungal culture. The patient informs you that he will get married soon and is planning to move out of state in a month to reunite with his fiancée. He wants to know if his condition is contagious. He also asks you about the side effects of the treatment. He had a severe reaction to penicillin as a child and is hesitant to take any medications.

4. **Review the treatment options for tinea capitis. Which agent would you prescribe for this patient?**

This patient has likely contracted the infection from the animals at his workplace. You should inform him that pets can harbor the infection and can lead to re-infection. Clothing, bedding, or personal items like combs can transmit dermatophytes as well. Topical antifungals are not effective against tinea capitis. Oral agents are required to penetrate the affected hair shafts. The prevalence of tinea capitis varies in different parts of the world depending on the local dermatophytes present. Immigration patterns contribute to the change of prevalent species. The resulting “labile” epidemiology of tinea capitis and resistant strains are the major limiting factors in antifungal therapy (Patel, 2011).

• **Griseofulvin** has been traditionally the treatment of choice in the U.S. Dosing recommendations vary from 375 mg/day to 500 mg/day, divided into two doses. Treatment with this agent requires prolonged therapy for at
At least six to eight weeks. Side effects include nausea, vomiting, headaches, and photosensitivity. This drug should not be used in patients with penicillin allergy, porphyria, liver disease, or in men planning to father children within six months of treatment because of the possible induction of defective spermatozoa. (Patel, 2011).

- **Itraconazole** is safe and effective. However it is a potent CYP3A4 inhibitor and if administered with other medications, drug interactions can lead to QT prolongation. It has also negative inotropic effects and should be avoided in patients with ventricular dysfunction. A typical adult dosing regimen would be 200 mg daily, which can be up titrated to 400 mg daily depending on outcomes. Recommended treatment duration is four to eight weeks.

- **Fluconazole** has weight-based dosing, 6 mg /kg for adults. It is considered safe and effective. Side effects include nausea, abdominal pain, headaches and transaminitis. Hepatotoxicity and QT prolongation are amongst the serious side effects. Treatment duration is 20 days for adults (Patel, 2011).

- **Terbinafine** is more effective against Trichophyton species infections, less so against Microsporidium species. It is dosed 250 mg daily for adults. Treatment duration is four weeks. “A meta-analysis of randomized trials in 2004 showed no significant difference with regard to adverse effects or tolerance of griseofulvin and terbinafine” (Patel, 2011). “Side effects are uncommon, although there is concern of liver toxicity and rarely Stevens-Johnson syndrome, thus encouraging liver function monitoring and careful follow up monitoring” (Patel, 2011).

Although griseofulvin is considered the treatment of choice, it is contraindicated in this patient due to his penicillin allergy. Since it also has a prolonged adverse effect on spermatozoa it would also be a poor choice in this case. This patient may be lost to follow-up when he moves out of state. A short treatment course is therefore ideal for this patient. Itraconazole requires a longer treatment duration. Terbinafine treatment can be completed in four weeks, however monitoring for liver toxicity might not be possible. Fluconazole therefore seems to be the best option for this patient. Treatment is effective, safe and requires only a 20-day course.

Adjunctive topical antifungal shampoos containing selenium sulfide (Selsun), ketoconazole (Nizoral) or pyrithione zinc (Selsun Blue- Itchy Dry Scalp) can decrease shedding of viable fungi and therefore reduce the risk of infection transmission (Grimalt, 2007).
CASE THREE:

One week later you see 30-year-old Mr. Globosa, who was referred to you by his coworker, the patient from Case Two. He states that he has been having itching and extensive scaling on his scalp for the last year. Since he also works in the animal shelter, he is worried that he has tinea capitis as well. His scalp examination is significant for diffuse erythema covered by large yellow scales that are easily removable. There are no areas of alopecia. You notice diffuse erythema of the skin around his eyebrows and in the paranasal area. The skin appears greasy with mild scaling. He states that he has had “dandruff” since he was a teenager.

5. How do you counsel your patient on the etiology of his scalp condition? What treatment options are available?
This patient has seborrheic dermatitis. Seborrheic dermatitis presents as waxy, scaly red patches commonly in the eyebrows, scalp and behind the ears. It occurs primarily in body areas that have a high sebum production. The chest, trunk, groin and even intergluteal folds can be affected as well. Dandruff and seborrheic dermatitis are both linked to the yeast Malassezia, previously known as Pityrosporum. They are considered to be the same condition on different ends of the severity spectrum and are believed to affect close to 50% of the world’s population (Grimalt, 2007). The prevalence is much higher in immune-compromised patients (e.g., AIDS patients) compared to healthy adults (Grimalt, 2007). Malassezia is part of the normal skin flora but not everyone develops seborrheic dermatitis. The yeast is believed to digest sebaceous triglycerides, producing free fatty acids. These penetrate the stratum corneum, leading to an inflammatory reaction causing the symptoms. This inflammatory response does not occur in everyone, which suggests that seborrheic dermatitis has a genetic component as well (Del Rosso, 2007).

Treatment of dandruff and seborrheic dermatitis utilizes three different classes of medications:

- **Keratolytics:** Agents in this class aid in removing the flakes (e.g., salicylic acid shampoo.)
- **Antifungals:** These agents eliminate Malassezia species. [e.g., pyrithione zinc (Selsun Blue-Itchy Dry Scalp or Head and Shoulders), selenium sulfide (Selsun Blue), ketoconazole (Nizoral), ciclopirox (Loprox) applied topically.]
- **Anti-proliferative/Anti-inflammatory agents:** These agents decrease epidermal proliferation and inflammation. (e.g., coal tar, topical steroids) (Grimalt, 2007).
Since the main causative agent in seborrheic dermatitis is the yeast, Malassezia, treatment should include an antifungal agent. No single ingredient from those listed above produces a cure. Therefore a combination of antifungal and anti-inflammatory agents is needed. Using multiple shampoos on a rotating basis is the cornerstone of therapy (Del Rosso, 2007). The shampoos should be used daily for several weeks until remission is achieved. Subsequent use of the shampoos on a weekly basis can aid in prevention of relapses. Recolonization with Malassezia after successful treatment is very common. Seborrheic dermatitis is, therefore, not a disease that is cured. However, treatment prolongs the time between relapses.
Primary Reference:


Additional References:


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CME Questions:

1. Which of the below is not associated with an increased risk for intertrigo?
   a. Obesity
   b. Parkinson’s disease
   c. Diabetes
   d. Urinary incontinence

2. Which agent is the best treatment option for tinea capitis in a 54-year-old male with liver cirrhosis?
   a. Griseofulvin po
   b. Ketoconazole shampoo
   c. Selenium sulfide shampoo
   d. Itraconazole po

3. Which one of the following statements is true?
   a. Seborrheic dermatitis is akin to psoriasis and is therefore mainly treated with antiproliferative agents like tar.
   b. Seborrheic dermatitis is a relapsing condition that can’t be cured completely.
   c. Seborrheic dermatitis is contagious and contact precautions amongst family members is advisable.
   d. Malassezia species appear as branching hyphae on microscopic examination of a KOH specimen.

Answers:

1. b  Obesity, diabetes and urinary incontinence predispose an individual to intertrigo. (Patients with Parkinson’s disease have a higher predisposition to seborrheic dermatitis.)

2. d  Topical therapy is not effective against tinea capitis. Although griseofulvin is considered the drug of choice, it should not be used in patients with liver disease.

3. b  The main causative agent of seborrheic dermatitis is the yeast Malassezia. Treatment has to involve an antifungal agent. Antiproliferatives and keratolytics are used in conjunction with antifungal therapy. The relapsing nature of seborrheic dermatitis is due to recolonization with Malassezia. The symptoms are mainly caused by a reaction to the free fatty acids and not the Malassezia itself; Malassezia is part of normal skin flora. This reaction is not present in every individual. Immune deficient states predispose to seborrheic dermatitis. Branching hyphae on a KOH specimen are consistent with dermatophytes (not yeast).