CLINICAL VIGNETTE

Staphylococcus-Associated Glomerulonephritis: A Complication from Scabies Infestation

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Case Report

A 52-year-old female with a history of DM and hyperlipidemia presented with a diffuse, intensely pruritic rash for 1 week that was worse at night. She also had a red and warm area on her right breast which was excoriated from scratching at night. She had no fever or chills. Her sister who was visiting from Australia had a similar pruritic rash for 2 weeks. The patient tried using over the counter cortisone cream and oral diphenhydramine with no improvement of the itching or the rash. Review of systems revealed a pink-tinged urine for 2 days. Her vital signs showed blood pressure 152/90, temperature 99 degrees F, heart rate 82 and a respiratory rate 12. Exam revealed diffuse pink papules and nodules with areas of excoriation throughout her body with greater concentration of lesions in her breasts, groin, buttocks, abdomen and interdigital spaces of both hands and feet. She had a warm and erythematous area on her right breast that was tender to touch. Closer inspection of the breast skin showed significant scratch marks and excoriation with yellowish drainage. She had no breast mass on exam. She had 1+ bilateral ankle edema. Laboratory results showed: Urinalysis with 3+ hematuria and 2+proteinuria, serum creatinine 2.1 with a glomerular filtration rate of 55, low C3 and normal C4. Wound culture from the right breast showed MRSA infection. Skin biopsy revealed scabies mites. She was treated with permethrin 5% cream on days 1 and 7 and diphenhydramine for pruritis. She was also given oral clindamycin for 10 days for MRSA cellulitis of the right breast. After 1 month, her blood tests showed normalization of serum creatinine and GFR. The pruritic rash has improved with no new lesions. Only residual hyperpigmented scarring from previous scabies infestation remained.

Discussion

Scabies is a common intensely pruritic skin disease caused by infestation with the itch mite *Sarcoptes scabiei* variety *hominis*, a parasitic arthropod that burrows into the skin causing the disease. It affects approximately 300 million people annually worldwide and occurs in all ethnic groups, all ages, and all socioeconomic levels.[1] It is more common in tropical climates. Important risk factors include poverty and crowded living conditions with higher risk of outbreaks in nursing homes, hospitals, and in immunocompromised hosts.[2] Children in developing countries are also susceptible.

Transmission

Human scabies is caused by the human itch mite *Sarcoptes scabiei* variety *hominis*. The adult female mites burrow into the epidermis where they live and deposit their eggs. The eggs hatch 2-3 days later giving rise to larvae which develop into adult mites in about 15 days. Mating occurs between a male and female mite and the cycle starts again. There are about 5-15 female mites living on a host in classic scabies but the number reaches hundreds even millions in cases of crusted scabies.

The predominant route of transmission is direct, prolonged skin to skin contact between humans. Humans are the sole source of infestation. Animals do not spread human scabies. Patients with crusted scabies carry as many as 2 million mites and because of the large number of mites they become highly infectious and may transmit infection through brief skin contact and by indirect contact by sharing clothing, bedding or furniture.

Disease and Symptoms

When a person is infested with the scabies mite for the first time, symptoms often do not appear for 2-6 weeks after onset of infestation. However, an infested person can spread scabies at this time even without symptoms. The most common symptoms of scabies are itching and skin rash. They are caused by sensitization, a type of "allergic reaction" to the mite feces and proteins. Severe itching and rash may affect the entire body and distributed in greater concentration in between fingers and toes, wrists, elbows, armpits, breasts, genitals, buttocks, waists and shoulder blades. The head, neck, face, palms and soles of feet are often involved in infants and young children but not in older children and adults. Tiny burrows are sometimes seen on the skin where they appear as tiny raised grayish-white or skin colored serpiginous lines on the skin.

Diagnosis

The diagnosis of scabies depends on the history and examination of the patient. Whenever possible, the diagnosis of scabies should be confirmed by identifying the mite, mite eggs or mite feces (scybala). This can be done by using the tip of a needle to remove the mite from the end of its burrow or scraping the skin of an infected patient looking for mite, mite eggs or scybala under the microscope. Skin biopsy may also be performed.

The typical presentation of scabies includes intense itching that is worse at night and generalized rash sparing the face and the head. Inflammatory papules are located in between fingers, flexural areas of the wrists, elbows, groin, buttocks, genitalia and breasts in women. Nodules and burrows are specific to scabies and when present are typically seen in the groin, genitalia and the axillae. Secondary nonspecific skin findings such as excoriations, impetigo, cellulitis and eczematous skin changes may also be present.

Crusted scabies in immunocompromised patients appear as erythematous scaly eruption on the face, neck and scalp and soles of the feet making the diagnosis of scabies more challenging. Because of the large number of mites present, crusted scabies is highly contagious and may be transmitted indirectly through fomites, often causing outbreaks among family members and among patients in hospitals.

Treatment

It is important to remember that patients with scabies may not have symptoms for 2-6 weeks after exposure. However, they may spread scabies during this asymptomatic period. In addition to the patient, all household members, sexual partners and individuals the patient had prolonged skin-to-skin contact within the preceding month should be treated.

Topical Permethrin 5% is the drug of choice for classic scabies in the United States, United Kingdom and Australia. It has an excellent record for safety and toxicity. A Cochrane meta-analysis concluded that permethrin is the most effective treatment currently available for scabies.[3] Recent studies report more than 90% cure rate at day 14 or 28.[4-10] Many studies show that permethrin is effective after a single dose but because permethrin's effectiveness as an ovicide remains unresolved, there are guidelines recommending second treatment on day 7 or day 15 to kill residual mites from recently hatched eggs. A significant limitation to the widespread use of permethrin is its cost as it is more costly than other topical treatments. It is unavailable in developing countries where there is a higher prevalence of scabies. In addition, there are emerging problems with resistance.

Benzoyl benzoate 25% is the drug of choice for Africa and parts of Europe. It is not available in the United States. It is effective, affordable and has no known resistance. It can sometimes cause significant immediate skin irritation limiting tolerance to this medication.

Lindane 1% is an organochloride insecticide that has been withdrawn from many regions worldwide due to potential side effect of neurotoxicity. In some countries, however, it remains the first and second-line treatment.[11]

Other Topical Agents

Precipitated sulfur 8-10%. It is effective but due to messy application and odor it is rarely used. It is still used in some areas due to its low cost and safety in infants and pregnant women.

Crotamiton 10% is an old drug that is still in use in some regions of the world due to its safety in infants. It requires multiple applications to increase efficacy and has useful antipruritic property.

Malathion 0.5% is an organophosphate insecticide that is currently a second-line treatment for scabies in the United Kingdom.

Systemic Treatment

Oral Ivermectin 200 microgram/kg is the current recommended dose. The primary indication is treatment of the most severe form of infestation called crusted scabies.[12] In addition, ivermectin is used in mass treatment setting and institutional outbreaks due to ease of use and compliance. Ivermectin is not approved for use in infants and pregnant or lactating women.

Scabies Complications

Throughout the world, scabies causes significant morbidity and mortality through direct effects and as a result of secondary bacterial infection. These complications are important and often underappreciated. Scabies imposes significant economic burden on individuals and families by way of cost of treatment and missed employment, and psychological effect due to stigma and feeling ostracized.

Crusted scabies or Norwegian scabies is a severe form of scabies infestation where thousands even millions of scabies mites are present. Individuals at risk include those who are immunocompromised, the very young and the very old and pregnant women. These patients are highly contagious that even minimal contact may lead to infestation.

Scabies infestation can provide a point of entry for bacteria which may lead to secondary bacterial infection including impetigo, cellulitis and abscess. Bacterial skin infections may predispose to invasive infections and sepsis. There are approximately 660,000 cases of invasive *Streptococcus pyogenes* throughout the world each year leading to more than 160,000 deaths[13] with comparable numbers for *Staphylococcus aureus* infection. In some cases, skin infections with S. pyogenes and S. aureus may lead to glomerulonephritis or rheumatic fever.

Discussion

Staphylococcus-associated glomerulonephritis (SGN) is an immune-complex mediated disease in which the antigen component of the immune-complex is derived from the infective agent. Unlike poststreptococcal-associated glomerulonephritis (PSGN), SGN occurs during active infection. The pathogenesis of SGN remains largely unknown but it likely involves glomerular deposition of preformed immune complexes. SGN requires continuous antigen production and

therefore persistent infection to sustain renal inflammation. Once the infection is properly treated, the glomerulonephritis improves or resolves. A similar mechanism applies to other non-streptoccoccal form of GN such as Hepatitis B, Hepatitis C and parasitic infections.

SGN is rare occurring primarily in middle aged or elderly patients, individuals with diabetes, alcoholism, cancer, or intravenous drug addiction. In a study of 14,138 native adult kidney biopsies over a period of 10 years, 86 patients had glomerulonephritis following a bacterial infection. The mean age for all 86 patients was 56 years. Staphylococcal and streptococcal infections were the most commonly associated bacterial infections. Adults with SGN typically present with a concurrent staphylococcal infection and frequently with hematuria, proteinuria, elevated serum creatinine, new onset hypertension and edema. New onset or exacerbated heart failure is not uncommon in elderly patients due to higher prevalence of underlying cardiovascular disease and reduced ability to handle the salt and water retention associated with glomerulonephritis. The site of infection in SGN usually involves the skin including wound infections (38%), lung infection/pneumonia (22%), heart/endocarditis (10%), deep-seated abscess (6%), urinary tract infection (6%), unknown source (6%).[14]

Diagnosis

The presence of SGN should be suspected in patients with clinical manifestations of active glomerulonephritis, hematuria with or without red cell casts, proteinuria and elevation in serum creatinine. These findings are present in conjunction with a known or suspected staphylococcus infection. The diagnosis is established by kidney biopsy.

The diagnostic criteria used for the diagnosis of SGN requires concurrent staphylococcal infection with onset of glomerulonephritis along with at least two of the following findings: hypocomplementemia (primarily low C3), endocapillary proliferation and exudative glomerulonephritis on light microscopy, C3 dominance staining on immunofluorescence microscopy, or hump shaped sub epithelial deposits on electron microscopy. However, hypocomplementemia with these pathological findings are not completely specific for glomerulonephritis due to a bacterial infection. Therefore, a confirmed diagnosis of Staphylococcal associated glomerulonephritis requires that the disease activity improve after successful treatment of the infection. This means that the hematuria and hypocomplementemia must resolve after treatment of the infection. In some cases, the serum creatinine and proteinuria persist indicating irreversible kidney injury.

In patients suspected of having staphylococcal associated glomerulonephritis, a kidney biopsy may not be required if all three of the following criteria are satisfied: 1) There is clear evidence of overt glomerulonephritis marked by glomerular hematuria, heavy proteinuria (greater than 1 gram per day), an abnormally elevated serum creatinine; 2) A serious infection is present, staphylococcus aureus is documented by a positive blood culture, wound culture or tissue culture; 3) The staphylococcal infection is concurrent with the development of glomerulonephritis.

Monitoring after diagnosis

Patients with SGN should be monitored for signs of resolution of active disease, including elimination of active infection, remission of hematuria, reduction in serum creatinine and resolution of hypocomplementemia.

Treatment

Treatment of Staphylococcus associated glomerulonephritis in adults involves eradicating the infection with antibiotics, controlling hypertension edema with antihypertensive drugs, diuretics and salt restriction.

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Submitted April 24, 2017
Last Revised March 20, 2018