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DERMATOLOGY CLINIC
What's Your Diagnosis?

Clustered Vesicles in a 7 Year Old Female

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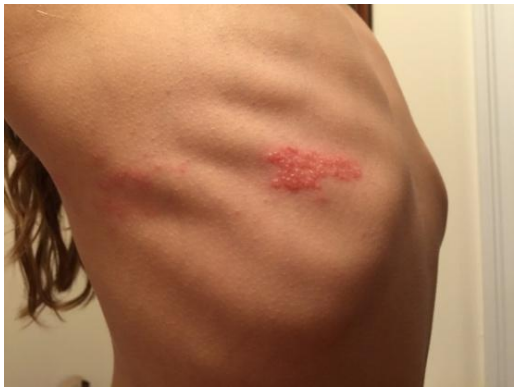
A 7 year old female presents with a 1 day history of rapidly-developing, fluid-filled vesicles on the right chest. The 2-3mm vesicles are clustered on a red base and appear to follow the distribution of her rib. She has no current fever or malaise and no recent illnesses. She has no history of underlying immunodeficiency. However, she did have an episode of bullous impetigo on her legs 2 months earlier. Her skin does not itch. However, the area is sensitive and she does complain of a deep ache in her right chest and abdomen area when she bends. The child thought that she might have banged herself while playing in the playground at school 2 days ago. Mom comments that the schoolyard does have poison ivy along the fenced-in area. Mom had a history of episodic cold sores on her lip, but has not had one recently. The child did not receive the varicella vaccine. She had a mild case of chicken pox at 6 months of age.

What's Your Diagnosis?

A. Cutaneous Herpes (Herpes Simplex)
B. Herpes Zoster (Varicella Zoster)
C. Allergic Contact Dermatitis
D. Bullous Impetigo



HERPES ZOSTER

This patient has a clinical diagnosis of Varicella Zoster, aka Shingles, an acute, unilateral, vesicular eruption caused by the re-activation of latent varicella-zoster virus (VZV). While diagnosis of both chickenpox and shingles are made clinically, confirmation is possible with Tzank smear from cells from the base of a vesicle, and viral culture or PCR studies of blister fluid. When a child gets chickenpox, there is a viremic phase followed by eruption of vesicles. The immune system develops T-cell mediated antibodies as well as an acute and memory T-cell response. That original VZV infects a sensory dorsal nerve root ganglion (the method of spread may be via infected T-cells, or otherwise), usually of the trunk (C2-L2) or a branch of the trigeminal or facial cranial nerves, where it lays dormant for years. If the patient becomes immune-compromised, if the T-cell mediated immunity wanes or if the induced immune response was never strong enough to begin with (particularly true in children who had chickenpox before 1 year of age), the antibodies cannot contain the VZV in its latent state. Dormant VZV can awaken in the nerve, cause nerve inflammation, irritation and can actively replicate, causing pain and a vesicular rash in the skin dermatome overlying the inflamed nerve. The lesions do not spread to other skin sites on the patient via auto-inoculation, though a rare patient may develop a distant vesicle. Another person cannot 'catch' shingles from someone with shingles. However, direct skin contact with shingles lesions, and sometimes aerosolized droplet exposure from a shingles patient with a low VZV antibody titre can infect a naïve person and spread generalized chickenpox to that contact.

In children, chickenpox infection presents as an itchy rash (pink papules, then vesicles, then crusts) and often fever, malaise and pharyngitis, which last about 1-2 weeks. The secondary complications in children can be severe. Cutaneous complications include *staph* and *strep* bacterial skin infections: impetigo, cellulitis and, most frighteningly, necrotizing fasciitis. Neurologic complications include: encephalitis, aseptic meningitis, post-viral cerebellar ataxia and transverse myelitis. When healthy children develop shingles, they can experience a prodromal fever and malaise associated with the viremia, as well as some scattered pink papules and vesicles, but they then develop the classic, clustered vesicles in a dermatomal distribution. The rash usually lasts about 1-2 weeks and, while patients can develop secondary soft-tissue bacterial infections, they usually do not experience significant post-herpetic neuralgia. In contrast, when adults develop chickenpox, they tend to have more severe and extensive rashes and 1/400 will develop a secondary pneumonia, which is associated with a 10-30% mortality rate. When adults develop shingles, they can have severe, painful exanthems that can take over a month to heal, and prolonged, often debilitating post-herpetic neuralgia that can last for months to years.

To prevent these severe and potentially life-threatening secondary complications, children in the US are vaccinated with 2 doses of an attenuated live VZV (Oka strain). The first dose is given after 12 months of age; so that the child's T cell immunity is

developed sufficiently to produce effective antibodies. It is repeated at age 4-6 years of age, in order to boost the T-cell response and increase both cellular and humoral immunity. Some studies have suggested that the second dose be administered in the second year of life, to increase the efficacy of the vaccine sooner, in order to prevent breakthrough varicella infections, when children may be exposed to VZV in daycare and nursery. This vaccine was first made available in 1995. In 1997, 27% of US children were vaccinated; by 2006, this number increased to over 80%. The single dose VZV vaccination program was shown to have an 85% efficacy at preventing clinical VZV infection. Further, a Massachusetts database demonstrated a 79% decrease in varicella (chickenpox) incidence from 2000 to 2010 and an 88% decrease in varicella-related mortality. However, once the 2-dose VZV vaccination protocol was initiated in 2006, the incidence of all varicella disease was decreased by 93%, and the incidence of severe disease was reduced by 99%.

It has been shown that the attenuated live Oka strain VZV virus in the VZV vaccine may remain dormant in a dorsal nerve root ganglion, similar to wild-type VZV after primary infection. As such, these children do have the potential to develop shingles in the future. However it has been noted that, to date, immunized children have a much lower incidence of developing shingles, than children with immunity from primary wild-type VZV infection, and that their presentation is less severe. It is hypothesized that this is due to the lower viral load that is induced with the attenuated strain.

Because most US children are vaccinated, there is decreased exposure to wild-type VZV in the US population; herd immunity. One concern is that children who are not vaccinated or do not mount a sufficient T cell immune response to infection (vaccine failure), will develop chickenpox if they are exposed to VZV at an older age, and that they will have a more severe case with higher potential for secondary complications. Another concern is that we do not yet know how long the vaccine-induced immune response to attenuated VZV will last. If immunity wanes, and there is no ‘booster’ effect by routine exposure to wild-type VZV in the environment, will vaccinated children develop primary chickenpox later in life? Will they be more prone to reactivation of their latent Oka-VZV virus, producing shingles, and, if so, at what age will this occur? As for adults, all acquired immunity wanes with age. If adults do not get intermittent mini-boosters to VZV through exposure to chickenpox from children, there is a theoretical concern that there will be an increased incidence of shingles in today’s ‘older’ adult population. Furthermore, this ‘older’ age may become significantly lowered with time, since younger parents are not being routinely exposed to VZV. In fact, the CDC reports that there has been an increase in shingles diagnoses reported to Medicare from 2000-2010, but, they do not specifically attribute it to the varicella vaccination program in children over a similar period. The lack of demonstration of the predicted increase in adult shingles due to universal VZV vaccination could be attributed to the idea that, for now, we are being exposed to mini-boosts of VZV more frequently than we think, through travel to unvaccinated countries, contact with adult wild-type shingles, and subclinical activation of latent VZV during periods of stress. A shingles vaccine of

limited efficacy is currently available to adults over the age of 50, to boost their T cell immunity to VZV, with a better vaccine on the horizon. But time will tell if a version of this vaccine will be necessary for younger patients who were vaccinated in childhood with Oka-vaccine and hope to maintain their VZV-immune state.

HERPES SIMPLEX

Herpes Simplex (HSV-1, HSV-2) is a double-stranded DNA virus that classically affects the lips and oral mucosa or the genital area. However, it can technically occur on any compromised (scratched, eczema, dry, cracked, cut) skin surface, presenting as clustered vesicles or erosions with crusts on a red base. These infections can complicate eczema or become secondarily infected, themselves. They are often mistaken for impetigo and even shingles. Primary HSV infections occur when the skin comes in direct contact with a herpes sore or with infected secretions from someone who has herpes. Incubation time is days to weeks, after which time most exposed persons will develop sub-clinical infection and antibody production. Some people may even develop a localized painful, crusted herpes sore, while neonates and immunocompromised individuals can develop CNS disease and/or disseminated disease. Recurrent HSV infection occurs in individuals who have already been infected and have circulating antibodies; these persons will develop recurrent lesions at the same (usually) muco-cutaneous site. These lesions are painful and tend to have a prodromal tingling or burning sensation before the lesion presents. HSV can be detected by Tzank smear of cells from the base of a vesicle, by viral culture of blister fluid, or of PCR studies of DNA in the blister fluid. Antiviral therapy is useful in reducing viral load and preventing development of the actual lesion, if it is taken within the first 2 days of prodromal symptoms. This patient has no previous history of HSV lesions at this location, even if her mother has a HSV of oral HSV lesions, the chest is an unlikely site of viral exposure, unless she touched a herpes lesion and then scratched her chest with her unwashed fingers, to introduce virus into the skin.

ALLERGIC CONTACT (RHUS) DERMATITIS

Skin exposure to urushiol, the sap of plants in the *Rhus* family (Poison Ivy, Poison Oak, Poison Sumac) can cause a Type 4, delayed-type contact allergic reaction in susceptible individuals. The skin must be washed clean of the sap within 5 minutes of exposure to prevent the development of a rash. Once 30 minutes have elapsed, predisposed individuals will not be able to prevent the itchy, blistery vesicles that will develop 24-36 hours after skin exposure. Of note, Type 4 allergic reactions develop after the *second* exposure to an allergen; antibodies are formed after the initial exposure. These lesions tend to present in patches, where the plant rubbed, or in linear streaks, where the individual scratched the unwashed skin and spread the urushiol sap to other skin sites. The *rash* of Poison Ivy and Poison Oak is not contagious and cannot be spread to other skin sites. It is a contact allergic reaction to skin that has been exposed to the allergen. Once the rash develops, symptoms can be managed with steroids, anti-histamines and drying agents. While this child might have been exposed

to Poison Ivy in the school yard, unless she fell into the plant and the bare skin on her chest was exposed to the plant or she touched the plant and proceeded to scratch her chest underneath her shirt, it is not the likely cause of her current rash.

BULLOUS IMPETIGO

Bullous impetigo is a localized, superficial blistering condition seen in children, and is due to exfoliative toxins (exotoxins A and B, released by *Staph aureus* phage group 2), which cleaves intercellular desmoglein 1. Shallow, flaccid blisters develop into large bullae that burst easily and leave red, moist erosions with surrounding fine scale. Non-bullous impetigo presents with honey-colored crusts. The bacteria can be cultured from the wound fluid, but diagnosis is usually made on clinical appearance. Treatment includes oral or topical anti-staph antibiotics. If MRSA is suspected, treat accordingly. Recurrent episodes of bullous impetigo can occur. This can often be prevented by treating the child for *Staph aureus* carriage. While this patient was recently treated for an episode of extensive bullous impetigo, the tiny, localized, clustered, intact, non-spreading vesicles she exhibits today do not look like the larger bullae of bullous impetigo.

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