Clinics in Dermatology (2015) **33**, 327–332

ELSEVIER

Clinics in Dermatology

Cutaneous reactions to vaccinations

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Abstract Vaccinations are important for infectious disease prevention; however, there are adverse effects of vaccines, many of which are cutaneous. Some of these reactions are due to nonspecific inflammation and irritation at the injection site, whereas other reactions are directly related to the live attenuated virus. Rarely, vaccinations have been associated with generalized hypersensitivity reactions, such as erythema multiforme, Stevens-Johnson syndrome, urticaria, acute generalized exanthematous pustulosis, and drug hypersensitivity syndrome. The onset of certain inflammatory dermatologic conditions, such as lichen planus, granuloma annulare, and pemphigoid, were reported to occur shortly after vaccine administration. Allergic contact dermatitis can develop at the injection site, typically due to adjuvant ingredients in the vaccine, such as thimerosal and aluminum.

Vaccinations are important to promote development of both individual and herd immunity. Although most vaccinations are considered relatively safe, there may be adverse effects associated with any vaccine. Cutaneous manifestations make up a large portion of the types of reactions associated with vaccines. There are many different reasons for the development of a cutaneous reaction to a vaccination. Some are directly related to the injection of a live attenuated virus, such as varicella or vaccinia (for immunity to smallpox), whereas others cause more nonspecific erythema and swelling at the injection site, as a result of local inflammation or irritation. Vaccinations have also been associated in rare reports with generalized hypersensitivity reactions, such as erythema multiforme, Stevens-Johnson syndrome, urticaria, acute generalized exanthematous pustulosis, and drug hypersensitivity syndrome. There have been case reports associating the administration of a vaccine with the new onset of a dermatologic condition, such as lichen planus, granuloma annulare, and Sweet syndrome. Finally, allergic contact dermatitis can develop at the injection site, typically due to adjuvant ingredients in the vaccine, such as thimerosal and aluminum.

Local site reactions

After administration of injectable vaccines, the most common reaction is a local nonspecific injection site reaction with erythema, swelling, and tenderness (Figure 1). Clinical manifestations usually resolve within a few days to weeks. Supportive treatment with cool compresses and acetaminophen is usually sufficient to reduce symptoms such as pruritus or pain until the cutaneous reaction clears. These findings occasionally may be accompanied by generalized malaise or fever. These symptoms may occur with any vaccine and are not specifically related to any of the vaccine components.[1]

Infrequently, patients may experience local injection site reactions that are specific to particular vaccines, as reviewed below.

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http://dx.doi.org/10.1016/j.clindermatol.2014.12.009
0738-081X/

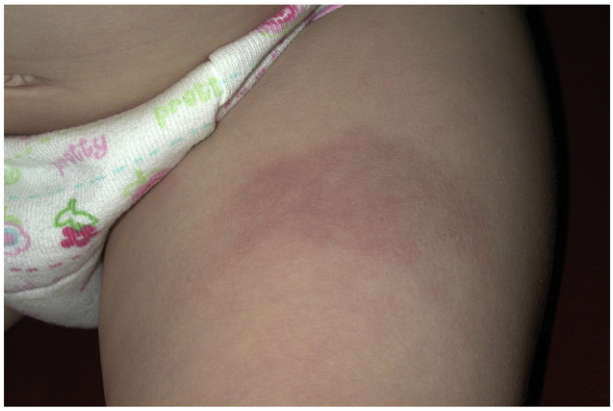

Fig. 1 Localized injection site reaction characterized by erythema and edema.

Nicolau syndrome (aka embolia cutis medicamentosa)

Nicolau syndrome is a local site reaction that can occur following any intramuscular drug injection, including many of the intramuscular vaccines, such as influenza, diphtheria-tetanus-pertussis, diphtheria and tetanus, and hexavalent vaccine (diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae*, and hepatitis B).[2] It is characterized by an acute onset of painful swelling, followed by livedoid erythema, circumscribed hemorrhagic patches, and ultimately necrosis of the cutaneous and soft tissues. These lesions may resolve with scarring but usually cause no long-term functional impairment. The pathogenesis of this condition is not completely understood but is thought to be due to vasospasm secondary to needle prick, embolization of the injected material, or pressure from the injected material around the vessel.[2] Early intervention to prevent necrosis is important. Improved local blood flow may be accomplished with the use of pentoxifylline, heparin, or hyperbaric oxygen. Local inflammation may be reduced with intralesional corticosteroids, being careful to withdraw before injection to avoid intravascular injection.[3] Systemic antimicrobials may also be administered to prevent secondary infection.[2]

Hepatitis B vaccine

In addition to erythema, edema, and tenderness at the injection site, patients receiving the hepatitis B vaccine have been found to develop nodules and granulomas at the injection site.[4] These lesions are less common; however, they usually persist longer than the nonspecific findings of edema, erythema, and tenderness.

Smallpox vaccine

The vaccine against smallpox, developed by Edward Jenner in 1798, was the first of its kind. Jenner had succeeded in demonstrating that immunity to cowpox was protective against smallpox. The smallpox vaccine is still in use today and is made from the virus causing cowpox, known as vaccinia virus. It does not contain the smallpox virus and cannot cause smallpox; however, it is a live virus vaccine with its own set of complications. Smallpox vaccination is not a routine component of the current vaccination schedule. Given recent concern about the smallpox virus being used for biologic warfare, vaccination of military personnel and other "first responders" has been performed since 2001. Increased research efforts have recently been undertaken in an effort to increase the safety of the vaccine, should there be a need for widespread use in the future.

After smallpox vaccine inoculation, erythema develops with a central eschar. In rare cases, a cutaneous reaction related to the introduction of the vaccinia virus via immunization may expand beyond the injection site. These reactions include progressive vaccinia, eczema vaccinatum, and generalized vaccinia. Progressive vaccinia is a rare complication seen in immunocompromised individuals in which the initial injection site fails to heal within 14 days. The nonhealing injection site develops an ulcer with central necrosis and eschar formation. Similar satellite lesions then appear at distant sites. Systemic symptoms usually occur late in the course of the illness. The degree and type of immunodeficiency determines the likelihood of developing progressive vaccinia and the severity of the illness. Progressive vaccinia may be fatal due to overwhelming viremia or secondary septicemia.[5]

Eczema vaccinatum is characterized by an acute onset of disseminated painful vesicles and pustules in a patient with a history of atopic dermatitis (Figure 2).[6] Positive viral cultures or direct observation of infected cells by direct immunofluorescence solidifies the diagnosis. Pathologic examination typically reveals balloon degeneration of keratinocytes with the presence of multinucleated epithelial cells. Fatality from this reaction ranges from 5-40%. Current guidelines exclude anyone with a personal history of atopic dermatitis from receiving the smallpox vaccine. In addition, vaccinated individuals should not be in contact with anyone with a history of atopic dermatitis until the injection site is completely healed. There have been cases of eczema vaccinatum developing in household contacts of vaccinated individuals.[7] Given that such a large percentage of the United States population has atopic dermatitis, this issue will likely be very complicated if widespread smallpox vaccination is necessary in the future. Newer vaccines for smallpox are under development that will not contain live inoculates and, therefore, will not be a potential cause of eczema vaccinatum.

Generalized vaccinia is a clinical diagnosis based on the development of a vesicular, pustular, and/or papular eruption in an otherwise healthy individual at sites distant from the vaccination site.[8] These lesions are thought to be due to hematologic spread of the virus. Recent diagnostic criteria require that smallpox virus be confirmed in these lesions by viral culture, immunohistochemistry, or polymerase chain reaction.