Henoch-Schönlein Purpura Following a Meningococcal Vaccine

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ABSTRACT. We report a 17-year-old girl who developed Henoch-Schönlein purpura 10 days after receiving a meningococcal vaccine (Menomune). To our knowledge, this is the first case report of Henoch-Schönlein purpura temporally associated with the tetravalent serogroups A, C, W-135, and Y meningococcal vaccine administered in the United States. Pediatrics 2003;112:e491–e494. URL: http://www.pediatrics.org/cgi/content/full/112/6/e491; Henoch-Schönlein purpura, meningococcus, Meningitec, vaccine, leukocytoclastic vasculitis, vasculitis.

ABBREVIATIONS. HSP, Henoch-Schönlein purpura; LCV, leukocytoclastic vasculitis; IgA, immunoglobulin A.

Henoch-Schönlein purpura (HSP) is a form of systemic leukocytoclastic vasculitis (LCV) characterized by the deposition of immunoglobulin A (IgA)-containing immune complexes in tissue. A meningococcal capsular polysaccharide vaccine has been administered for the past 30 years. The Advisory Committee on Immunization Practices currently recommends that colleges inform incoming students, particularly those who plan to reside in dormitories and face an increased risk of meningococcal disease compared with the general population, about the disease and the availability of a safe and effective vaccine.

CASE REPORT

A healthy 17-year-old girl with no significant medical history presented with 5 days of a nonpruritic eruption that began on her ankles and spread rapidly to her legs and thighs. She denied any new contacts or medications and had started taking Viactiv, a calcium supplement, 1 week before the onset of the rash. She received the Menomune meningococcal polysaccharide vaccine, groups A, C, Y, and W-135 (Aventis Pasteur, Swiftwater, PA), 10 days before the onset of the eruption.

At presentation, a physical examination revealed an otherwise well teenager with multiple purpuric papules, some with darker centers and purpuric halos and others with central ulceration on the bilateral lower extremities, buttocks, volar hands, and left elbow. She denied having abdominal pain, hematuria, fever, cough, or change in bowel movements. In the next couple of weeks, new lesions developed on bilateral elbows and ankles, and the existing lesions progressed to hemorrhagic bullae and then to more prominent purpuric bullae and ulcers (Fig 1). Clobetasol cream twice a day, rest, and lower extremity elevation were prescribed.

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DISCUSSION

HSP is the most common type of vasculitis diagnosed in childhood and is seen less frequently in adults. The main clinical manifestations of HSP include palpable purpura, arthritis, abdominal pain, gastrointestinal bleeding, and nephritis. The symptoms are caused by a LCV caused by IgA deposits in vessel walls. Although the precise etiology of HSP is unknown, IgA is certainly involved. There are increased serum IgA concentrations, increased serum
polymeric IgA, circulating immune complexes that contain IgA, and IgA rheumatoid factor demonstrable in most cases.\textsuperscript{1}

The mean age of children affected by HSP is 6 years, and 90% of children afflicted with HSP are <10 years old.\textsuperscript{2} HSP is most common in the fall and winter and frequently follows an upper respiratory infection. It has been inconclusively attributed to pharyngitis caused by \textit{Streptococcus pyogenes}, hepatitis B infection, varicella infection, human immunodeficiency virus, adenovirus, mycoplasma, herpes simplex virus, \textit{Helicobacter pylori}, \textit{Toxocara canis}, human parvovirus B19, and coxsackie virus as well as drugs and environmental factors.\textsuperscript{3,4}

The tetravalent serogroups A, C, Y, and W-135 meningococcus vaccine is administered in the United States. The vaccine contains specific purified bacterial capsular polysaccharides.\textsuperscript{5} Menomune, the meningococcal polysaccharide vaccine, groups A, C, Y, and W-135, involved in this report, is indicated for a select population \textsuperscript{2} years old to prevent \textit{Neisseria meningitidis} meningitis. Serogroups B, C, and Y are equally responsible for most sporadic meningococcal disease in the United States today. Although serogroup B was responsible for epidemic meningococcal disease in the 1990s, serogroup C is implicated in most North American meningococcal epidemics and is the most common serogroup to affect young adults.\textsuperscript{6}

Standard vaccination of US inhabitants is not recommended, because there is a low disease incidence, vaccine protection is short, and the vaccine is not very effective in children \textsuperscript{<2} years old, who are most likely to have sporadic disease. The meningococcal vaccine is recommended for use to prevent and control serogroup C meningococcal outbreaks; for people with terminal component complement deficiencies; for people with anatomic or functional asplenia; travelers to countries with hyperendemic meningitis; and individuals with occupational exposure to \textit{N. meningitidis} aerosol. Most germane to this report, the Advisory Committee on Immunization Practices recommends that college students (especially those planning to reside in dormitories) and their parents be informed about their increased risk for meningococcal disease and the existence of a safe and effective vaccine.\textsuperscript{7}

With >6 million meningococcal vaccinations administered, there have been very few reports of serious adverse events. Side effects consist mainly of tenderness and erythema at the injection site,\textsuperscript{8} transient fevers,\textsuperscript{9} headache, malaise, dizziness, and chills seen in a minority of patients.\textsuperscript{10,11} There have not been any previous reports of temporally associated HSP. Unexplained IgA nephropathy has been associated with Menomune vaccinations on rare occasions (Aventis Pasteur Inc, unpublished data, 2003, available at www.micromedex.com). This association is of particular interest to this report, because HSP and IgA nephropathy are associated with identical histologic findings in the kidney.

In the case we report, the patient was 17 years old, did not have a preceding upper respiratory infection, and developed HSP at the beginning of the summer. The temporal relationship of the development of HSP and the Menomune meningococcal polysaccharide vaccine, groups A, C, Y, and W-135, are notable. There was a 2001 report from the United Kingdom of a case of HSP that was temporally associated with the serogroup C meningococcal conjugate vaccine C (Meningitec).\textsuperscript{12} There have been several reports of vasculitis following various immunizations. HSP has been associated with the influenza vaccine\textsuperscript{13} and measles vaccine.\textsuperscript{14} LCV has been associated with the pneumococcal vaccine,\textsuperscript{15} and vasculitis has been reported after hepatitis B and bacillus Calmette-Guérin vaccines\textsuperscript{16,17} Although a relationship between the vaccination and the development of HSP may be coincidental, past reports of temporally associated vaccinations and vasculites without other identifiable etiologies or historical factors set a precedent for association, albeit with different vaccines and antigens.

Previous observations suggest that there may be an immunopathogenic association between meningococcal diseases and vasculitis. There have been

![Fig 1. Multiple purpuric papules, some with darker centers and purpuric halos and others with central ulceration, on the bilateral lower extremities.](http://pediatrics.aappublications.org/)
multiple reports of cutaneous LCV associated with chronic meningococcemia. Although chronic meningococcemia is associated with intermittent bacteremia and antibiotic administration may impede a positive bacterial culture, nearly all reported skin lesion cultures have been negative for *N. meningitidis*. Attempts to demonstrate antigens and IgA specificity have been similarly futile.18 These aseptic lesions suggest an immunologic mechanism rather than direct bacterial invasion.19 Immune complexes have been demonstrated in the lesional skin and synovial fluid of patients with acute meningococcal meningitis who developed cutaneous lesions and arthritis. A decrease in circulating meningococcal antigen titer, followed by a rise in antibody level to the same antigen immediately subsequent to the onset of skin lesions, was also observed in some of these patients.20 Although endotoxins and disseminated intravascular coagulation may be responsible for the vasculitis associated with acute meningococcal meningitis, this evidence of decreasing antigens and increasing antibodies supports the proposed hypothesis of vasculitis resulting from an immunologic response to meningococcal antigen, either naturally or possibly (as in this case) iatrogenically.

The temporal association between the meningococcal vaccine and the development of HSP is notable. We cannot explain the immunopathogenic link between the meningococcal polysaccharide vaccine, groups A, C, Y, and W-135, and vasculitis, but we think that practitioners should be aware of this possible complication and evaluate further cases of post-vaccination vasculitis with causality in mind. However, HSP is extremely rarely associated with the meningococcal vaccine and should not affect vaccine usage.

REFERENCES


Fig 2. (A) Biopsy of lesional skin of the leg shows superficial perivascular neutrophils with karyorrhectic debris, associated with fibrin in and around venular walls, typical of LCV (hematoxylin/eosin, original magnification ×20). (B) Direct immunofluorescence of lesional skin demonstrates bright granular labeling surrounding and within venular walls with IgA (original magnification ×40)
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