

Generalized Vaccinia 2 Days after Smallpox Revaccination

To the Editor: Hospital and public health personnel are currently receiving smallpox vaccination in a national effort to increase preparedness for a possible deliberate release of smallpox (1). Generalized vaccinia (GV) is a typically self-limited adverse event following vaccination (incidence 23.4–238.2 cases per million primary vaccinees and 1.2–10.8 cases per million revaccinees) (2,3).

We report the clinical course and laboratory diagnosis of GV in a 37-year-old woman with a history of at least one uncomplicated childhood inoculation that left a vaccination scar. She was revaccinated on March 12, 2003. Before revaccination, the patient reported no contraindications to vaccination and denied any conditions that typically weaken the immune system (including HIV/AIDS, leukemia, lymphoma, other cancers, radiation, chemotherapy, organ transplant, post-transplant therapy, immunosuppressive medications, severe autoimmune disease, and primary immune deficiency). The patient also confirmed that she did not have a skin disease or a history of eczema or atopic dermati-

tis, nor was she pregnant or allergic to a vaccine component.

On March 14, some 44 hours after vaccination, the patient reported headache, chills, pruritus, chest pain (described as chest “heaviness”), recurrent vomiting, and maculopapular lesions. The lesions, characterized by the patient as “mosquito bites,” first appeared on the face, then the legs, and then the trunk and upper extremities. Maximum oral temperature was 37.7°C. Over the next 4 days, approximately 30 pustules developed, several of which began to drain. Nausea persisted, and the patient had a stiff neck and recurring chest tightness, but physical examination, echocardiography, electrocardiography, and chest radiography results were within normal limits. By March 25, the patient’s lesions had all scabbed, the scabs had fallen off, and she felt well enough to return to work. Pustular material obtained on March 18 from two unroofed lesions on the shoulder (Figure) and back tested positive at the Wadsworth Center-Axelrod Institute, New York State Department of Health, for vaccinia virus DNA by a TaqMan (Applied Biosystems, Foster City, CA) real-time polymerase chain reaction assay provided by the Laboratory Response Network, Centers for Disease Control and Prevention. The presence of

ortho-poxvirus was confirmed by electron microscopy of lesion fluid.

This case is the first report of a laboratory-confirmed case of GV among recent civilian vaccinees and is notable for the GV occurrence in a revaccinee. GV was not reported among 132,656 military personnel recently revaccinated (4). A single case of GV in a revaccinee among 38,514 recent civilian vaccinations (5) yields a ratio that exceeds the rate in revaccinees observed in earlier reports and the difference would be even greater if civilians who received primary vaccinations were excluded.

This laboratory confirmation of GV demonstrates the potential of laboratory testing to determine the cause of a post-vaccination rash. Possible cases of GV in earlier surveillance efforts represented a mixed group of rashes, some of uncertain etiology (6). This patient’s clinical course is notable for the onset of GV 2 days after vaccination, as compared to a mean of 9 days (range 1–20+) after (generally primary) vaccination (2) and suggests that viremia can occur quickly after vaccination.

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Figure. Pustular lesion on patient’s shoulder, 6 days after revaccination.

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***Salmonella* enterica Serovar Enteritidis, Japan**

To the Editor: Nontyphoidal salmonellae are the important causative agents of foodborne diseases in Japan and other industrialized countries. *Salmonella enterica* serovar Enteritidis has risen to the leading cause of infection among *Salmonella* spp. since 1989 (1). Emergence of drug-resistant *S. Enteritidis* has been rarely reported while *S. Typhimurium*, another serovar of major public health concerns, has been reported to acquire multidrug resistance such as DT104 resistance to ampicillin, chloramphenicol, streptomycin, sulfonamide, and tetracycline (R-ACSSuT) (2).

We previously reported outbreaks caused by strains resistant to ampicillin and streptomycin (resistance type R-AS, herein); the strains' reac-

tions against the phages used in bacteriophage typing did not conform to any known reaction patterns (phage type [PT] RDNC-a, herein, with the following reactions: (-) for #3, 5-7, 11-13, 15, and 16 phages; (+++) for #2 phage; opaque lysis [OL] for #4 and 9 phages; <OL for #10 phage; and ambiguous reactions (-/+++)) were observed for #1, 8, and 14 phages) (3). To investigate the characters of the R-AS strains more extensively, we surveyed isolates from outbreaks that occurred from 1997 to 2002 for antimicrobial drug susceptibility and bacteriophage typing.

S. Enteritidis strains from 899 outbreaks that occurred from 1997 to 2002 were tested. Bacteriophage typing was done according to the Public Health Laboratory Service (PHLS), London, United Kingdom guidelines (4). Antimicrobial drug susceptibility testing was done with a disc diffusion method on Mueller-Hinton II agar (Becton Dickinson Microbiology Systems, Cockeysville, MD) as previously described (5). Antimicrobial drugs used in this study were ampicillin, streptomycin, tetracycline, kanamycin, nalidixic acid, gentamycin, sulfamethoxazole-trimethoprim, trimethoprim, chloramphenicol, cefotaxim, and ciprofloxacin.

Dominant phage types were PT4 (36.9%) and PT1 (26.9%). They have been dominant among outbreak-related strains since 1992 (1). Other types were also identified at certain frequencies. For example, RDNC-a, PT47, PT6, PT6a, and PT21 accounted for 4.4%, 5.3%, 4.0%, 3.2%, and 2.0% of the phage types, respectively.

Strains sensitive to all the antimicrobial drugs tested were the most predominant (55.1%), followed by those resistant to only streptomycin (34.8%). R-AS was the third most predominant, accounting for 4.1%. A correlation existed between drug resistance and phage types in that all the R-AS strains (n = 37) showed RDNC-a in bacteriophage typing, and

all the RDNC-a strains (n = 40) were resistant to at least ampicillin including two R-A and one R-AST strains.

Since previous studies described the correlation between drug resistance and phage types as a result of acquisition of an R-plasmid (6), we focused on the relationship between RDNC-a and ampicillin resistance. Plasmid profiles analysis of the RDNC-a strains showed that all but one (R-AST) had at least two kinds of plasmids, and all but one were approximately 50 kb and 60 kb in size. The last could be the so-called serovar-specific plasmid (7). Southern blot analysis by using the ampicillin resistance gene of pBluescript KS (+) (Stratagene, La Jolla, CA) as a probe indicated that a resistance gene was carried on the 50-kb plasmid. Furthermore, when *Escherichia coli* DH10B cells (Invitrogen Corporation, Carlsbad, CA) were transformed with plasmids isolated from an RDNC-a R-AS strain and plated onto Luria broth plates containing 100 mg/L of ampicillin, the 50-kb, but not 60-kb, plasmid could be isolated from the ampicillin-resistant transformants. And the 50-kb plasmid from the transformants was hybridized to the probe for ampicillin resistance described above. Thus, the 50-kb plasmid of RDNC-a R-A or -AS strains was suggested to be an R-plasmid responsible for ampicillin resistance.

A representative 50-kb plasmid (p981123) was prepared from the DH10B transformant cells described earlier for further characterization. Southern blot analysis suggested that a 6-kb *EcoRI* fragment contained the resistance determinant. Sequences for the fragment were analyzed done by using ABI PRISM 310 sequencer and BigDye Terminator Cycle Sequencing Ready Reaction Kit (Applied Biosystems, Foster City, CA). The resulting sequence showed high similarities to *Pseudomonas aeruginosa* Tn801 (accession no. AF080442; 98% identical) and *E. coli* Tn3 (accession