SUMMARY OF ADVERSE EVENTS FOLLOWING CIVILIAN AND MILITARY SMALLPOX VACCINATION—LOS ANGELES COUNTY, 2003

BACKGROUND

The US discontinued routine childhood smallpox immunization in 1971 and routine immunization of health care workers in 1976 with the last reported smallpox case reported in Somalia in 1977. In 1980, the World Health Organization (WHO) Global Commission for the Certification of Smallpox Eradication officially declared that smallpox eradication had been achieved. Since 1977, there have been no indigenous cases of smallpox despite extensive surveillance [1]. In the fall of 2002, the Los Angeles County (LAC) Department of Health Services Immunization Program prepared a smallpox vaccination plan for selected health care workers, public health workers and first responders in response to renewed concerns that the smallpox virus might be used as a biological weapon against military or civilian targets. In February 2003, LAC Immunization Program initiated Phase I of the smallpox vaccination plan with the vaccination of selected public health workers, hospital based teams, and first responders. The military initiated their smallpox vaccination program earlier that year, January of 2003. This renewed direction to initiate a smallpox immunization program within the US raised concerns many health care workers would be confronted with smallpox vaccination reactions for the first time in their professional careers.

Smallpox vaccine is made from live vaccinia virus and protects against the disease smallpox caused by the variola virus. It does not contain variola virus, the causative agent of smallpox [1]. Because viral replication and shedding occurs at the vaccination site (beginning 2-5 days post-vaccination), unintended transmission is possible from the time immediately after vaccination until the scab separates from the skin, approximately 2-3 weeks [2]. Although virus exists in the scab, it is bound in the fibrinous matrix, and the scab is not believed to be highly infectious. During the smallpox eradiation era, transmission usually required close interaction and occurred most often in the home [3]. Adverse events following vaccination can occur following individual smallpox vaccination or as a result of unintended transmission of vaccinia virus from recently vaccinated immunized persons. Adverse reactions following smallpox vaccination have been well documented during the years of universal vaccination in the US. Most adverse reactions are diagnosed on the basis of clinical examination and history. Most reactions can be managed by observation and supportive care; they are usually self-limited include fever, headache, fatigue, myalgias, chills, local skin reactions, nonspecific rashes, erythema multiforme, lymphadenopathy, and pain at the vaccination site [3]. Other reactions are most often diagnosed through a completed history and physical and might require additional therapy. Adverse reaction that might require further evaluation or therapy include: inadvertent inoculation, generalized vaccinia, eczema vaccinatum, progressive vaccinia, postvaccinia central nervous system disease, and fetal vaccinia. An in depth discussion of the diagnosis, treatment, prevention of the above noted adverse events is provided by the CDC [2]. This report summarizes the smallpox vaccination adverse events reported to the ACDC from February 26 to May 9, 2003.

METHODS

Smallpox vaccination adverse events reports were obtained through passive surveillance. Adverse events were reported to ACDC by both medical providers and by infection control practitioners from hospital facilities that suspect smallpox adverse events.

Case definition: A smallpox vaccination adverse event was defined as a reaction following the vaccination that did not meet the criteria of a normal vaccination response or unintended or “inadvertent” vaccinia transmission to an unvaccinated person due to close contact with a recently vaccinated person.

In preparation for the start of a limited smallpox vaccination program (Phase I) involving volunteer public health and medical workers and selected first responders, LAC medical providers were made aware of

potential adverse events following smallpox vaccination that they might encounter in their clinical setting through a mass mailing. The mass mailing was sent to all LAC medical providers and included: recommendations from the CDC [2], a memorandum from the health officer mandating reporting of smallpox adverse events within one day, description of the treatment available for smallpox adverse events, and directions for clinicians needing clinical consultation and treatment for adverse events through our program (ACDC). Once a report was called to an ACDC physician, a standardized Vaccine Adverse Event Reporting System (VAERS) report form was completed by the clinician and submitted to ACDC. This report was then faxed to the LAC Immunization Program, State of California Immunization Program and the CDC Immunization Program. All serious adverse events that required treatment consideration with vaccinia immune globulin (VIG) or antiviral therapy with cidovifir were made with in collaboration with the ACDC, the treating physician, and the CDC smallpox adverse event expert consultation line. Clinicians were requested to submit clinical specimens to the LAC Public Health Laboratory for testing for the presence of vaccinia virus. All clinical specimens submitted for vaccinia testing had nucleic acid polymerase chain reaction (PCR) testing, direct fluorescent antibody testing (DFA) to assess the presence of vaccinia virus in addition to other viral testing that could clinically mimic an adverse event which included herpes simplex virus (PCR) and varicella virus (DFA).

RESULTS

From February 26 through May 9, 2003, seven adverse events related to smallpox vaccination were reported to the ACDC. These seven included, 4 were female and 3 were male, median age=28 (range 19 to 53 years). There were no deaths reported.

Of the seven individuals, four (three female and one male) had adverse events secondary inadvertent vaccinia transmission from close physical contact with military contacts that had recently been vaccinated with the smallpox vaccination, and three cases were civilian smallpox vaccinees.

Three civilian smallpox adverse reactions were reported from vaccines. The first report was a 23 year-old male health care worker reported pleuritic chest pain 7 days following vaccination. Medical evaluation did not reveal evidence of myocardial or pulmonary damage. His symptoms resolved in 7 days. The second was a 53 year-old male physician who presented with a radicular pain syndrome involving the neck. His medical workup did not show spinal cord damage and his symptoms resolved in 2 days. The third report was in a 38 year-old public health worker who was diagnosed with generalized vaccinia 12 days following smallpox immunization. None of these individuals required hospitalization, treatment with VIG or cidofovir, and all recovered uneventfully.

Four adverse events were documented due to inadvertent transmission from their military close contacts. The first documented and most serious adverse event occurred in a female contact to military contact developed ocular vaccinia with conjunctivitis. She presented to multiple emergency rooms with presumed bacterial conjunctivitis until she was eventually hospitalized and the correct diagnosis was made. Her diagnosis was confirmed by the LAC Public Health Laboratory when her conjunctival specimen revealed vaccinia by DFA and PCR testing. This person received specific treatment with VIG and made an uneventful recovery after 3 days [4]. The remaining three individuals with inadvertent inoculation of the vaccinia virus from their intimate military contacts were not hospitalized, did not require specialized therapy, and recovered uneventfully. Vaccinia lesions due to close contact were described on these individuals' forearm, digit and mid-thorax, and one person had pustular lesions on her scalp and forearm. In two of the four cases, vaccinia was demonstrated in the lesions by DFA and PCR technology. In one of the four cases, no specimen could be obtained and in the other cases the specimen did not reveal vaccinia and the diagnosis were made by clinical examination and medical history. Following May 9, 2003, no further adverse events were reported to ACDC.

DISCUSSION

On March 28, 2003, the CDC reported cases of cardiac adverse events among vaccinated recently with smallpox vaccine [5]. This included 10 cases of myopericarditis among approximately 240,000 primary

vaccines in the military vaccination program, and two such cases (one with myocarditis and one of pericarditis) had been reported among civilian vaccinees. Additionally, the CDC received reports of five civilian patients with cardiac ischemic events after smallpox vaccination, including three patients with myocardial infarctions and two patients with angina. Two of the five individuals died due to myocardial infarction. With the documentation of cardiac adverse events following smallpox vaccination in both the military and civilian population, the Advisory Committee on Immunization Practices (ACIP) issued new emergency recommendations that persons be excluded from pre-event smallpox vaccination program who have known underlying heart disease, with or without symptoms, or who have three of more known major cardiac risk factors [6]. With these noted cardiac adverse event reports, smallpox vaccination requests severely dropped off in LAC. In total, 243 non-military persons received smallpox vaccination in 2003 in LAC. The drop off in civilian smallpox vaccine doses and possibly stricter guidance to military smallpox vaccines regarding transmission to their close contacts following vaccination may have contributed to the sharp cut-off of reported adverse events following smallpox vaccination.

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