Case Report

Human cowpox virus infection acquired from a circus elephant in Germany

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1. Introduction

Cowpox virus is an orthopox virus causing localized skin efflorescences in mammals. Other members of the orthopox genus are monkeypox, camelpox, gerbilpox, mouselpox (ectromelia), vaccinia, and variola virus. In 1798, the British physician Edward Jenner showed that cowpox infection protects against smallpox (variola). Consequently, cowpox virus and later vaccinia virus were used as live vaccines against smallpox. Worldwide vaccination programs led to the eradication of smallpox, with the last 'wild' case occurring in 1977. Here we describe the clinical course of a case of human cowpox, directly acquired from an Asian circus elephant.1

2. Case report

A 19-year-old male was admitted to the hospital with a vesicle on his right forearm of 1 cm in diameter, and a surrounding erythema of 1–3 cm in diameter. Palpation showed one non-tender lymph node about 1 cm in diameter in the right axilla. The physical examination was otherwise normal. With the exception of C-reactive protein (30.2 mg/l; normal <5 mg/l), all routine laboratory parameters were normal. A bacterial swab detected Staphylococcus aureus in large quantities, sensitive to all antibiotics tested, except penicillin.

The patient had cared for four female Asian elephants in a circus. One of these elephants, who had been bought in 1979 at the age of 14 years from a Danish zoo, developed apathy and malaise. Two weeks later, vesicles erupted around the mouth and the trunk and evolved into ulcers up to 15 cm in diameter. The patient never wore gloves when caring for this elephant, and he remembered minor wounds on his fingers. Another week later, 22 days before hospital admission, the patient noticed a vesicle on the radial side of the distal end of his right forearm. The elephant had to be euthanized, and PCR revealed cowpox virus DNA in the ulcers.1 The other three elephants had been separated from the diseased animal and have remained healthy.

A swab of the patient’s lesion (Figure 1) was processed for virus isolation and polymerase chain reaction (PCR). Orthopox virus sequences were amplified from DNA directly extracted from the swab. The virus was propagated in the African green monkey kidney cell line MA 104; a cytopathogenic effect was seen 36 h later. The virus was identified as an orthopox virus with the Orthopox Light Cycler Kit (Qiagen, Hilden, Germany), and the entire open reading frame of the hemagglutinin gene (921 base pairs) was sequenced. Comparison with sequences in the NIH
GenBank data base showed that the sequence obtained here had the highest identity (99%) with four cowpox virus strains, isolated from a monkey, two elephants, and a cat (sequence numbers AY298785, AY900298, AY900270, and AY9002300). No virus could be isolated from a swab taken on day 46 (Figure 1) since disease onset, after the scab had fallen off, and the amount of orthopox virus genomes as detected by PCR was approximately 10 000-fold less than the amount detected on day 22.

DNA sequence analysis revealed identity of the strains isolated from the patient, from the elephant, and from rats present in the elephant's winter quarters.1

In our patient, orthopox virus antibodies were confirmed by plaque reduction test. The titer was 1:80 on day 22, 1:320 on day 26, and 1:160 on days 32, 39, and 46.

In the absence of systemic disease, no antiviral treatment was started. The patient was isolated during his hospital stay, and the ulcer was disinfected daily and kept covered with dry and sterile dressings. The staphylococcal superinfection was treated orally with amoxicillin plus clavulanic acid. The surrounding erythema subsided within one week, the CRP level fell to 7.6 mg/l, but some fluid oozed from the ulcer. Within two weeks, the diameter of the black lesion increased from 1 to 2 cm.

After three weeks, the ulcer started to heal, and the patient was discharged. He was informed that the skin lesion would remain infective until the last scab had disappeared. He was instructed to keep the ulcer covered with a sterile dressing and to avoid contact with other persons and with animals, until the ulcer had healed completely. Healing was complete within 10 weeks after the onset of symptoms, leaving behind a scar of 1 cm in diameter.

3. Discussion

Until now, cowpox viruses have only been found in Europe, Turkmenistan, Israel, and possibly Egypt.2 Contrary to its name, cowpox is not enzootic in cattle.2 During the last 20 years, there have only been two reports of cow-derived human cowpox infections,4,5 and one report of a cowpox outbreak in cattle.5

Our patient was infected by direct inoculation from a circus elephant. The hemagglutinin gene of the patient's virus isolate was 100% identical with the hemagglutinin sequence of the strain isolated from the elephant.1 The elephant, in turn, was infected by rats, since the same virus strain was identified in rats caught in the elephant's stable.3

Mice, voles, and rats can act as cowpox reservoirs.7 One study from England found cowpox antibody prevalence rates of 20% in wood mice, and of 20% and 33% in bank and field voles, respectively.7 In small rodents, cowpox virus infection delays the birth of the first litter by 20–30 days, without causing other symptoms.8 Feeding on small rodents infects cats, where the disease spectrum includes subclinical infections, skin lesions, coryza, and severe systemic disease.9 The first case of feline cowpox was discovered in England in 1977.10 Since then, cowpox prevalence may have increased in cats, with orthopox antibody rates reaching 2% in England, 4% in Austria, 10% in Norway, and 14% in Germany.11 Like cats, zoo animals probably contract cowpox by ingesting small rodents. In the elephant described here, the appearance of mouth and trunk lesions is compatible with such a pathway of infection.

Cowpox or cowpox-like viruses have been isolated in outbreaks among captive animals including okapis, elephants, cheetahs, and anteaters and big cat carnivores.12,13 Most human cases are cat-derived,2 and two reports have described rat-to-human transmission.14,15 Aerogenic or droplet infection has not been described.

Cidofovir, which is used in human cytomegalovirus retinitis, prevents death in balb/c mice infected by aerosolized cowpox virus.16 There are no reports of cidofovir use in human cowpox. Nevertheless, cidofovir is probably effective in this disease. However, since the patient had no complications, cidofovir was not given.

In immunocompetent humans, cowpox usually remains localized. Skin lesions typically heal within 12 weeks, leaving behind a permanent scar. In our patient, cowpox virus was cultured from a swab obtained at day 22, but not from a swab obtained at day 46, after the scab had fallen off. However, poxvirus DNA was still detectable at day 46, albeit at only 1/10 000 of the original quantity.

Whether the number of human cowpox cases would increase after discontinuing smallpox vaccination is a question that has been raised.3 A Medline search revealed 21 cases (at least nine unvaccinated)13 between 1944 and 1977, while 35 reports of human cowpox were published between 198717 and 2008.18 At least 18 of these 35 patients were born after the discontinuation of smallpox vaccination in 1980. The vaccination status of the other 17 patients was unknown. Therefore, the increasing number of published cases during the last 20 years may reflect an emergence of cowpox, rather than just an increased interest. Among these 33 cases, seven had a nonfatal generalized disease14 and two had a fatal generalized disease.19,20 One of the two patients who died from cowpox had received steroids for asthma.19 The case fatality rate of human cowpox may be similar to the 1–3% reported for controlled inoculation of smallpox virus (variolation) performed in the pre-Jenner days to protect against fatal smallpox.3

Since rats, mice, and voles can carry cowpox virus, contact between captive animals and small rodents should be avoided. Pets, zoo animals, and circus animals with skin lesions should be investigated for cowpox and caregivers should wear gloves.

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References


