Human Monkeypox Infection: A Family Cluster in the Midwestern United States

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Background. The outbreak of monkeypox in the Midwestern United States during June 2003 marks the first documented human infection in the Western Hemisphere. Consistent with those in outbreaks in Africa, most cases in this outbreak were associated with febrile rash illness. We describe a cluster of monkeypox in a family with a spectrum of clinical illness, including encephalitis, and outline the laboratory confirmation of monkeypox.

Methods. Standardized patient information was collected by questionnaire and medical chart review; all cases described were laboratory confirmed. Laboratory methods included nucleic acid detection, viral culture, serologic testing, histopathologic evaluation, and immunohistochemical testing.

Results. Of 3 family members with monkeypox, 2 had rash illness only, and 1 required hospitalization for severe encephalitis. The family member with the mildest clinical course had previously received smallpox vaccination. Diagnostic testing by both polymerase chain reaction and culture revealed infectious monkeypox virus in skin lesions of all 3 patients; 2 patients had orthopoxvirus detected by immunohistochemistry in skin lesions. The patient with encephalitis had orthopoxvirus-reactive immunoglobulin M (IgM) in cerebrospinal fluid. All patients had detectable IgM responses to orthopoxvirus antigens.

Conclusions. These 3 patients illustrate a spectrum of clinical illness with monkeypox despite a common source of exposure; manifestation and severity of illness may be affected by age and prior smallpox vaccination. We report that monkeypox, in addition to causing febrile rash illness, causes severe neurologic infection, and we discuss the use of novel laboratory tests for its diagnosis.

In June 2003, an outbreak of human monkeypox that had been transmitted from infected exotic pets was identified in the United States [1, 2], representing the first time that human monkeypox infection has been documented in the Western Hemisphere. The source of the US outbreak was traced to native prairie dogs (genus Cynomys) housed with exotic pets imported from Africa at an Illinois pet distributor; the index animal source is suspected to be imported wild rodents from Africa, where the disease is endemic [1]. Subsequent close contact between humans and infected pets led to laboratory confirmation of 37 human infections as of January 2004. Most cases were associated with a mild, self-limited febrile rash illness [2]; we describe a cluster of cases of monkeypox in a family with a common source of exposure, including a case of severe encephalitis.

PATIENTS AND METHODS

Case Investigation

Inquiry of these patients was performed as part of a public health response; verbal consent was obtained, and a standardized questionnaire collecting data on demographics, exposures, and signs, symptoms, and risk factors of infection was completed by interview and chart review. Assessment of the patient with encephalitis was performed in the context of routine medical care. Patient samples (e.g., skin lesion tissue and cerebrospinal fluid [CSF]) were sent to the Centers for
Disease Control and Prevention (CDC; Atlanta, GA) for monkeypox-specific testing.

**Laboratory Methods**

**Nucleic acid detection.** Real-time and standard polymerase chain reaction (PCR) assays were used to identify *Orthopoxvirus* genus and monkeypox species nucleic acid signatures in clinical specimens. Homogenates of skin tissue and CSF were evaluated. Standard assays included single-gene PCR, followed by restriction fragment–length polymorphism [3–5]. An additional novel multiplex standard PCR assay [6] discriminated monkeypox virus from vaccinia and variola viruses. Real-time PCR assays included evaluation of the presence of a specific monkeypox nucleic acid signature encoded in an envelope gene designated B6R [7] and 2 independent orthopoxvirus nucleic acid signatures in the DNA polymerase gene. Positive controls included monkeypox DNA; negative controls consisted of no-template controls and other orthopoxvirus DNAs. Internal controls for sampling adequacy and nucleic acid extraction detected human β-actin. Real-time PCR assays specific for human herpesviruses (HHVs) 1 and 2 were performed by use of a commercial assay kit (Artus Biotech USA), in accordance with the manufacturer’s instructions; PCR assays specific for varicella-zoster virus (VZV) were also performed [8, 9].

**Culture.** All clinical specimens were evaluated for the presence of viable infectious virus by use of standard methods [10].

**Immunohistochemistry.** Immunohistochemical (IHC) tests using the immunoalkaline-phosphatase technique were performed. The primary antibodies used included a rabbit anti–variola (smallpox) virus antibody, a mouse anti–vaccinia virus antibody, and a rabbit anti–monkeypox virus antibody [11]. IHC tests for various human HHVs, including HHV-1, -2, and -3, were also performed. Positive controls included orthopoxvirus- and HHV-infected cells; negative controls consisted of patient tissue sections incubated with normal rabbit or mouse serum.

**Serologic testing: orthopoxvirus IgM capture, serum, and CSF.** For the IgM ELISA, microtiter plates (Immulon II) were coated with 100 μL of a 1:800 dilution of goat anti–mouse IgG horseradish peroxidase (HRP) conjugate (KPL) and added for 30 min at 37°C. Plates were washed, and tetramethyl benzidine (TMB–1 component peroxidase substrate) (KPL) was added, and development was allowed to proceed for 5–20 min. Plate reactions were stopped by addition of stop solution (KPL) and read at 450 nm on a SoftMax Pro optical density reader (Molecular Devices).

**Serologic testing: indirect IgG ELISA, serum, and CSF.** Microtiter plates (Immulon II) were coated with 100 μL of vaccinia virus (purified) at a concentration 0.01 μg of DNA/well, in carbonate buffer, overnight at 4°C. Plates were then blocked for 30 min at room temperature with assay diluent, followed by washing. Patient samples were then added at a 1:100 dilution, for serum, and at 1:20, 1:40, 1:80, and 1:160 dilutions, for CSF, and were incubated for 1 h at 37°C. Plates were washed, and goat anti–human IgG HRP conjugate was added at a 1:2000 dilution for 1 h at 37°C. Plates were washed, and TMB-1 component substrate was added, and development was allowed to proceed for 5–15 min. Stop solution was added, and reactions were read at 450 nm. Values reported represent the average of duplicate wells of each sample. Positive and negative control serum samples were used as assay controls. Negative controls were used to generate a cutoff value for each plate by averaging the negative controls and adding 3 × SD.

**RESULTS**

**Case Reports**

On 18 May 2003, a 30-year-old woman (patient A), her 33-year-old husband (patient B), and the couple’s 6-year-old daughter (patient C) purchased 2 prairie dogs from a pet trade show; both animals appeared to be healthy at the time of purchase. All 3 family members, none of whom had a medical history of significance, had extensive contact with the animals. On 21 May, 1 of the animals was noted to appear to be ill, displaying lethargy, wasting, and anorexia; on 24 May, the animal died. The following day, the second animal developed similar signs, and it died 2 days later. On 29 May, all 3 family members developed illness, as described below. Each of the 3 family members was identified at a local health facility as having a vesiculopustular rash illness consistent with a poxvirus infection; awareness of the outbreak of monkeypox infection in nearby states via print journalism, CDC and Marshfield Clinic Web sites, and elicitation of prairie-dog exposure eventually led to the suspected diagnosis.

**Patient A.** On 29 May 2003, patient A developed sore throat, headache, fever, and malaise concurrent with development of a small painless papule on her left cheek. Over the course of the next 48 h, throat soreness and malaise worsened, and additional lesions developed, most prominently on the chest and arms. On 2 June, the patient presented to a primary-
care physician, who noted a vesiculopustular rash with focal areas of hemorrhage progressing in a uniform manner to include the entire body, most prominently on the trunk and including the palms and soles (figure 1); ∼150 lesions were present at this time. She was referred to a dermatologist, who made a diagnosis of possible staphylococcal infection; no treatment was rendered. That same evening, the patient experienced acute worsening of throat soreness, as well as a sense of airway obstruction; she was seen in an emergency room, where she was given a bolus of prednisone, resulting in subsequent improvement of dyspnea. On 4 June, her daughter, patient C, was hospitalized with new-onset seizures. At this time, patient A was noted to have ∼200 lesions, covering the entire body; all lesions had a similar morphological appearance, and no scabbing was noted. By 7 June, several of the lesions began to scab, and patient A experienced improvement of systemic symptoms. On 9 June, on the basis of suspicion of monkeypox infection, due to an ongoing epidemic in the surrounding area, skin biopsies of several lesions were performed; by 11 June, sloughing of scabs had begun, and patient A remained otherwise well. By 16 June, all lesions had developed scabs, most of which had sloughed. Patient A subsequently remained asymptomatic with no further lesions.

**Patient B.** Patient B had received smallpox vaccination as a child; a scar was documented on the left arm. On 29 May, the patient developed a mild flulike illness with mild body aches and sore throat. These symptoms resolved over the next 48 h. On 1 June, he noticed a small raised nonpruritic vesicle on his right palm, followed 2 days later by a similar lesion over his left eyebrow. He remained free of systemic symptoms, however, and no further lesions developed. The patient did not seek medical care; however, on 9 June, along with patient A, skin biopsy was performed on his palmar lesion, on the basis of suspicion of monkeypox infection. The patient subsequently remained asymptomatic with no further lesions.

**Patient C.** Patient C was a previously healthy 6-year-old girl. Her childhood immunizations were up-to-date, with the exception of varicella vaccine. On 29 May 2003, she was febrile to 39.4°C and had sore throat, malaise, anorexia, and headache. Two days after onset of symptoms, she was evaluated in an emergency department, where she was found to have enlarged tonsils, cervical adenopathy, and a vesiculopapular rash limited to a small area on the back; she was treated with cefdinir and antipyretics for presumed group A streptococcal infection and released. Over the next 24 h, the rash spread to the face, trunk, distal extremities, palms, and soles. On 4 June, she was reevaluated at the same emergency department. During evaluation, she was febrile and somnolent and became acutely unresponsive, with pupillary dilatation and muscle rigidity; with resolution of presumed seizure activity, she was administered lorazepam, intubated, and transferred to another facility for intensive care.

On examination on arrival to the intensive care unit, she

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**Figure 1.** Photograph of skin lesions on patient A. Hemorrhagic-appearing palmar lesions are depicted.
was febrile to 39.4°C and tachycardic; her blood pressure was 102/52 mm Hg, and respirations were 40/min with chest-wall retraction. Oxygen saturation was 95% on a nonrebreather mask; the lungs were clear to auscultation. Examination of the pharynx revealed tonsillar enlargement, with pharyngeal erythema and edema, and profuse, thick exudate. Oral cavity lesions were not noted in the presence of the exudate. Skin evaluation revealed ∼90 discrete vesiculopustular lesions with erythematous bases. Some were umbilicated; none were scabbed or necrotic. All lesions were of uniform stage and morphologic appearance. The lesions predominated on the distal extremities, with fewer lesions on the face and trunk.

On initial neurologic examination, the patient was unresponsive to verbal commands but withdrew appropriately to noxious stimuli. The pupils were equal and reactive; fundoscopic examination revealed mild optic disc edema without retinal hemorrhages or exudates. Corneal and gag reflexes were diminished. Her neck was supple. Deep tendon reflexes were depressed throughout; sustained ankle clonus was elicited on the left, and the toes were up-going bilaterally.

Laboratory tests were significant for an arterial blood gas profile consistent with respiratory failure, a peripheral leukocytosis, and CSF pleocytosis with normal levels of protein and glucose (table 1). Other admission laboratory studies, including electrolytes, hematological analysis, and liver-function tests, were normal. A noncontrasted computed tomogram of the head was normal. A diagnosis of VZV encephalitis, herpes simplex encephalitis, or enterovirus or meningococcal disease was suspected on the basis of the presence of rash and encephalopathy; smallpox was considered on the basis of the rash. She was immediately placed in strict isolation and given empiric intravenous ceftriaxone, acyclovir, phenobarbital, and midazolam.

During the next 48 h, the patient was extubated. A brain magnetic resonance imaging (MRI) scan obtained on 7 June showed diffuse cortical, thalamic, and brain stem edema, meningeal enhancement, and left thalamic and right parietal signal abnormality (figure 2). An electroencephalogram (EEG) showed diffuse slowing with no epileptiform activity. Ceftriaxone was discontinued because CSF and blood cultures were without bacterial growth. Laboratory studies for metabolic and infectious etiologies for encephalitis—including bacterial and viral cultures, fungal serology panels, latex agglutination of serum, CSF for bacterial pathogens and cryptococcal antigen, and CSF VDRL—were negative.

On 9 June, her skin lesions began to scab, but she remained febrile and stuporous with variable response to verbal commands and tactile stimulation. A repeat CSF profile showed improvement of pleocytosis (table 1). Suspicion of monkeypox infection led to submission of skin biopsy specimens, serum, and CSF for definitive monkeypox virus testing. On 12 June, her fever resolved, and phenobarbital was stopped. A repeat brain MRI scan obtained on 13 June revealed decreased brain edema with resolution of the abnormal meningeal enhancement. The cerebral hemispheres, thalami, and pons demonstrated increased signal consistent with parenchymal edema secondary to meningoencephalitis. Encephalopathy subsequently improved, and, 12 days after admission, she began responding verbally and was able to follow simple commands. Fourteen days after admission, she was conversing appropriately, ambulating with assistance, and eating solid foods. She was discharged 2 days later. Over the next several days, the patient’s strength and mobility continued to improve; a follow-up neurologic examination performed on 2 July was normal, with no neurologic sequelae noted. At that time, all skin lesions had scarred, and scabs had fallen off.
Laboratory Diagnostic Tests

Nucleic acid testing and viral isolation. Laboratory testing of skin biopsy specimens from all 3 family members displayed definitive evidence of an infectious Orthopoxvirus species, speculated as monkeypox virus, by a combination of PCR and culture (table 2). PCR results for monkeypox were concordant for ≥2 monkeypox-specific genes, in addition to orthopoxvirus generic tests. In direct examination of nucleic acid extracted from CSF, there was no evidence, by PCR, for HHV-1 or -2, VZV, or orthopoxvirus.

Immunohistochemistry. Histopathologic evaluation of skin sections from patient A displayed an intradermal vesicle with focal spongiosis and ballooning degeneration of epidermal keratinocytes, dense cytoplasmic granules, and reactive nuclei (figure 3A). The dermis showed mixed perivascular inflammatory infiltrates. IHC testing demonstrated abundant staining of orthopoxviral antigens within the cytoplasm of keratinocytes (figure 3B) and karyorrhectic debris. Tissue from a leg vesicle that developed later during illness in patient C showed a small fragment of fibroadipose tissue with scant neutrophilic infiltrates. Rare, focal staining of orthopoxviral antigens was identified within the cytoplasm of fibrohistiocytes. No staining of HHV-1 or -2 or VZV was identified in the skin biopsy specimens from either patient.

Serologic testing. Robust orthopoxvirus-reactive IgM was present in both CSF and serum (figure 4) from patient C. An IgM peak on or before day 10 of illness and a concurrent increase in IgG peak at day 13 of illness were demonstrated (figure 4). Of uncertain significance was a weakly positive HHV-2 IgM CSF test; HHV-1 and -2 IgG serologic testing was nonreactive 2.5 weeks after onset of illness. Both parents showed evidence of orthopoxvirus IgM in serum samples (table 2) obtained 2 weeks after onset of illness. Orthopoxvirus IgG seroreactivity was seen in patient B.

DISCUSSION

Human monkeypox was first identified in Zaire, now the Democratic Republic of Congo (DRC), in 1970, near the end of smallpox eradication efforts in Africa [12]. Outbreaks of human illness have been documented in the DRC in recent years, involving >450 suspected cases [13–15]; additional cases have been sporadically reported in other western and central African countries. Previous studies of the disease conducted in western and central Africa describe clinical characteristics similar to those of smallpox. The recent US outbreak represents the first time that human monkeypox has been identified outside of Africa. Clinicians initially evaluating patient C included smallpox as a possible differential diagnosis. After accessing the CDC Web site and its information on the recently observed human monkeypox disease associated with prairie dog exposure, they realized that the pustular rash lesions were more likely to be from the closely related orthopoxvirus monkeypox.

Monkeypox virus is a double-stranded DNA virus of the genus Orthopoxvirus; it is genetically distinct from other orthopoxviruses, including variola virus (the cause of smallpox) and vaccinia virus (the virus used as smallpox vaccine) [16]. Descriptive studies conducted in Africa through 1986 have provided most of our understanding of human disease and epidemiology. Transmission is primarily by large droplets or direct contact. Compared with the transmissibility of smallpox, transmission of monkeypox is inefficient; however, recent studies suggest that, as the number of individuals who have never been vaccinated against smallpox has increased, the number of secondary transmission events has also increased [16, 17].

<table>
<thead>
<tr>
<th>Patient, specimens evaluated</th>
<th>Tests performed</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient A (30-year-old woman)</td>
<td>Viral culture, PCR, IHC test&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Positive</td>
</tr>
<tr>
<td>Skin lesion</td>
<td>ELISA (IgM), ELISA (IgG)&lt;sup&gt;bd&lt;/sup&gt;</td>
<td>Positive (IgM and IgG)</td>
</tr>
<tr>
<td>Serum</td>
<td></td>
<td></td>
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<tr>
<td>Patient B (33-year-old man)</td>
<td>Viral culture, PCR</td>
<td>Positive (IgM and IgG)</td>
</tr>
<tr>
<td>Skin lesion</td>
<td>ELISA (IgM), ELISA (IgG)</td>
<td>Positive (IgM and IgG)</td>
</tr>
<tr>
<td>Serum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient C (6-year-old girl)</td>
<td>Viral culture, PCR, IHC test&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Positive</td>
</tr>
<tr>
<td>Skin lesion</td>
<td>ELISA (IgM), ELISA (IgG)</td>
<td>Positive (IgM and IgG, see figure 4)</td>
</tr>
<tr>
<td>Serum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebrospinal fluid</td>
<td>Viral culture, PCR</td>
<td>Negative</td>
</tr>
<tr>
<td>Cerebrospinal fluid</td>
<td>ELISA (IgM)</td>
<td>Positive</td>
</tr>
</tbody>
</table>

<sup>a</sup> B-SC-40 tissue culture; a positive result signifies isolation of monkeypox virus from that specimen.
<sup>b</sup> Polymerase chain reaction (PCR) assays for Orthopoxvirus genus and >2 monkeypox species nucleic acid signatures.
<sup>c</sup> Immunohistochemical (IHC) test for orthopoxvirus antigens using broadly reactive anti–variola, anti–vaccinia, and anti–monkeypox virus antibodies.
<sup>d</sup> ELISA for orthopoxvirus IgM (antigen-capture assay) and IgG (indirect ELISA) antibodies.
Figure 3. Histopathologic features and immunohistochemical staining of cutaneous lesions of monkeypox. A, Marked nuclear atypia and ballooning degeneration of keratinocytes (hematoxylin-eosin; original magnification, ×150). B, Immunohistochemical staining of monkeypox virus predominantly in cytoplasm of infected epithelial and connective tissue cells (immunoalkaline phosphatase with naphthol fast-red substrate and hematoxylin counterstain; original magnification, ×150).

After an incubation period of 7–19 days, clinical monkeypox is characterized by a prodrome of fever, headache, and fatigue. Adenopathy is common and may distinguish this infection from smallpox [14]; although many patients in the US outbreak had extensive adenopathy [2], this feature was noted in only 1 of our patients. Generally, the rash evolves uniformly as macules, papules, vesicles, and pustules and then crusts over the course of 2–3 weeks. Lesions are most prominent on the head and extremities and often involve the palms and soles. This classic centrifugal distribution manifested in patients A and C. The areas of focal hemorrhage within lesions in these patients have previously been described with cowpox but not with monkeypox. It is unknown whether this is a clinical feature associated with this strain of monkeypox virus or whether skin pigmentation may be responsible for this observation. The lesions of monkeypox may be differentiated from those caused by VZV, a virus also associated with encephalitis. VZV lesions, in contrast to those of monkeypox, are small, superficial, concentrated mainly on the trunk, and classically evolve in different stages (crops) [18].

Encephalitis has rarely been associated as a complication of monkeypox infection, having been described only once previously [14, 19]. Vaccinia virus, a related orthopoxvirus, has been associated with a complication known as postvaccinal encephalomyelitis (PVE) when administered as vaccination against smallpox [20, 21]. Cases of PVE have variably displayed clinical and diagnostic features suggestive of a postimmunization demyelinating encephalomyelitis (acute disseminated encephalomyelitis) or direct viral infection of the central nervous system (CNS) [21–23]. In patient C, who had monkeypox-specific IgM antibodies in CSF, the diagnosis of monkeypox-associated encephalitis was confirmed by skin biopsy and encephalopathy. Since IgM does not normally cross the blood-brain barrier, detection of IgM in CSF is suggestive of active infection of the CNS with intrathecal antibody production and, although dependent on the timing of testing relative to disease progression, serves as the laboratory diagnostic standard for several infectious encephalitides [24]. The presence of intrathecal IgM, cytotoxic changes demonstrated by diffuse and focal edema, and the absence of demyelination all support the association of monkeypox as the cause of acute encephalitis in patient C. Weakly positive HHV-2 IgM, generally associated with genital herpes infections, was observed in CSF from patient C; however, this result is discordant with the more-sensitive nonreactive HHV-1 and -2 PCR testing on CSF. Additionally, although patient C had been treated with high-dose acyclovir, clinical features pathognomonic for herpes simplex virus encephalitis, including signal abnormality or hemorrhage of the temporal lobe by neuroimaging [25] and periodic lateralizing epileptiform discharges by EEG [26], were absent, and no HHV-1 or -2 seroreactivity was seen up to 2.5 weeks into her illness.

Smallpox vaccine affords protection against monkeypox both by preventing disease and by decreasing disease severity [14]. In the African series, severe disease (e.g., that requiring intensive
nursing care or that with the presence of >99 rash lesions) was more common among persons not vaccinated with smallpox vaccine (73.9%) than among vaccinated persons (39.5%) [17]. In contrast, milder disease (that without physical incapacitation or that with the presence of <25 rash lesions) was more common among persons vaccinated with smallpox vaccine (37.2%) than among unvaccinated persons (7.5%) [17]. These studies demonstrated 85% protection with smallpox vaccine against disease acquisition within households. This is consistent with the mild clinical course of patient B, the only family member to have received smallpox vaccination as a child. The unvaccinated mother and child, on the other hand, developed "severe" disease, by the African criteria. Also, human and animal studies suggest that disease susceptibility and severity is greater in persons of younger age [17].

There is currently no US Food and Drug Administration–approved treatment for monkeypox; however, several options may be of potential benefit. Cidofovir is an antiviral medication with documented in vitro activity against poxviruses, including vaccinia and monkeypox [27, 28]; it has been recommended as a second-line agent in the management of possible smallpox-vaccine adverse events [29] and may be an agent for consideration in the treatment of monkeypox. The administration of vaccinia immune globulin (VIG) may have efficacy in the treatment of monkeypox, on the basis of serologic cross-protection among the orthopoxviruses [30]. Under an investigational new

![Figure 4. A, Detection of orthopoxvirus-specific IgM in cerebrospinal fluid (CSF) from patient C, collected on 4 and 9 June 2003. A dilution series of CSF were tested and compared with a panel of control CSF from patients not associated with an orthopoxvirus infection. B, Detection of orthopoxvirus-specific IgG and IgM in serum from patient C. Serum samples were tested and compared with a cutoff value (COV) generated with 5 negative control serum samples from patients not associated with an orthopoxvirus infection. OD₄₅₀, optical density at 450 nm.](https://academic.oup.com/jid/article-abstract/190/10/1833/2191730)
drug protocol, VIG is recommended as treatment for severe adverse events of vaccinia used as smallpox vaccine [29]. It may have efficacy in treatment of complications of monkeypox attributable to viral replication. In patient G, recovery followed supportive care alone.

Clinicians should consider monkeypox in the differential diagnosis of atypical vesiculopustular rash illness, including cases of encephalitis associated with rash. The differential diagnosis of encephalitis in patients with rash should include the common causes of rash-associated viral encephalitis, particularly varicella and HHV infection, but, given our report, should be broadened to include monkeypox in the appropriate context, such as the presence of atypical rash illness, exposure to exotic pets, or recent travel to Africa.

A range of novel diagnostic methods—including PCR, serologic testing, and IHC testing—can be used to confirm various orthopoxvirus infections, including monkeypox. Anti–orthopoxvirus IgM reactivity in CSF may be useful in diagnosing encephalitis due to orthopoxviruses. With further validation, the demonstration of seroconversion to IgM and then an anti–orthopoxvirus IgG response will be a useful tool in diagnosing infectious orthopoxvirus illness. Although there are no quantitative data on potential dose and specific exposure types, this case series represents a unique exploration of the range of monkeypox disease presentation seen in different human hosts exposed to the same viral strain emanating from a common source.

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