CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 24-2022: A 31-Year-Old Man with Perianal and Penile Ulcers, Rectal Pain, and Rash

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PRESENTATION OF CASE

Dr. Vivian De Oliveira Rodrigues Gama (Medicine): A 31-year-old man was admitted to this hospital because of perianal and penile ulcers, rectal pain, and vesiculopustular rash.

The patient had been in his usual state of health until 9 days before this admission, when he noticed several itchy white "bumps" around the anus that subsequently evolved into ulcerative lesions. The next day, he sought evaluation at a primary care clinic of another hospital. Tests for human immunodeficiency virus (HIV), syphilis, gonorrhea, and chlamydia were performed. An injection of penicillin G benzathine was administered, and treatment with valacyclovir was started.

During the next 5 days, the perianal ulcers did not abate, and the patient stopped taking valacyclovir. Painful proctitis with rectal bleeding and malodorous, mucopurulent discharge developed, along with fever, chills, drenching sweats, and new tender swelling in the groin. Three days before this admission, a new painless ulcer appeared on the penis that was similar in appearance to the perianal ulcers. Two days before this admission, new scattered vesicular lesions appeared on the arms and legs, and the patient presented to the infectious disease clinic of this hospital for evaluation.

Additional history was obtained from the patient. Fourteen years before this evaluation, sore throat and upper body rash developed; he received a diagnosis of secondary syphilis and was treated with penicillin G benzathine. He also had a history of recurrent oral herpes simplex virus (HSV) infection, for which he was treated intermittently with valacyclovir. He took daily oral emtricitabine and tenofovir for HIV preexposure prophylaxis (PrEP). There were no known drug allergies.

The patient lived in a suburban area of Massachusetts with two roommates and a cat. Two weeks before this evaluation, he had traveled to an urban area of southeastern Canada. During this trip, he had had sex with male partners without the use of barrier protection. There was no other recent travel. The patient did not smoke cigarettes or use illicit drugs; he drank alcohol rarely.

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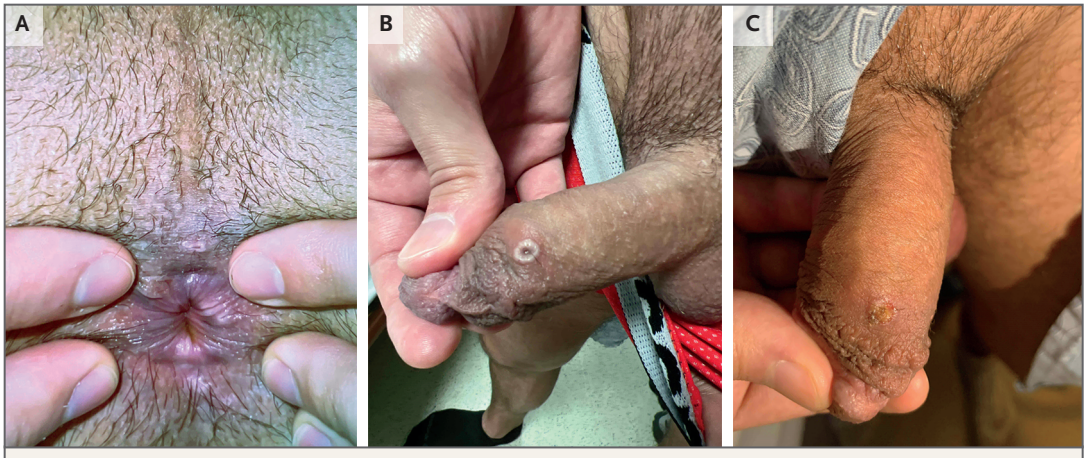

Figure 1. Photographs of Perianal and Penile Ulcers from 2 Days before Admission.

Panel A shows a tender perianal ulcer, measuring less than 1 cm in diameter, with raised, firm margins. Panel B shows an ulcer on the dorsum of the penile shaft, measuring 7 mm in diameter, that is similar in appearance to the perianal ulcer. Panel C shows that the ulcer has heaped margins around a central dry base. In all panels, the patient's hands are shown.

On examination, the temperature was 36.5°C, the blood pressure 130/86 mm Hg, the pulse 75 beats per minute, and the oxygen saturation 98% while the patient was breathing ambient air. The body-mass index (the weight in kilograms divided by the square of the height in meters) was 23.9. There were six tender perianal ulcers, measuring less than 1 cm in diameter, with raised, firm margins. There was also one ulcer on the dorsum of the penile shaft, measuring 7 mm in diameter, with raised borders (Fig. 1). Painful bilateral inguinal lymphadenopathy was present. The perianal skin was weeping, and there was proctitis with severe tenderness that precluded digital rectal examination. In addition, there were approximately 12 papulovesicular lesions scattered across the chest, back, arms, and legs. The lesions measured 2 mm in diameter, were filled with clear fluid, and had surrounding erythema (Fig. 2A and 2B).

Blood levels of electrolytes and glucose were normal, as were the results of kidney-function and liver-function tests. A blood test for treponemal antibodies was positive; a rapid plasma reagin (RPR) test was reactive at a dilution of 1:1. A blood test for HIV was nonreactive, and tests of urine and rectal specimens for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* nucleic acids were negative. A test of a specimen obtained from a perianal ulcer for HSV nucleic acids was performed, and a blood sample was obtained for bacterial culture. An injection of ceftriaxone was administered, and treatment with valacyclovir and doxycycline was started.

During the next 2 days, the ulcers did not abate and the rectal pain worsened, such that the patient was not able to sit, sleep, or have bowel movements. Additional skin lesions appeared. The patient returned to the infectious disease clinic for evaluation. Anoscopy revealed intense rectal and anal inflammation with shallow ulcerations and purulent exudate, findings consistent with proctitis (Fig. 3). The patient was admitted to this hospital.

On examination, the patient appeared uncomfortable because of rectal pain. Skin lesions that had become pustular with an erythematous base were scattered across the scalp, chest, back, legs, and arms, including one on the palm (Fig. 2C). There were no lesions in the mouth. Multiple tender, enlarged inguinal lymph nodes, measuring more than 1 cm in diameter, were present. The perianal and penile ulcers were tender and had heaped margins around a central dry base. The complete blood count and the white-cell differential count were normal. Swabs from a perianal ulcer and a chest skin lesion were obtained for bacterial culture.

Treatment with intravenous acyclovir was started, and doxycycline was continued; stool softeners and hydromorphone were administered. A blood test for HIV type 1 RNA was performed.

A diagnostic test was performed.

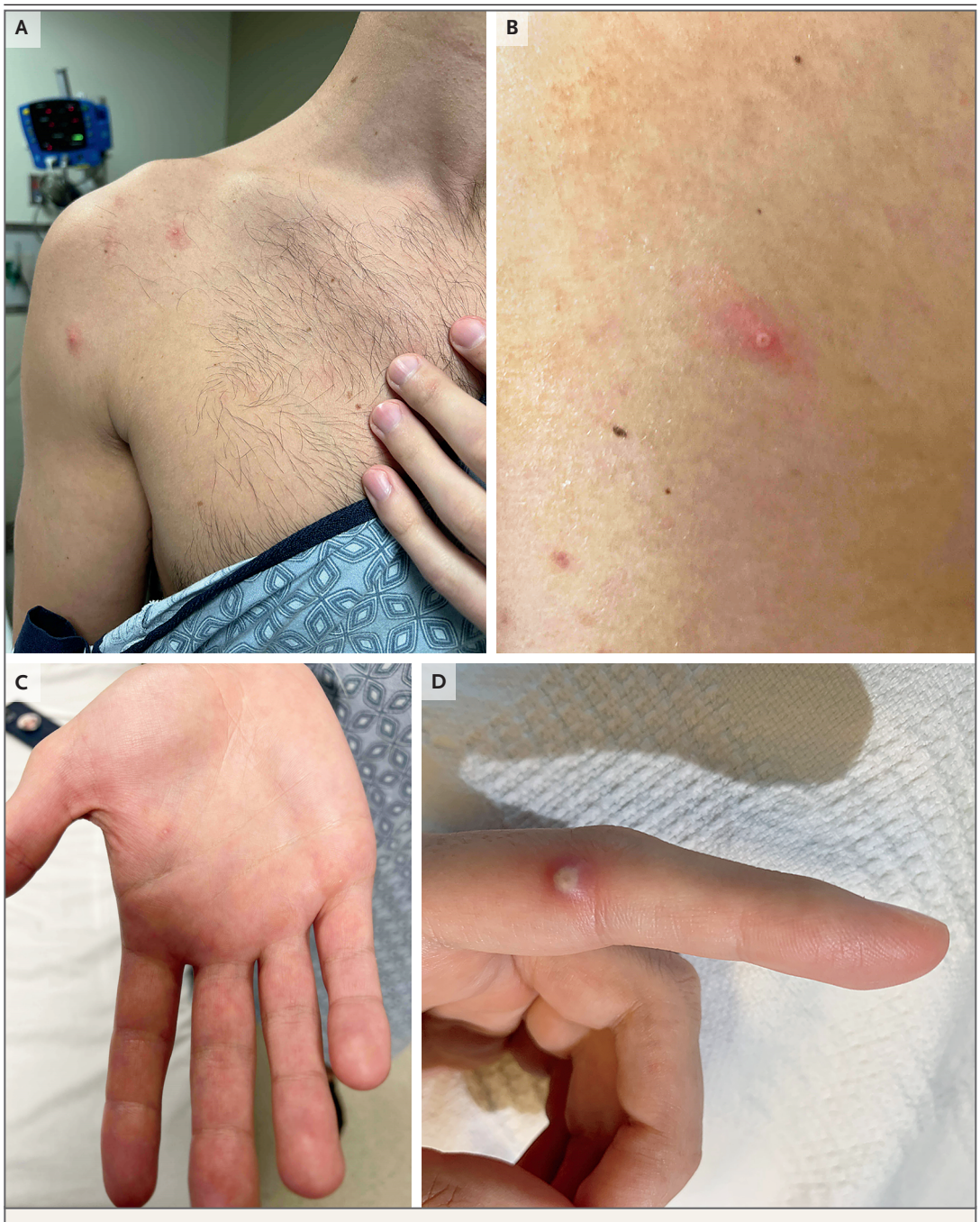

Figure 2. Photographs of the Rash.

Panels A and B show scattered papulovesicular lesions on the chest that were present 2 days before admission. The lesions measure 2 mm in diameter, are filled with clear fluid, and have surrounding erythema. Panel C shows a lesion on the right palm that was present at the time of admission. Panel D shows a papulovesicular lesion on the left second finger, which was one of the last skin lesions to develop, approximately 2 weeks after the onset of symptoms.

DIFFERENTIAL DIAGNOSIS

Dr. Nesli Basgoz: I was involved in the care of this patient, and I am aware of the final diagnosis. This 31-year-old man was admitted to the hospital with an illness that began with rash, with anogenital and cutaneous lesions, followed by regional lymphadenopathy, systemic symptoms,

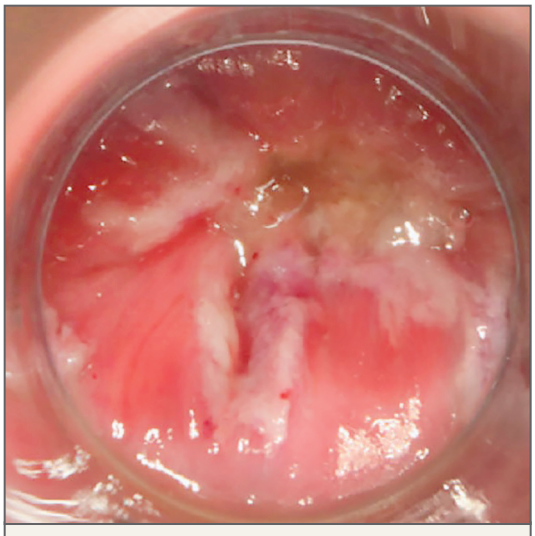

Figure 3. Photograph from Anoscopic Examination.
A photograph obtained during anoscopy, performed on the day of admission, shows intense rectal and anal inflammation with shallow ulcerations and purulent exudate, findings consistent with proctitis.

and progression of disseminated papulovesicular and papulopustular skin lesions. On the basis of the timing of his presentation, his illness was best described as subacute, although the daily progression of symptoms was rapid enough to prompt admission. At the time of admission, symptoms had been present for more than a week, so many hyperacute infections could be ruled out.

The patient's only recent travel had been to Canada. His status as a man who has sex with men and his history of syphilis placed him at increased risk for sexually transmitted infections (STIs) as well as other infections that are transmitted through close contact. He had no known sick contacts or contacts with similar symptoms, at least initially. There were two important antimicrobial exposures. He took daily emtricitabine and tenofovir for HIV PrEP, which dramatically reduces the risk of acquiring HIV. He also took oral valacyclovir several times per year for outbreaks of oral HSV infection. He was not known to have any systemic, anatomical, or functional alterations that would increase his risk of infection; specifically, he did not have any conditions or receive any treatments that would suppress the immune system, and he did not have a chronic medical illness such as liver disease, kidney disease, or diabetes.

During the patient's two outpatient visits at this hospital, a broad differential diagnosis was considered and extensive testing was performed. Initial treatments included penicillin G benzathine, ceftriaxone, and oral valacyclovir and doxycycline. When his symptoms continued to worsen despite these treatments, he was admitted to the hospital. Laboratory test results were normal.

Integration of the clinical presentation with epidemiologic and host factors, along with use of a medically modified Bayesian analysis (Fig. S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org), led us to develop a tripartite differential diagnosis, which I call the "three Ls":

First, what is most *likely*? Which infection is most probable? Although we began by respecting the principle of medical parsimony, there were reasons to consider multiple infections in this patient.

Second, what is most *lethal*? Are any infections likely to rapidly harm the patient and his contacts if not detected and treated early?

Third, what is *left*? Among infectious disease physicians, noninfectious illnesses are often relegated to this category, although they represent a substantial proportion of the cases we encounter. Finally, uncommon infections need to be considered.

With these principles in mind, we considered the typical human pathogens that could be associated with this patient's presentation.

VIRAL INFECTIONS

Genital Herpes

Many features of the patient's presentation could be explained by anogenital HSV infection, known as genital herpes. Genital herpes can be caused by either HSV type 1 (HSV-1) or HSV type 2 (HSV-2), although most cases are caused by HSV-2. The incubation period for genital herpes ranges from 2 to 14 days, with an average of 4 to 5 days, which would fit with this patient's sexual history. The severity of his symptoms would be most consistent with genital herpes due to primary HSV infection, which has a variable clinical course but is often relatively severe, with painful ulcers, inguinal lymphadenopathy, fever, malaise, and headache. The lesions associated with primary HSV infection — which can be vesicles, pustules, or relatively shallow ulcers —

have an erythematous base. Concurrent perianal disease, proctitis, and genital disease can occur.

However, several features of this patient's presentation were atypical for genital herpes. First, the perianal lesions were not clustered, and the penile lesion was solitary. Second, on the basis of the severity of his symptoms, primary HSV infection would be most likely, but primary infection occurs in patients who do not have a history of HSV infection. Conversely, on the basis of his history of recurrent oral HSV infection, nonprimary HSV infection with a first episode of genital involvement would be more likely, but nonprimary infection is often associated with milder disease. Finally, multiple vesiculopustular lesions at distant sites were present at the time of presentation. Although viremia occurs in up to one quarter of patients with primary genital herpes, widespread cutaneous lesions are unlikely to develop in immunocompetent patients. This patient's history and the findings on physical examination and laboratory testing did not suggest a preexisting immunocompromised state.

Varicella

Could this patient have varicella–zoster virus (VZV) infection? Vaccination has reduced the incidence of primary VZV infection, known as varicella or chickenpox. In patients with chickenpox, skin lesions can show progression from maculopapular features to vesiculopustular features (with the appearance of "a dew drop on a rose petal"), a change observed in some of the skin lesions in this patient. VZV is typically acquired through a respiratory route, but it may be transmitted through contact with skin lesions. Could cutaneous contact result in anogenital disease followed by viremia and generalized rash? There have been rare reports of chickenpox occurring in a "diaper rash" distribution in children, but we could find no such reports in adults. Reactivation of VZV infection, known as herpes zoster or shingles, in a dermatomal distribution can involve the anogenital area, but the anatomical distribution in this patient did not fit with this diagnosis.

HIV Infection

We considered the possibility that this patient had acquired HIV despite the use of PrEP. Primary HIV infection is associated with exanthems and enanthems, lymphadenopathy (which is usually generalized), and systemic symptoms. The patient did not have the typical laboratory abnormalities associated with HIV infection, had a negative test for HIV antigens and antibodies, and later had a negative polymerase-chain-reaction (PCR) test for HIV RNA; these findings ruled out this diagnosis.

Molluscum Contagiosum

Molluscum contagiosum virus is a poxvirus that causes a skin infection known as molluscum contagiosum. The associated skin lesions are typically flesh-colored papules measuring 2 to 5 mm in diameter. They can be umbilicated and can appear anywhere on the body. Sexually transmitted molluscum contagiosum involves the groin, genitals, lower abdomen, and upper thighs. The lesions are occasionally inflamed. In patients with HIV infection and other immunocompromised patients, molluscum contagiosum lesions may be extensive and progress rapidly. In this patient, some of the early lesions were consistent with molluscum contagiosum, but the palm involvement and the progressive disease were not. Furthermore, molluscum contagiosum would not explain the proctitis, lymphadenopathy, or systemic symptoms.

BACTERIAL INFECTIONS

Gonorrhea

Gonorrhea is an STI caused by *N. gonorrhoeae*. It is a common cause of urethritis in men and cervicitis in women. Although genital and extragenital gonorrhea can be asymptomatic, proctitis can occur, making the infection indistinguishable from other STIs. Disseminated gonococcal infection is reported in 1 to 3% of patients with gonorrhea. Case series highlight two different forms of disseminated gonococcal infection — purulent monoarthritis or oligoarthritis and a syndrome of dermatitis, tenosynovitis, and migratory polyarthralgias — but the clinical spectrum is heterogeneous. Cutaneous findings are reported in 50 to 75% of patients with bacteremia. The skin lesions may resemble the vesiculopustular lesions seen in this patient. However, patients with disseminated gonococcal infection do not commonly have signs and symptoms of a localized gonococcal infection (e.g., proctitis) at the time of diagnosis, and perianal and penile ulcers would not be explained by gonorrhea.

Syphilis

Syphilis is an infection caused by the spirochete *Treponema pallidum*. The average incubation period is 2 to 3 weeks, although symptoms have been reported only 3 days after exposure. The primary lesion, or chancre, is typically an ulcer measuring 1 to 2 cm in diameter with an indurated margin. Penile lesions are common; perianal lesions can also be seen. Chancres are usually painless but may be associated with pain in some cases. The presence of multiple chancres is uncommon. The secondary stage of syphilis, known as secondary syphilis, is associated with systemic symptoms and lymphadenopathy (which is typically more generalized than the lymphadenopathy observed in this patient), as well as rash and a positive RPR test. The rash can be pustular. Involvement of the palms and soles is a common feature. However, extensive painful perianal disease and proctitis would not be explained by syphilis.

Lymphogranuloma Venereum

C. trachomatis is the most common bacterial cause of sexually transmitted genital infection in the United States. Lymphogranuloma venereum is a disease caused by the L1, L2, and L3 serovars of *C. trachomatis*. Lymphogranuloma venereum can lead to proctitis or proctocolitis, and outbreaks among men who have sex with men have been reported in the United States. The primary lesion is a genital or anal ulcer that develops 3 to 12 days after exposure and is often asymptomatic. The secondary stage of lymphogranuloma venereum is characterized by involvement of regional lymph nodes. The groove sign (which indicates involvement of both the inguinal nodes and the femoral nodes just below them) and inguinal buboes (which may suppurate and drain) may be present but are not universal features. The secondary stage is often associated with systemic symptoms. Persistent perianal and penile ulcers and disseminated skin lesions have not been described with this illness.

Chancroid

Chancroid is an infection caused by the bacterium *Haemophilus ducreyi*, which is an uncommon cause of genital ulcer disease and lymphadenopathy in the United States. Chancroid is associated with the development of one or more deep, painful genital or perianal ulcers and with tender inguinal lymphadenopathy. Proctitis has not been attributed to this infection alone, and disseminated skin lesions have not been described.

HOSPITAL COURSE

Dr. Sascha N. Murillo (Medicine): When this patient was admitted to the hospital, we benefited greatly from the seamless transition of care between the physician in the outpatient infectious disease clinic and our internal medicine team. We considered briefly whether antimicrobial resistance could be playing a role. Multidrug-resistant gonorrhea is an increasing threat worldwide and has been reported in the United States. However, all testing for gonorrhea from multiple sites, including the blood, both before and after ceftriaxone treatment was negative. Acyclovir-resistant HSV infection was also considered. Although this patient took valacyclovir intermittently for oral HSV infection, he did not have a history of frequent high-titer infections in the context of an immunocompromised state, which is predictive of acyclovir resistance. Unfortunately, the painful perianal ulcers and proctitis persisted, and new skin lesions continued to develop in a wide distribution, although at a slower rate than they had developed previously.

Dr. Basgoz: It seemed increasingly clear that there must be a feasible alternative infectious disease diagnosis. We noted that some of the vesiculopustular lesions had taken on a more umbilicated appearance and that some were crusting and healing. We also noted that the persistent perianal ulcers were firm and deeply ulcerated. During the first week of the patient's hospitalization, we received the results of HSV and VZV PCR tests performed on swabs from skin lesions and blood, all of which were negative. The patient reported that he had been talking to two sexual contacts in Canada who had illnesses like his own. Their illnesses had also defied initial diagnosis and failed to resolve with empirical treatment. At this point, we contacted our local public health authorities to ask whether they had received any reports of similar illnesses and to request that they communicate with their Canadian counterparts.

Very early one morning, I awoke thinking

about the possibility of a poxvirus. A PubMed and general Internet search that included the terms "poxvirus," "outbreak," and "sexually transmitted infection" revealed a report that had been posted on the same day by public health authorities in the United Kingdom. It described four cases similar to this one, in which a diagnosis of monkeypox had been confirmed. It was at this point that I contacted the infection control unit at our hospital to report my concern that the patient may have monkeypox.

DR. NESLI BASGOZ'S DIAGNOSIS

Infection with monkeypox virus.

INFECTION CONTROL MANAGEMENT

Dr. Erica S. Shenoy: Several hours before I was notified of the concern that the patient may have monkeypox, he had been placed in a standard single-bed room because of a new exposure to severe acute respiratory syndrome coronavirus 2. Personal protective equipment (PPE) — including a gown, gloves, eye protection, and an N95 respirator — had been instituted for all health care personnel entering the room. The same PPE is currently recommended when caring for patients with suspected or confirmed monkeypox in health care settings.

Given the concern about monkeypox in this patient, we contacted the Massachusetts state epidemiologist to discuss whether testing for monkeypox virus was warranted. At that time, the Centers for Disease Control and Prevention (CDC) had recommended that patients with suspected or confirmed monkeypox be placed in an airborne infection isolation room, and we determined that admitting the patient to this type of room, in the Special Pathogens Unit of this hospital, was indicated.[1] The Special Pathogens Unit is a general medical unit that includes 10 airborne infection isolation rooms. Staff in this unit have received training and participate in preparedness activities related to the role of this hospital as a Regional Emerging Special Pathogens Treatment Center (RESPTC). Ten RESPTCs were established in 2015, by the assistant secretary for preparedness and response in the Department of Health and Human Services, for the management of high-consequence infectious diseases, such as monkeypox. However, all health care facilities must be able to effectively identify suspected cases of high-consequence infectious diseases, to implement appropriate isolation, and to engage local infection prevention and control, as well as public health partners.

Dr. Catherine M. Brown: In May 2022, the World Health Organization issued a report identifying cases of monkeypox that had been diagnosed in persons living in multiple countries where the disease is not endemic.[2] Most of the cases had occurred in persons with no history of travel to Africa, and many had occurred in men who have sex with men. Persons infected with monkeypox virus are thought to be infectious beginning with the onset of symptoms. The virus is introduced into breaks in the skin or mucous membranes through direct contact (exposure to bodily fluids or monkeypox lesions) or indirect contact (exposure to fomites, such as those in clothing or bedding); it can also be introduced through large respiratory droplets after prolonged face-to-face contact. Household transmission has been documented in both endemic and nonendemic areas,[3,4] whereas only a single case of nosocomial transmission in nonendemic areas had been described before the current outbreak.[5]

During the incubation period, which lasts approximately 7 to 14 days, monkeypox virus initially replicates at the site of inoculation, spreads to local lymph nodes, and causes viremia. After this period, a prodromal illness develops that is characterized by fever, headache, and lymphadenopathy; the presence of lymphadenopathy can distinguish monkeypox from smallpox. Not all patients report a febrile illness. Thereafter, rash occurs, with lesions progressing through several stages. Given this patient's clinical presentation and his social and travel history, we were concerned that he was at high risk for monkeypox, and the decision was made to test for monkeypox virus.

DIAGNOSTIC TESTING

Dr. Sandra C. Smole: Swab specimens obtained from skin lesions and the throat were sent to the Massachusetts State Public Health Laboratory, which is part of the Laboratory Response Network. Real-time PCR testing detected the presence of nonvariola orthopoxvirus DNA, a finding

that specifically ruled out smallpox.[6] Additional clinical swab specimens and serum were sent in parallel to the CDC, where species-specific real-time PCR testing confirmed the presence of monkeypox virus, West African clade.[6] After the West African clade was confirmed, the Massachusetts State Public Health Laboratory notified the CDC Federal Select Agent Program that select agent regulations did not apply. Serologic testing identified anti-orthopoxvirus IgM in the absence of recent vaccination.

There are two distinct clades of monkeypox virus. The Congo Basin clade (which is endemic in Central Africa) is associated with case fatality rates of up to 11%, and human-to-human transmission is well documented.[6] The West African clade is associated with less severe disease (case fatality rates of <3%),[7] and in the past, limited human-to-human transmission has been reported.[8] Recent outbreaks of the West African clade in Nigeria suggest that transmission between close contacts may be more common than initially reported.[9] Death is most likely to occur in children[10] and immunocompromised patients[7]; the pooled case fatality rate is lower for the West African clade (3.6%) than for the Congo Basin clade (10.6%).[10]

LABORATORY DIAGNOSIS

Infection with monkeypox virus, West African clade.

CONTACT TRACING AND EXPOSURE INVESTIGATION

Dr. Shenoy: While awaiting confirmation of the diagnosis, we began the process of contact tracing and exposure investigation to identify and subsequently assess risk for persons with confirmed exposure to the patient during the period when he was not isolated. This period included his outpatient visits, an encounter in the emergency department, and his inpatient admission. All health care personnel with a confirmed exposure of any risk level (high, intermediate, or low or uncertain) were monitored for symptoms. We worked with the Massachusetts Department of Public Health to identify options for postexposure prophylaxis for persons with high-risk exposures or with specific intermediate-risk exposures.

PUBLIC HEALTH CONSIDERATIONS

Dr. Brown: Once the diagnosis of monkeypox was established, epidemiologists from the Massachusetts Department of Public Health coordinated with the hospital to initiate case investigation and contact tracing. Interviews of the patient elicited an epidemiologic profile consistent with that observed in other recent cases, including no history of travel to an endemic region and no known contacts with monkeypox. Contact tracing initially identified more than 200 possible contacts among health care personnel and personal contacts. Further assessment, performed with the application of criteria for exposure risk level, reduced this number. Contacts with an exposure of any risk level are to be monitored for symptoms (fever or chills, lymphadenopathy, and rash) for 21 days after the exposure. Monitoring is to be overseen by the public health department or health care institution; frequent communication between contacts and monitors is advised.[11]

Dr. Lawrence C. Madoff: Smallpox vaccination provides protection against monkeypox; however, routine smallpox vaccination in the United States ended in 1972, after disease eradication. Thus, postexposure prophylaxis with the use of the smallpox (vaccinia) vaccine (ACAM2000) or the smallpox and monkeypox vaccine (JYNNEOS) is recommended after high-risk exposures and can also be considered for intermediate-risk exposures. Given its safety profile and ease of administration, JYNNEOS, which has been approved by the Food and Drug Administration for the prevention of both smallpox and monkeypox,[11,12] was obtained from the Strategic National Stockpile and made available to occupational health services at the hospital. Within the first week after diagnosis, several contacts were tested for monkeypox, and none had positive tests.

Current guidance indicates that infected persons should remain in isolation until all skin lesions have resolved and a fresh layer of skin has grown. Because this patient had mucous membrane lesions, reepithelialization of ulcerated mucosal surfaces was thought to be required.

Most patients with monkeypox have mild, self-limited disease and are treated with supportive care only, but some patients have severe disease. Currently, no medical countermeasures have been approved for the treatment of monkeypox. However, two antiviral agents (tecovirimat and cidofovir) and vaccinia immune globulin intravenous are available in the Strategic National Stockpile as options for treatment. To date, among reported cases in the United States in the current outbreak, at least one patient has been treated with tecovirimat.[13] These medical countermeasures should be considered in patients with monkeypox who have severe disease or have a high risk of severe disease, including immunocompromised patients, children, pregnant or breast-feeding patients, and those with one or more complications of illness. In accordance with current CDC recommendations, treatment should also be considered in patients with monkeypox caused by accidental implantation in the eyes, mouth, or other areas.[14]

HOSPITAL MANAGEMENT AND INSTITUTIONAL RESPONSE

Dr. Paul D. Biddinger: The evaluation of even a single patient with a high-consequence infectious disease, such as monkeypox, can be extremely complex and challenging for any hospital. Hospital leaders must have complete confidence in the ability of their staff to access and safely use PPE, following appropriate infection control procedures in potentially high-risk situations. Immediate just-in-time refresher training for staff may be needed. There is also a need for frequent communication and coordination with city, state, and federal public health authorities, and the communications internally to the hospital community and externally to the public can be complex and labor intensive. In addition, the hospital must be able to make resources available to support contact tracing and perform exposure investigations, to possibly establish vaccination clinics for postexposure prophylaxis, and to make rapid changes to the electronic health records system to support infection prevention and control, among other activities.

Dr. Joshua J. Baugh: Because of this complexity, the safe and appropriate care of a patient with a high-consequence infectious disease often necessitates activation of the hospital emergency operations plan and use of the hospital incident command system. At our hospital, the response to this case involved more than 30 hospital leaders participating in the hospital incident command system, as well as hundreds of frontline staff members.

FOLLOW-UP

Dr. Murillo: Approximately 2 weeks after the onset of symptoms in this patient, we noted the development of the last new lesions: small sores inside the left naris, under a toe, and on the left second finger (Fig. 2D). We estimated that over the course of his illness, he had had approximately 25 skin lesions at different stages of evolution. Although the patient had malaise and fatigue, he did not have fever during the hospitalization. The inguinal lymphadenopathy began to abate. On the ninth hospital day, all the lesions had scabbed and fallen off, with adequate reepithelialization. The patient was no longer considered to be infectious and was discharged home.

FINAL DIAGNOSIS

Infection with monkeypox virus, West African clade.

This case was presented as a tabletop exercise for the purpose of rapidly disseminating information about the first confirmed case of monkeypox in the United States during the 2022 outbreak.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank the many clinicians and support staff members at Massachusetts General Hospital for their contributions to the evaluation and treatment of this patient.

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