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Oral Manifestations of Monkeypox: A Report of 2 Cases

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Monkeypox is a zoonotic infection caused by the monkeypox virus. It is a double-stranded DNA virus belonging to the *Orthopoxvirus* genus and the poxvirus family.[1] In the past, the clinical relevance of monkeypox was limited to Western and Central Africa, with transient outbreaks in the Western Hemisphere linked to either international travel or trade of exotic pets.[2,3] Currently, the Centers for Disease Control and Prevention and World Health Organization are tracking an outbreak of monkeypox cases, which began in May 2022. At the time of writing, approximately 15,000 cases have been reported in nearly 70 countries. Of these cases, more than 98% have occurred in locations where monkeypox has not traditionally been reported.[4–6] In the majority of these cases, international travel to endemic regions was not documented, suggesting community spread. There have been more than 2,000 cases reported in the United States during this outbreak, with many of these cases occurring in patients who identify as either homosexual or bisexual.[5,7]

Patients with monkeypox infection will often report fever, fatigue, and influenza-like symptoms such as headaches, muscle aches, and swollen, painful lymph nodes. Most notably, patients will develop a pustular rash involving the skin.[1,8] Monkeypox infection can spread from person to person via close contact with an infected individual. Transmission may occur via direct contact with the rash, respiratory secretions, or through fomites that have previously come in contact with an infected individual. Vertical transmission from infected mother to fetus through the placenta has also been documented.[9]

Although the cutaneous rash of monkeypox infection has been well documented, oral monkeypox lesions have only been infrequently described. Herein, we report 2 cases of oral manifestations of monkeypox infection. In both cases, the diagnosis of monkeypox was confirmed via laboratory testing shortly after the onset of the oral lesions.

Case Report

CASE 1

A 38-year-old male presented to an oral and maxillofacial surgeon for the evaluation of a recent onset anterior tongue lesion. The patient reported that the area was tender to palpation and endorsed worsening sensitivity in association with hot and spicy foods and beverages. He could not recall any clear history of trauma to his tongue. He reported that the lesion had been present for a few days before his appointment. The patient denied any underlying medical conditions, although he did endorse that he uses emtricitabine-tenofovir (Truvada) for the prevention of HIV. He also stated that he took Valacyclovir for a few days following the onset of his tongue lesion. At the time of presentation, the patient mentioned that he had a fever and fatigue but denied the presence of any additional oral or skin lesions. Clinical examination revealed an approximately 1 cm tan-gray, well-defined ulcerated lesion involving the tip of the tongue along the midline. In addition, smaller, clustered tan-gray vesiculo-ulcerative lesions were seen along the anterior ventral aspect of the tongue (Fig 1). A swab of the tongue lesions was performed and was positive

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for the monkeypox virus. Subsequently, the patient reported the development of approximately 20 skin lesions involving his arms, legs, and torso (Fig 2). He was prescribed tecovirimat and is currently recovering, although he is still symptomatic at this time.

CASE 2

A 30-year-old male presented to the emergency department of Columbia University Irving Medical Center for the evaluation of a painful oral lesion involving the anterior dorsal aspect of his tongue. The patient also endorsed a 3-day history of fever, sore throat, and neck soreness. With regard to the oral lesion, he described a painful, "pimple-like" tender nodule of the tip of his tongue, which increased in size before his presentation to the emergency department. At the time of evaluation, a well-defined, tan-gray ulceration of the anterior tongue measuring approximately 1.0 cm in size was identified (Fig 3). No other oral lesions were observed, and no cutaneous lesions were identified on initial presentation. The patient's past medical history was significant for HIV, which was first diagnosed in 2016. At present, he reported that his viral load was undetectable, although he was unsure of his CD4 cell count. His past medical history was also significant for a prior diagnosis of syphilis. With regard to his social history, the patient reported that he was sexually promiscuous with multiple male partners over the past 6 months.

Given the patient's clinical symptoms and reported social and medical history, the initial differential diagnosis included a wide range of infectious pathologies, including syphilis, a deep fungal ulcer, an atypical herpetic lesion, and tuberculosis. A traumatic ulcer was also considered, given the tip of tongue location. During his hospital stay, the patient subsequently developed a pustular, rash-like process involving the skin of his groin region, finger, back, and shoulders (Fig 4). Swabs from the cutaneous lesions and the tongue lesion were performed and were positive for monkeypox virus deoxyribonucleic acid (DNA) by nucleic acid amplification test with probe detection.

Discussion

Human monkeypox is a viral zoonosis belonging to the *Orthopoxvirus* genus. This genus also includes variola virus (the etiologic agent of smallpox), vaccinia virus, and cowpox virus.[1] The first documented case of monkeypox in humans occurred in 1970 in a 9-month-old male in the Democratic Republic of the Congo.[10] Monkeypox is known to be endemic to Western and Central Africa, and sporadic cases of monkeypox infection have been reported in multiple countries, including Cameroon, the Central African Republic, Congo Brazzaville, Ivory Coast, Gabon, Liberia, Nigeria, Sierra Leone, and South Sudan.[11,12] In addition, a single outbreak of 122 cases occurring in Nigeria was documented during 2017 to 2018.[13] The first reported cases of monkeypox infection in the United States occurred in 2003 and were due to exposure to infected African wildlife.[14] Monkeypox infection has traditionally been of limited clinical concern in Europe and North America, with infrequent cases being linked to a history of travel to an endemic area.

FIGURE 1. Painful tongue lesions of acute onset. A tissue swab of these lesions was positive for the monkeypox virus.

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In May 2022, multiple countries in Europe, North America, South America, and Asia began to report a rising number of monkeypox infections. More than 98% of these cases were from locations not considered endemic for monkeypox infection.[5] Furthermore, a history of travel to endemic areas or exposure to infected wildlife was not reported, suggesting that this current outbreak is growing via community spread. Trends in the current outbreak include a higher frequency of cases in individuals who are homosexual or bisexual or are males who have sexual intercourse with other males. Other higher risk groups include individuals who are immunosuppressed, pregnant women, and health care or laboratory workers.[15] Monkeypox is spread via close contact with an infected individual. It can be transmitted via direct exposure to the pustular rash, from respiratory droplets, or by touching surfaces that have come in contact with an infected individual. It can also be spread via direct contact with an infected animal or by consuming or using infected animal meat or products.[15,16]

FIGURE 2. (*A* and *B*) Pustular skin rash (marked by *arrows*), which manifested several days after the oral lesions.

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Symptoms of monkeypox infection include fever, fatigue, chills, cervical lymphadenopathy, and muscle soreness. The most characteristic feature of Monkeypox infection is the development of a vesicular or pustular rash, which often involves the skin of the face, upper and lower extremities, torso and abdomen, and anogenital region. The development of the rash may occur before or after the onset of constitutional symptoms.[1] Monkeypox infection is a self-limiting illness, which resolves in most patients over a course of 2 to 4 weeks.[1,17]

Although the monkeypox rash has been reported to involve the oral mucosa, documentation of oral manifestations of monkeypox infection to date has been poor.[18] This report describes 2 cases of oral lesions in patients with confirmed monkeypox infection. Although it is

FIGURE 3. A tan-gray ulcerated lesion of the anterior tongue. The patient reported that this lesion had been present for 3 days before his arrival at the emergency department.

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not possible to make sweeping generalizations based on such a limited number of cases, there were some findings in both that merit further discussion. In both patients, the oral lesions preceded the development of the skin rash by 1 or more days. In addition, the oral lesions appeared to have a somewhat midline distribution along the anterior aspect of the tongue. Both patients reported constitutional symptoms of fever, fatigue, and soreness before the onset of the oral lesions.

Because of the limited clinical relevance of monkeypox before the May 2022 outbreak, it is often not initially considered in differential diagnosis. The differential diagnosis may include other infectious pathologies. Syphilis should be ruled out, given the presence of a papular rash. Other viral infections, including chickenpox, smallpox, and molluscum contagiosum, should also be excluded. Herpetiform drug eruptions may also be considered.[1,19] With regard to the oral findings in particular, the differential diagnosis will often include more commonly encountered inflammatory and infectious processes. Traumatic ulcerations from biting may be considered in cases where the lesion presents as a tan-gray ulceration involving the anterior tongue. In the presence of constitutional symptoms such as fever, fatigue, and malaise, consideration may be given to primary herpetic gingivostomatitis, although this condition occurs more frequently in children. In patients with a history of immunosuppression, atypical manifestations of recurrent herpes simplex virus, as well as Epstein Barr Virus mucocutaneous ulcers, and ulcers caused by cytomegalovirus should be excluded. Syphilis may also present intraorally, and the oral lesions of monkeypox may resemble mucous patches of secondary syphilis infection. Oral manifestations of tuberculosis, although rare, may also present as ulcerated lesions of the oral mucosa.

Diagnosis of monkeypox infection is confirmed via tissue swab of an active lesion.[20] Testing of skin lesions is typically performed. If the oral lesions of monkeypox precede the development of the skin rash, then analysis of these lesions may help expedite diagnosis. Monkeypox infection is a self-limiting disease but

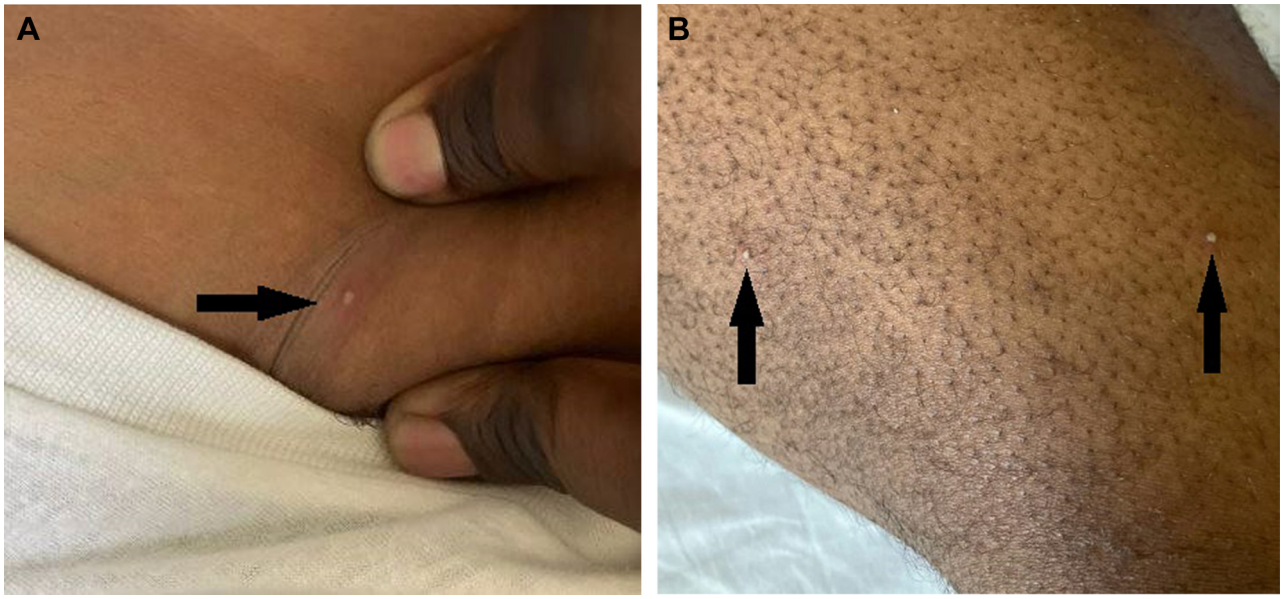

FIGURE 4. Representative cutaneous lesions involving the neck (*A*, marked by *arrows*) and arm (*B*, marked by *arrows*). These lesions developed during the patient's hospital stay.

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rarely can be fatal in those who are very young or immunosuppressed. For individuals at higher risk for serious illness, antipoxviral drugs such as tecovirimat may be used. Tecovirimat is a medication used in the treatment of smallpox; however, its use for monkeypox infection has not been approved by the Food and Drug Administration. It is currently being used based on nonresearch expanded access investigational new drug protocol authorized by the Centers for Disease Control and Prevention. Based on these guidelines, it is recommended that tecovirimat be administered to patients who are immunocompromised, pediatric patients below the age of 8 years, individuals who are pregnant or breastfeeding, patients with atopic dermatitis or other exfoliative skin conditions, or in those with disease course complications, such as secondary bacterial infection or lesions involving high-risk anatomical sites such as the eyes or mouth.[20] It can be administered either orally or intravenously. Vaccination for monkeypox does exist, although its use is currently limited to those who are considered high risk for developing monkeypox infection or who have been exposed to an individual with monkeypox.[21]

Human monkeypox infection is a rare viral zoonosis with increasing clinical relevance due to a recent global outbreak of cases. Oral manifestations of monkeypox infection are infrequently reported but may play a role in the diagnosis and management of this condition. Monkeypox should be considered in the differential diagnosis of acute onset oral ulcerations, especially in patients who are at higher risk for developing this condition.

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