Concomitant group A Streptococcus and disseminated mpox infection mimicking relapsed diffuse large B-cell lymphoma

Viviane Liao, BA,[a] Sarah Nocco, MD,[b] Puja H. Nambiar, MD,[c] Alexander P. Boardman, MD,[d] Fergal Kavanagh, MD,[e] Yildirim Onur, MD,[f] Liang Deng, MD, PhD,[a] and Shamir Geller, MD[a]

Key words: CAR-T; diffuse large B-cell lymphoma; Group A streptococcus; Mpox; pharyngitis.

INTRODUCTION

Mpox, a viral infection transmitted primarily through close skin-to-skin contact, was first described in the Democratic Republic of Congo.[1] There are 2 main clades of the Monkeypox virus that cause mpox: Clade I which is endemic to Central Africa and associated with more severe disease and Clade II which is endemic to West Africa and associated with milder disease.[1] Clade II Monkeypox virus spread worldwide in 2022, peaking in the summer, primarily among men who have sex with men.[1] Mpox co-infection with human immunodeficiency virus (HIV) and other sexually transmitted infections occur commonly, exacerbating disease severity and prolonging the recovery process.[2] Rare cases of bacterial co-infection have been reported and co-infection may complicate diagnosis of mpox.[2,3] Here, we present a case of disseminated mpox with concomitant Group A Streptococcal infection mimicking relapsed diffuse large B-cell lymphoma (DLBCL).

Abbreviations used:

CAR:	chimeric antigen receptors
DLBCL:	diffuse large B-cell lymphoma
GAS:	group A Streptococcus
HIV:	human immunodeficiency virus

CASE REPORT

A 30-year-old man with a history of T-cell histiocyte-rich DLBCL, in complete remission following chimeric antigen receptors (CAR) T-cell therapy 4 years earlier, presented with diffuse monomorphic firm papules and pustules with central crusting and umbilication.

One week prior, the patient was evaluated for sore throat and dysphagia. He tested positive for group A Streptococcus (GAS) and was prescribed a course of oral amoxicillin. Over the next 3 days, he experienced worsening sore throat and severe dysphagia, dysphonia, and pyrexia despite adhering to his antibiotic regimen. Computed tomography of his neck demonstrated increased cervical adenopathy with new diffuse nasopharyngeal, oropharyngeal, and posterior hypopharyngeal thickening, suspicious for lymphomatous involvement (Figs 1, *A* and *B*, and 2, *A* and *B*). Endoscopic examination of the pharyngolarynx showed edema with cobblestoning and white exudate on the posterior pharyngeal wall (Fig 3, *A-C*). Lactate dehydrogenase was at the high end of normal at 249. Given the imaging and endoscopic findings, along

From the Dermatology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York[a]; Department of Pathology and Laboratory Medicine, Memorial Sloan Kettering Cancer Center, New York, New York[b]; Infectious Disease Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York[c]; Lymphoma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York[d]; Department of Head and Neck Surgery, Memorial Sloan Kettering Cancer Center, New York, New York[e]; and Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, New York.[f]

Funding sources: This research was funded in part through the NIH/NCI Cancer Center Support Grant P30 CA008748.

Patient consent: The authors attest that they have obtained written consent from patient/s, their legal guardian/s or person/s with legal authority, for their photographs and medical information to be published in print and online and with the understanding that this information may be publicly available. Patient consent forms were not provided to the journal but are retained by the authors to be made available upon request.

IRB approval status: Not applicable.

Correspondence to: Shamir Geller, MD, Dermatology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, 530 E 74th St, New York, NY 10021. E-mail: gellers@mskcc.org.

JAAD Case Reports 2025;61:45-50.
2352-5126

https://doi.org/10.1016/j.jdcr.2025.04.015

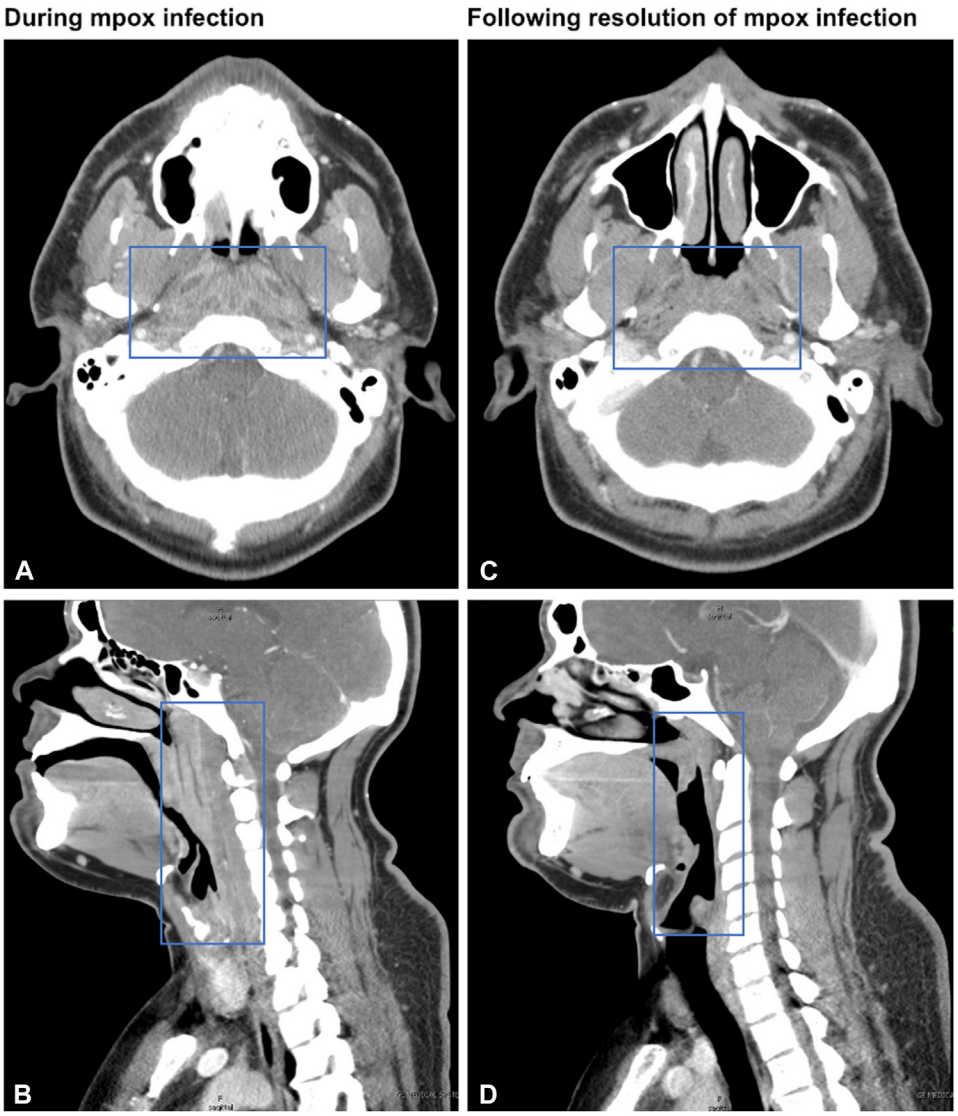

Fig 1. Nasopharyngeal soft tissue thickening on CT neck resolved following mpox treatment. **A,** Diffuse symmetric soft tissue thickening in the nasopharynx during active mpox infection. **B,** Nasopharyngeal airway narrowing during active mpox infection. **C** and **D,** Reduction in nasopharyngeal soft tissue thickening and clearing of nasopharyngeal airway 7 months following mpox treatment. *CT*, Computed tomography.

with a history of persistent fluorodeoxyglucose avid lymphadenopathy with sporadic B symptoms over the past several years, the leading differential diagnosis included lymphoma recurrence versus an infectious or inflammatory process. The patient was admitted and treated with high-dose intravenous dexamethasone and ampicillin/sulbactam, resulting in significant improvement in pharyngeal swelling and symptoms. After 4 days of treatment, he was discharged on dexamethasone and amoxicillin-clavulanate.

Two days following discharge, dermatology was consulted for a painless, nonpruritic, papulo-pustular rash (Fig 4). The patient reported that the initial lesions appeared on his arms during his hospitalization and then spread to the palms, legs, back, scalp, and penile shaft. He endorsed having unprotected oral intercourse with multiple male sexual partners, most recently 2 weeks ago. Sexually transmitted infection testing, including HIV serologies and herpes simplex virus polymerase chain reaction, was negative. However, mpox virus polymerase chain reaction from a skin lesion was positive. He received a 14-day course of tecovirimat 600 mg twice a day, leading to complete resolution of the rash and sore throat. Post-treatment computed tomography of the neck also demonstrated a reduction in pharyngeal edema, airway narrowing, and cervical adenopathy (Figs 1, *C* and *D*, and 2, *C* and *D*).

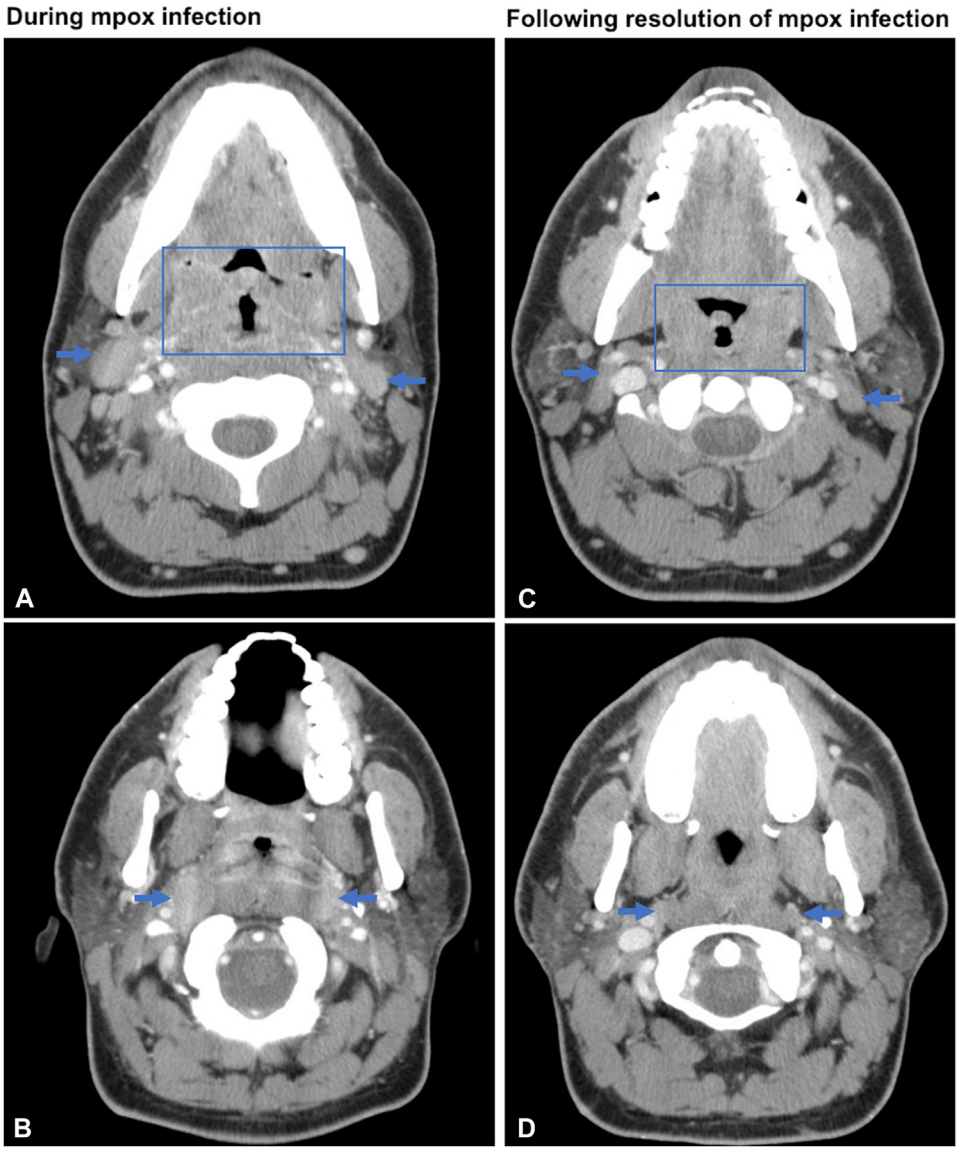

Fig 2. Bilateral palatine tonsil and retropharyngeal adenopathy on CT neck resolved following mpox treatment. **A,** Bilateral palatine tonsil (box) and level 2 lymph node enlargement (*arrows*) during active mpox infection. **B,** Bilateral retropharyngeal adenopathy and airway narrowing during active mpox infection. **C** and **D,** Reduction in bilateral palatine tonsil enlargement, adenopathy (*arrows*), and airway narrowing 7 months following mpox treatment. *CT,* Computed tomography.

DISCUSSION

Although lymphoma recurrence was initially a concern in our case, it is important to recognize that tonsillitis, sore throat, and dysphagia occur in approximately 10% of patients with mpox infection. In some cases, severe oropharyngeal manifestations may precede the appearance of cutaneous mpox lesions.[4] Mpox can also be complicated by pharyngeal co-infection with *Streptococcus* or other pathogens.[3] Common oropharyngeal manifestations include pharyngitis, epiglottitis, odynophagia, and oral or tonsillar lesions, with oral lesions often appearing before skin lesions.[4] Recognizing noncutaneous presentations are critical for early suspicion and identification of mpox, particularly given the potential for asymptomatic viral transmission. Awareness is especially important as Clade IIb continues to pose a public health threat alongside the emerging Clade I strain.[5]

While we were unable to obtain a pharyngeal swab to confirm mpox infection of the pharynx, this diagnosis is strongly supported by lack of response

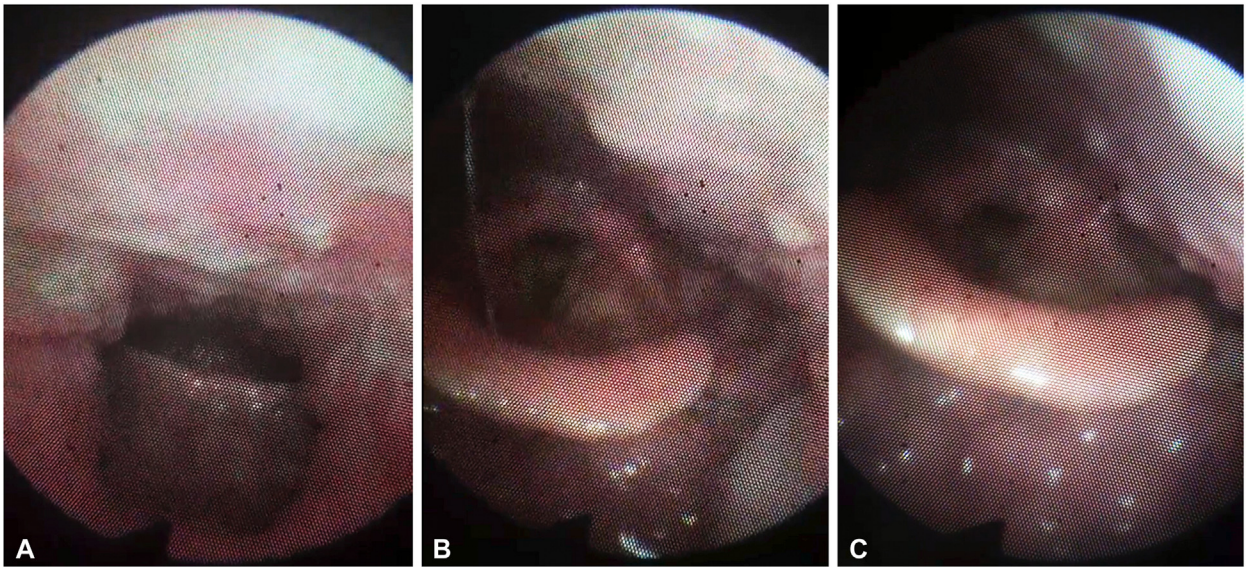

Fig 3. Posterior pharyngeal wall edema and cobblestoning on endoscopic examination. **A,** Endoscopic view of the pharyngolarynx captured from the nasopharynx, demonstrating marked edema of the posterior pharyngeal wall with inflamed mucosal tissue and the presence of exudates. The base of the tongue appears bulky and edematous. **B,** Endoscopic visualization of the larynx, highlighting the glottis and vocal folds. Significant edema and exudate are observed along the posterior pharyngeal wall. **C,** Endoscopic image of the pharyngolarynx, showing diffuse edema of the posterior pharyngeal wall and prominent swelling of the base of the tongue tissue.

to appropriate antibiotics for GAS and ultimate resolution of pharyngeal swelling following mpox-directed treatment. The patient's oral-receptive sexual history suggests he was infected through the oropharyngeal route. Although our patient's immune markers were largely within normal ranges—white blood cell count 6.4, absolute $CD4^+$ T-cells 487, $CD8^+$ T-cells 848, B cells 289, $CD3^-56^+16^+$ NK cells 108, and $CD3^+56^+16^+$ NKT cells 54, with immunoglobulin levels (G, A, and M) also within normal limits—his history of DLBCL with CAR T-cell therapy may have caused lasting immune alterations,[6] predisposing him to infection with both GAS and mpox virus.

Pharyngeal co-infection of mpox and GAS has been previously reported in 2 cases—one treated with antibiotics alone and another requiring intubation, broad-spectrum antibiotics, systemic corticosteroids, intravenous tecovirimat, and intravenous cidofovir.[3] Treatment with systemic corticosteroids and tecovirimat, an antiviral initially developed for smallpox, was effective in resolving pharyngeal symptoms and swelling in our patient. Animal models and early human trials have demonstrated promise for tecovirimat in treating mpox, with early administration significantly reducing the likelihood of disease progression, particularly among patients with HIV.[7] Although resistance to tecovirimat among patients with mpox has been reported, the incidence remains low, affecting less than 1% of treated patients.[8]

While our patient had not received an mpox vaccination prior to this event, vaccination remains a key preventive strategy, particularly for high-risk populations. The nonreplicating modified vaccinia Ankara vaccine is the primary vaccine recommended for mpox prevention and has demonstrated significant efficacy.[9] Given the heightened risk of severe disease in immunocompromised individuals, including those with a history of lymphoma or prior CAR T-cell therapy, vaccination should be strongly considered in these populations to reduce morbidity and prevent transmission.

Atypical presentations of mpox, as seen in our patient, can complicate diagnosis. Symptoms such as tonsillitis, proctitis, lymphadenopathy, or sparse cutaneous lesions can mimic a range of other conditions including bacterial tonsillitis, primary syphilis, oral or genital herpes, and bacterial proctitis.[10] These variable presentations highlight the importance of obtaining a thorough exposure history and reconsidering the diagnosis if initial treatment proves ineffective. Furthermore, co-infection with other pathogens like GAS can also occur and the identification of 1 infection should not preclude testing for mpox when clinical features are suggestive.

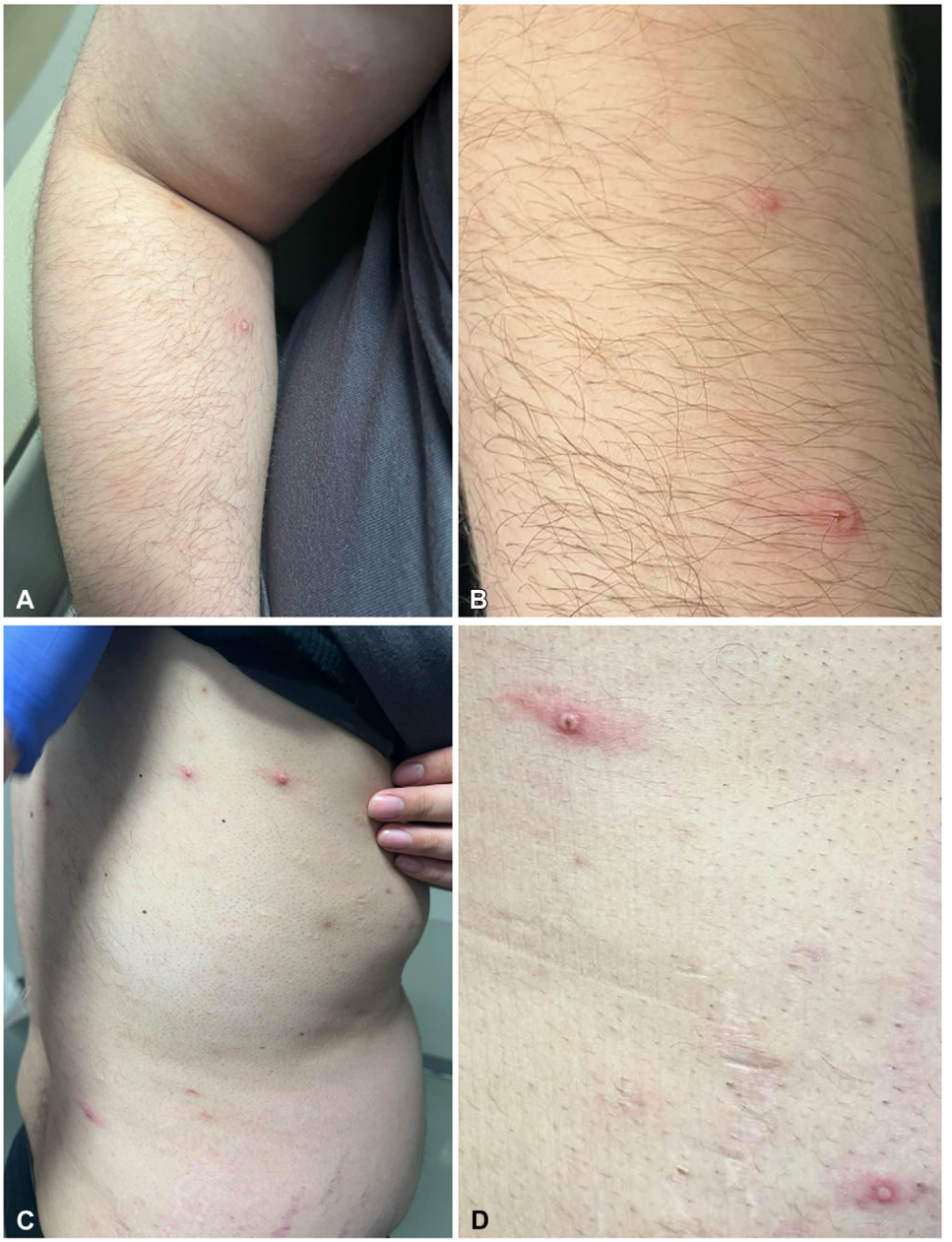

Fig 4. Papulopustular eruption on the arms and trunk. **A** and **B,** Papulopustular eruption on right forearm and arm. **C** and **D,** Umbilicated papules with an erythematous base on the right flank.

Conflicts of interest

None disclosed.

REFERENCES

1. Titanji BK, Hazra A, Zucker J. Mpox clinical presentation, diagnostic approaches, and treatment strategies: a review. *JAMA*. 2024; 332(19):1652-1662. https://doi.org/10.1001/jama.2024.21091
2. Liu BM, Rakhmanina NY, Yang Z, et al. Mpox (Monkeypox) virus and its co-infection with HVI, sexually transmitted infections, or bacterial superinfections: double whammy or a new prime culprit? *Viruses*. 2024;16(5):784. https://doi.org/10.3390/v16050784
3. Kaiser RM, Cash-Goldwasser S, Lehnertz N, et al. Pharyngeal co-infections with Monkeypox virus and group A Streptococcus, United States, 2022. *Emerg Infect Dis*. 2023;29(9): 1855-1858.
4. Tarin-Vicente EJ, Alemany A, Agud-Dios M, et al. Clinical presentation and virological assessment of confirmed human Monkeypox virus cases in Spain: a prospective observational cohort study. *Lancet*. 2022;400(10353):661-669. https://doi.org/10.1016/S0140-6736(22)01436-2
5. Vakaniaki EH, Kacita C, Kingada-Lusamaki E, et al. Sustained human outbreak of a new MPXV clade I lineage in eastern

Democratic Republic of the Congo. *Nat Med*. 2024;30(10): 2791-2795. https://doi.org/10.1038/s41591-024-03130-3

6. Luan D, DeWolf S, Fei T, et al. Dynamics of immune reconstitution and impact on outcomes across CAR-T cell products in large B-cell lymphoma. *Blood Cancer Discov*. 2024;6(2):119-130. https://doi.org/10.1158/2643-3230.BCD-24-0163
7. Aldred B, Lyles R, Scott J, et al. Early tecovirimat treatment for mpox disease among people with HIV. *JAMA Intern Med*. 2024;184(3): 275-279. https://doi.org/10.1001/jamainternmed.2023.7696
8. Smith TG, Gigante CM, Wynn NT, et al. Tecovirimat resistance in mpox patients, United States, 2022-2023. *Emerg Infect Dis*. 2023; 29(12):2426-2432. https://doi.org/10.3201/eid2912.231146
9. Deputy NP, Deckert J, Chard AN, et al. Vaccine effectiveness of JYNNEOS against mpox disease in the United States. *N Engl J Med*. 2023;388(26):2434-2443. https://doi.org/10.1056/NEJMoa2215201
10. Wieder-Feinsod A, Zilberman T, Erster O, et al. Overlooked Monkeypox cases among men having sex with men during the 2022 outbreak - a retrospective study. *Int J Infect Dis*. 2023; 128:58-60. https://doi.org/10.1016/j.ijid.2022.12.014