Monkeypox presenting as supraglottitis in an immunocompromised patient

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SUMMARY
We describe a young man with AIDS who presented to the ear, nose and throat team with a severe sore throat mimicking supraglottitis. He had a 3-day history of sore throat, hoarse voice, fevers and myalgia. On examination, he had cervical lymphadenopathy and profuse pus overlying his right tonsil. On flexible nasoendoscopy, this pus was seen to track down to the supraglottis, with associated mucosal ulceration. The patient was treated for supraglottitis and he improved. 24 hours post admission, a pustule suspicious for monkeypox developed on the patient’s hand. The diagnosis was confirmed by PCR testing. The patient was isolated and treated supportively and recovered fully. This case highlights that monkeypox may present with a severe sore throat without cutaneous lesions. Monkeypox is a growing public health concern. Its early symptoms are non-specific and healthcare professionals should be alert to it.

BACKGROUND
The early symptoms of monkeypox are non-specific and may be missed, resulting in poor infection control and public health risks. Given the current multicountry outbreak, which was declared a public health emergency of international concern in October 2022, it is important that clinicians are aware of the breadth of potential monkeypox presentations. We highlight that a severe sore throat may be the main presenting feature and that cutaneous lesions may not be present initially.

Monkeypox is a zoonotic viral disease similar to, though milder than, smallpox. It is caused by an enveloped, double-stranded DNA virus belonging to the Orthopoxvirus genus of the Poxviridae family. It was first described in 1970 in the Democratic Republic of Congo, with the majority of cases since distributed across central and West Africa.1,2 However, in early summer 2022, multiple cases of monkeypox were diagnosed in non-endemic countries. No direct travel links to endemic countries were identified, and cases were mainly identified in primary care and sexual health clinics among men who have sex with men (MSM).2 This outbreak has occurred on the background of a resurgence of monkeypox in both endemic and non-endemic countries hypothesised to be due to the fact that, following eradication of smallpox in 1980, smallpox vaccination (which provides some immunity to monkeypox) has waned.1

Human-to-human monkeypox transmission is through close contact with lesions, body fluids, respiratory droplets and contaminated materials.

The incubation period is 5–21 days. Symptoms begin with the ‘invasion period’ (lasting 0–5 days), characterised by fever, headache, lymphadenopathy, myalgia and fatigue. Within 1–3 days of the onset of fever skin lesions usually develop, mainly across the face, hands and feet. The rash develops in a manner similar to chickenpox: macules to papules to vesicles then to pustules and eventually dry crusts. Monkeypox is generally self-limiting though complications may occur and underlying immune deficiencies may lead to worse outcomes.1,2 Public health management of the condition includes contact tracing, risk assessment and smallpox vaccination.3

As the outbreak starting in May 2022 progressed, reports emerged of more varied presentations of monkeypox.4 This included upper aerodigestive tract manifestations such as oropharyngeal lesions and tonsillar erythema.4 In a case series of 528 reported in the New England Journal of Medicine, 113 patients (21%) presented with pharyngitis. More severe aerodigestive tract manifestations are rarer. There has been one reported case of peritonsillar abscess4 and one of epiglottitis4 associated with monkeypox infection.

CASE PRESENTATION
A man in his 40s presented to the emergency department with a 3-day history of sore throat, hoarse voice, odynophagia, reduced oral intake, fevers, cervical lymphadenopathy and myalgia. He was HIV positive with a low CD4+ count. He had a background of previous Kaposi’s sarcoma of the palate and an isolated lymph node, which had been treated with excision. He took dolutegravir, tenofovir and emtricitabine alongside prophylactic azithromycin and co-trimoxazole. The patient is a MSM. He had travelled within Europe 8 weeks prior to becoming unwell.

On initial presentation, he had a hoarse voice and was drooling, though he had no stridor. He was slightly tachycardic. His other observations were normal and he self-reported fevers and rigours at home.

On examination of the oropharynx, there was peritonsillar erythema bilaterally, with profuse, thick, white tonsillar exudate on the right. There was noted to be one small vesicle on the left posterior palate. There was marked tender level II cervical lymphadenopathy bilaterally, worse on the right than the left.

Flexible nasoendoscopy showed thick, white plaques of sticky exudate and ulcerated lesions spreading from the right side of the base of tongue to the right supraglottic area, with multiple white...
ulcerated lesions over the right aryepiglottic fold (see figure 1). There was mild swelling of the epiglottis and aryepiglottic folds. There was no airway obstruction, and the vocal cords were moving normally. These features can be seen on the video of the flexible nasoendoscopy (see video 1).

There was a widespread, macular, erythematous rash over the patient’s back and chest which was pre-existing, having developed when the patient commenced antiretroviral therapy some months prior. Otherwise, examination of the chest and abdomen was normal.

Twenty-four hours after admission, it was noted that the patient had a pustule on his hand (see figure 2). This was highly suspicious for monkeypox in appearance. The patient was therefore transferred to an isolation room and infection control processes initiated. A viral swab was taken from the vesicle on the hand by deroofing it and swabbing the fluid within. This sample was sent to the Rare and Imported Pathogens Laboratory, and a diagnosis of monkeypox was confirmed shortly thereafter.

INVESTIGATIONS
Blood tests on admission showed: normal electrolytes with stage 1 acute kidney injury (urea 10.3 mmol/L, creatinine 117 µmol/L), C reactive protein 188 mg/L and white cell count 5.9×10⁹/L. Full blood count, renal function tests and liver function tests were otherwise within normal ranges.

CT neck with contrast was performed. It showed generalised thickening of the right side of the neck (see figures 3 and 4) with superficial enhancement of the right tonsillar fossa and base of tongue (see figures 5 and 6). There was a sizeable 1.7 cm enhancing focus (presumed node) at right level IIa and a similar finding at level IIb. Contralateral level II nodes were noted but were not as large. The internal jugular vein (IJV) on the right could not be identified so thrombosis was suspected. IJV thrombosis was confirmed on a bedside ultrasound doppler.

Due to the HIV positive status of the patient, thorough microbiological investigation was undertaken. Relevant results include: CD4 count 20 cells/µL; HIV viral load undetectable; blood and throat cultures negative; SARS-CoV-2 RNA and antigen negative, sputum acid-fast bacilli negative.

DIFFERENTIAL DIAGNOSIS
The key differential diagnoses for this patient was supraglottitis. This can be a life-threatening airway emergency. However, findings on flexible nasoendoscopy were atypical for supraglottitis. It was postulated that this could be caused by an atypical organism, for example, diphtheria, as suggested by the thick exudate seen on the right tonsil. Other infective differential diagnoses were considered due to the background of immunocompromise. These included possible Epstein-Barr virus (given the systemic features and marked lymphadenopathy) fungal, mycobacterial or streptococcal infection. Given the suspicion of IJV thrombosis on the CT scan Lemierre’s syndrome (septic thrombophlebitis of the jugular vein) was also a differential diagnosis. Given the medical history, we considered mucosal Kaposi’s sarcoma as a non-infective differential diagnosis, with possible metastatic lymphadenopathy.
TREATMENT
The patient was treated with intravenous dexamethasone, intravenous broad-spectrum antibiotics, nebulised epinephrine, intravenous fluids and analgesia. After the identification of the skin lesion, he was transferred to a tertiary centre under the infectious diseases team. He responded well to treatment; his general condition improved and throat symptoms resolved within a week of admission. He remained an inpatient for isolation purposes until all skin lesions had resolved. The patient’s IJV thrombosis was treated with treatment dose low-molecular-weight heparin while an inpatient, then direct oral anticoagulant on discharge.

OUTCOME AND FOLLOW-UP
The patient had regular input from the HIV team, and new Kaposi’s sarcoma lesions were noted alongside the monkeypox rash. These are undergoing monitoring. Once he was no longer infectious, he was discharged with ongoing HIV team follow-up.

DISCUSSION
Monkeypox is an important emerging disease in the UK. Our case highlights that severe sore throat in the absence of skin lesions may be a defining early feature of monkeypox. Awareness of this fact, particularly when seeing a patient from a higher risk group (MSM or HIV positive) may enable clinicians to make an early diagnosis, thus preventing further transmission of monkeypox in hospital and the community. There are no reported cases of transmission from patient to healthcare worker. However, examination of the upper aerodigestive tract puts the clinician in close contact with the patient. Oropharyngeal examination and

Figure 3  Coronal slice from CT scan of the neck with contrast showing generalised thickening of the right neck.

Figure 4  Axial slice from CT scan of the neck with contrast showing generalised thickening of the right neck.

Figure 5  Coronal slice from CT scan of the neck with contrast showing superficial enhancement of the right tonsillar fossa and base of tongue.

Figure 6  Axial slice from CT scan of the neck with contrast showing superficial enhancement of the right tonsillar fossa and base of tongue.
flexible nasoendoscopy generate aerosols, exposing the clinician to the risk of transmission. An awareness of the upper aerodigestive manifestations of monkeypox ensures that appropriate infection control measures can be taken.7

Severe sore throat with associated systemic signs of infection may be a sign of supraglottitis, a potentially life-threatening disease characterised by inflammation and oedema of the supraglottic structures of the larynx.8–10 There is a risk of rapidly progressive airway compromise, requiring emergency intubation or tracheostomy, or potential respiratory arrest.8–10 Immuno-compromised patients are at higher risk of supraglottitis. Our patient had some concerning features for supraglottitis (drooling and hoarse voice). We; therefore, had a low threshold for starting him on empiric treatment for supraglottitis.

It was deemed appropriate to give corticosteroids. They are believed to reduce airway inflammation, stabilise endothelial permeability and decrease tissue oedema.11 Epinephrine nebulisers have long been used to treat supraglottitis and are believed to reduce airway oedema through vasoconstriction.12 In the case of our patient, this treatment seemed to have a rapid beneficial effect. He went from drooling to eating and drinking within twelve hours. However, it is worth noting that corticosteroids may reduce the diagnostic yield of any lymph node biopsies that may be required, so a risk–benefit decision must be considered. Antibiotics were given to cover superadded bacterial infection, though they would not have been effective for treating monkeypox.

Our patient was diagnosed with an IJV thrombosis on imaging of the neck. IJV thrombosis may be unprovoked (no cause identified) or provoked (eg, by local infection, cancer or central venous catheter insertion).13 In our patient’s case, there were several risk factors for IJV thrombosis, notably significant local inflammation with severe cervical lymphadenopathy, alongside dehydration and systemic upset. IJV thrombosis is associated with morbidity and mortality.14 No established guidelines for treatment of IJV thrombosis exist.15 Treatment is usually based on protocols for treating other deep vein thromboses16 and is dependent on cause. This case highlights jugular vein thrombosis as a potential complication of monkeypox.

This patient’s case required multidisciplinary specialist input including ear, nose and throat, HIV, microbiology, infectious diseases, radiology, haematology and public health. Clear communication between clinicians and with the patient was essential to ensure care was delivered effectively. Monkeypox remains largely an ‘unknown’ to patients, as it emerges within countries such as the UK and is reported in mainstream media, it is important we communicate adequately with patients to try and reduce anxiety surrounding the diagnosis that may be present. It is also important to be sensitive to the stigma surrounding monkeypox and the distress that this may cause patients.

Contributors DA researched and drafted the paper. JC edited the paper. DTW supervised the project.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s).

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES