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ABSTRACT

Introduction:

Mpox emerged as a public health crisis with limited research describing co-occurring HIV and sexually transmitted infections (STIs). We present a case of severe proctitis secondary to Mpox with concomitant HIV (Human Immunodeficiency Virus), syphilis, HSV (Herpes Simplex Virus), and chlamydia and review presentation, diagnosis, treatment, and prevention of Mpox with concurrent STIs.

Case Presentation:

34-year-old male living with HIV (LWH) presenting with worsening rectal pain, multiple anal papules, and fever. His laboratory workup revealed simultaneous positive results for orthopoxvirus, chlamydia, and HSV-1 PCR. We initiated tecovirimat due to rectal involvement and uncontrolled pain. He subsequently developed lesions on hands as rectal pain improved. He completed tecovirimat treatment and the lesions cleared by outpatient follow-up.

Discussion:

Among published studies of Mpox patients, 40% were LWH, and a significant percent were found to have co-occurring gonorrhea (23%), chlamydia (20%), syphilis (8%), and HSV (1%) with presentations including fever (62%), lymphadenopathy (49%), malaise (39%), and rectal pain (25%). We recommend Mpox and full STI diagnostic testing for unknown anogenital lesions and early treatment should be considered. Early initiation of Tecovirimat treatment should be considered in severe disease, immune deficiency, or those at high-risk for serious sequelae, in accordance with CDC guidelines.

Learning Points:

- Identify the differential diagnosis for unknown rectal lesions
- Describe the clinical presentation of Mpox
- Summarize the diagnostic approach and interpretation of diagnostic results
- Identify treatment options and considerations by patient populations
- Review preventative strategies and high-risk populations for Mpox transmission

INTRODUCTION

Mpox is a viral zoonotic orthopoxvirus first identified in humans in 1970 in the Democratic Republic of Congo.[1] Outbreaks were mainly limited to Africa until a 2003 outbreak infecting 70 Americans from prairie dog contact.[2] A 2017 Mpox outbreak in Nigeria signaled its reemergence in West Africa but was predominantly among young adult males and attributed to person-to-person secondary transmission. Due to travel, genome mutations, and international gatherings, Mpox emerged as a public health crisis in 2022. Growing published case series and outbreak reports have described concurrent HIV (Human Immunodeficiency Virus) and Mpox; however, few have reported cases of other concurrent STIs with Mpox.[3,4,5,6,7] As Mpox prevalence increases, comparing Mpox presentation with similar appearing STIs has increasing clinical importance. We present a case of severe proctitis secondary to Mpox with concomitant HIV, syphilis, HSV (Herpes Simplex Virus), and chlamydia treated with tecovirimat and review current literature on presentation, diagnosis, treatment, and prevention of Mpox with concurrent STIs.

CASE PRESENTATION

A 34-year-old male LWH since 2018 with intermittent antiretroviral therapy (ART) adherence and a history of prior STIs presented to the Emergency Department (ED) with severe, burning rectal pain and chills for 3 days. He endorsed anal sex with multiple partners and intermittent condom use over the last year. Examination revealed three gray/white, shallow perirectal ulcerations with drainage. He was diagnosed with hemorrhoids, and testing for syphilis and HSV were performed. At discharge, he was presumptively treated with valacyclovir and pain medications.

He re-presented to ED two days later with worsening rectal pain, chills, and new onset fever (Tmax 103°F) with diarrhea. On re-examination there was inguinal lymphadenopathy and 10 white papules surrounding the anal canal. Labs revealed leukocytosis, a positive rectal swab for HSV-1 PCR, absolute CD4 count 295, and HIV viral load 66,149 copies/mL (Table 1). RPR titers from the prior ED visit were elevated compared to prior (Table 1). CT pelvis revealed extensive rectal wall thickening and no drainable collection.

On hospital day (HD) 2, he continued to endorse severe, constant rectal pain. On HD 3, infectious disease consultants recommended Mpox PCR testing, a 21-day doxycycline course for chlamydia treatment, and single dose intramuscular penicillin G for syphilis treatment. Mpox PCR testing was performed due to the patient's known Mpox risk factors, systemic symptoms consistent with Mpox, and increased local transmission. On HD 4, tecovirimat was initiated twice daily for 14 days due to extensive rectal involvement, immune deficiency, and significant pain management requiring hospitalization. On HD 8, he developed lesions on his hands and fingers, and Mpox diagnostic testing resulted positive (Figure 1). He noted substantial

improvement in pain with tecovirimat treatment. Due to unstable housing and Mpox isolation guidelines, he was discharged after tecovirimat completion. On outpatient follow-up he denied residual rectal pain and had clearing of the lesions.

DISCUSSION

Mpox emerged in the U.S. to epidemic levels with nearly 30,000 cases and 20 deaths reported as of January 2023.[8] We present the first known case of Mpox with four co-occurring STIs and complete resolution of lesions with tecovirimat. Growing U.S. and global cross-sectional studies suggest HIV and other STIs are highly prevalent among persons diagnosed with Mpox.[4,6,9,10] A recent case report outlined Mpox with co-occurring gonorrhea and chlamydia with proctitis and absence of anogenital lesions.[7] CDC data found that among 1,969 U.S. persons with Mpox, 38% had HIV and 41% had an STI diagnosed in the preceding year.[4] Furthermore, an international case series found Mpox co-infection common with HIV (39%) or other STIs (29%).[6] Among published studies of Mpox with co-occurring STIs globally, we found STIs included HIV (40%), gonorrhea (23%), chlamydia (20%), syphilis (8%), and HSV (1%) (Table 2). There is more robust surveillance of Mpox and STI data in the U.S. rather than global settings, which highlights a limitation to this study and greater need for Mpox data reporting in global populations.

Signs and Symptoms

The incubation period of Mpox is 5-21 days with symptoms lasting 2-4 weeks.[2] We found in published Mpox cases with co-occurring STIs, clinical presentation included fever (62%), lymphadenopathy (49%), malaise (39%), headache (28%), and rectal pain (25%) (Table 2).

Furthermore, this patient initially presented with white anorectal papules progressing to bilateral hand and arm vesicles. Literature review found 95% cases reported skin lesions in anogenital (67%), extremities (39%), trunk (30%), and palms/soles (16%) areas. Lesions varied in magnitude from singular to thousands of lesions and character including macules, papules, vesicles, or pustules that coalesced to large sections.

Diagnosis

The differential diagnosis of unknown rectal lesions can include syphilis, gonorrhea, chlamydia, HSV, malignancy, and Mpox. This patient initially presented with multiple rectal papules and prior STI diagnoses. However, Desgranges and colleagues document a patient with Mpox with two co-occurring presenting with severe proctitis and no anogenital lesions.[7] The wide array of documented Mpox presentations can make distinguishing between STIs clinically difficult without further diagnostic testing. We recommend orthopoxviral PCR and a full STI screening panel for all sexually active individuals with unknown anogenital lesions or proctitis, and especially among populations with recent or high-risk exposure, consistent with CDC guidelines. In the setting of little to no clinical improvement despite concurrent STI treatment, pretest probability of Mpox diagnosis increases.

Treatment

Typically, Mpox is a self-limited condition, treated with supportive care. However, underlying immune deficiencies have been associated with worse patient outcomes.[2] This patient was empirically treated with tecovirimat due to uncontrolled HIV, rectal lesions with risk of severe

sequelae, and uncontrolled rectal pain.[13] Providers should consider referral to Study of Tecovirimat for Human Mpox Virus (STOMP) sites for treatment.[14] If not feasible, we recommend initiating tecovirimat in patients with uncontrolled pain, severe disease, or involvement of areas (*i.e.,* pharynx, anogenital, eye) prone to serious sequelae. Tecovirimat is administered for 14 days and is available in oral and IV formulation and is a weak inhibitor of CYP2C8 and CYP2C19, so providers should verify drug interactions.[11,13,15] Mpox treatment should also consider multi-modal pain management due to documented lesion-associated pain.

Prevention

Currently, two FDA-approved vaccines have been administered as pre- or post-exposure prophylaxis to high-risk populations to prevent Mpox transmission.[2] Specifically, CDC recommends vaccination for gay, bisexual, and other men who have sex with men and transgender, non-binary, and gender-diverse people who have any of the following risk factors: multiple partners, sex at a commercial venue, a new (within 6 months) STI diagnosis, planned attendance at large gatherings, or anticipated/current partners with these risk factors.[16] We recommend following CDC guidance on Mpox vaccination.

CONCLUSION

As the prevalence of Mpox with concurrent STIs increases globally, we present a rare case of Mpox in a patient LWH with several co-occurring STIs. In the setting of unknown anogenital lesions, we recommend testing for Mpox and STIs due to the varied and overlapping clinical presentations and shared risk factors. Mpox should be included on the differential diagnosis

among other STIs and utilizing epidemiological data may be helpful in delineating and expanding this differential diagnosis during Mpox outbreaks. Early treatment and potential hospitalization in patients with severe disease, immune deficiency, or high-risk for serious sequelae with tecovirimat may prevent morbidity and mortality.

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TABLES AND FIGURES

Table 1. Patient lab values on diagnostic workup

Hospital Day Lab Collected	Lab	Lab Value	Reference Range
Hematology and Chemistry			
1	WBC	13,310/uL	3,700-10,300/uL
1	Hemoglobin	11.8 g/dL	13.7- 17.5 g/dL
1	Sodium	132 mmol/L	136-145 mmol/L
1	Potassium	3.7 mmol/L	3.7-4.8 mmol/L
1	Creatine	0.83 mg/dL	0.8-1.3 mg/dL
Microbiology			
1	Blood culture (two sets)	No growth at day 5	No growth
1	Urine culture	No growth at 30 hrs	No growth
Infectious Disease			
2	Absolute CD4 count (% CD4)	295 (16%)	490-1730 cells/ uL
2	HIV Viral Load	66,149 copies/mL	<40 copies/mL
Prior encounter	Rapid Plasma Reagin	Reactive	Nonreactive
Prior encounter	Rapid Plasma Reagin Titer	1:16 (1:4 10 months prior)	<1:1
Prior encounter	HSV-1 PCR	Detected	Not detected
2	Chlamydia trachomatis DNA PCR	Detected	Not detected
2	Neisseria gonorrhea DNA PCR	Not detected	Not detected
3	Lymphogranuloma venereum IgG antibodies	1:64	<1.1
3	Lymphogranuloma venereum IgG antibodies	<1:10	<1:10
3	Orthopoxvirus (including Mpox) PCR	Detected	Not detected

Table 2. Literature review of published case reports, case series, and cross-sectional studies of populations diagnosed with Mpox and co-occurring sexually transmitted infections

	Ogoina *et al.*, 2020 [5]	Perez Duque et al., 2022 [10]	Iñigo Martínez *et al.*, 2022 [9]	Thornhill *et al.*, 2022 [6]	Antinori et al., 2022 [11]	Angelo *et al.*, 2022 [8]	Curran *et al.*, 2022 [4]	Bížová *et al.*, 2022 [3]	Overall
Study Design	Cross-sectional	Case Series	Cross-sectional	Case series	Case series	Cross-sectional	Cross-sectional	Case report	
Time Period	2017	Apr-May 2022	Apr-Jun 2022	Apr-Jun 2022	May 2022	May-Jul 2022	May-Jul 2022	2022	
Location	Nigeria	Portugal	Spain	Global	Italy	Global	U.S.	U.S.	
Male Sex Assigned at Birth % (n)	81% (17)	100% (27)	99% (503)	>99% (527)	100% (4)	100% (226)	74% (1466)	100% (1)	**84%** (2771/3284)
Men having Sex with Men % (n)	---	95% (18)	93% (397)	98% (519)	100% (4)	92% (208)	---	100% (1)	**95%** (1147/1205)
Mpox Cases (n)	21	27	508	528	4	226	1969	1	**3284**
Sexually Transmitted Infections % (n)									
STI Sample Size	17	27	508	See Below [t]	4	193	1969	1	
HIV	6% (1)	52% (14)	44% (225)	41% (89/218)	50% (2)	48% (92)	38% (755)	100% (1)	**40%** (1179/2953)
Chlamydia	--	--	--	5% (20/377)	--	1% (1)	25% (489)		**20%** (510/2539)
Gonorrhea	--	--	--	8% (32/377)	--	5% (9)	28% (546)		**23%** (587/2539)
Syphilis	18% (3)	--	--	9% (33/377)	75% (3)	3% (5)	8% (165)	100% (1)	**8%** (210/2561)
Herpes Simplex Virus	--	--	--	1% (3/337)	--	1% (1)	--		**1%** (4/530)
Multiple STIs	--	--	--	1% (5/377)	--	1% (1)	21% (420)		**17%** (426/2539)
Symptoms % (n)									
Symptoms Sample Size	21	27	508	528	4	226	1969	1	
Fever	90% (19)	48% (13)	64% (324)	63% (330)	50% (2)	58% (131)	--	100% (1)	**62%** (820/1315)
Sweats	62% (13)	--	--	--	--	--	--	--	**62%** (13/21)
Lymphadenopathy	62% (13)	52% (14)	44% (225)	56% (295)	--	36% (82)	50% (983)	100% (1)	**49%** (1613/3280)
Malaise	62% (13)	26% (7)	36% (185)	41% (216)	--	41% (93)	--	--	**39%** (514/1310)
Headache	57% (12)	26% (7)	32% (162)	--	--	15% (35)	--	--	**28%** (216/782)
Odynophagia	--	--	28% (143)	--	--	--	--	--	**28%** (143/508)
Myalgia	24% (5)	19% (5)	--	31% (165)	25% (1)	14% (32)	--	--	**26%** (208/806)
Proctitis/Rectal Pain	--	--	16% (81)	14% (75)	--	15% (33)	31% (609)	--	**25%** (798/3231)
Pharyngitis	41% (9)	--	--	21% (113)	--	24% (54)	--	--	**23%** (176/776)
Cough	19% (4)	--	--	--	--	--	--	--	**19%** (4/21)
Rectal Bleeding	--	--	--	--	--	4% (8)	16% (322)	--	**15%** (330/2195)
Pruritis	67% (14)	--	--	--	--	8% (18)	--	--	**13%** (32/247)
Lesions % (n)									
Any site	100% (21)	26% (7)	98% (498)	95% (500)	100% (4)	99% (221)	--	100% (1)	**95%** (1252/1312)
Anogenital	48% (10)	22% (6)	71% (359)	73% (383)	100% (4)	55% (124)	--	100% (1)	**67%** (887/1315)
Extremities	--	--	44% (222)	--	75% (3)	26% (56)	--	--	**39%** (281/725)
Trunk	--	--	31% (159)	--	50% (2)	27% (57)	--	--	**30%** (218/727)
Face/Head	--	--	35% (177)	25% (134)	--	24% (51)	--	100% (1)	**29%** (363/1250)
Oral	52% (11)	0% (0)	0% (0)	23% (50)	0% (0)	19% (43)	--	100% (1)	**21%** (105/491)
Palms/Soles	--	--	24% (124)	10% (51)	25% (1)	11% (24)	--	--	**16%** (200/1265)

[t] Sample sizes for each reported sexually transmitted infection (STI) in the Thornhill et al. study differed based on number of participants data was collected from. The number of participants included in each STI category are included below.

Figure 1. Patient presentation and hospital course timeline