

1 **CASE REPORTS**

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3 **Clinical presentation of Monkeypox among people living with HIV in South Florida: a case**
4 **series**

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6 **Running title: Monkeypox among people living with HIV**

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22 **SUMMARY**

23 Introduction: Monkeypox, historically a zoonotic disease caused by monkeypox virus, is a new
24 global health emergency. Since May 2022, dozens of non-endemic countries have seen new
25 cases with rapid spread. Generally a self-limited disease, there are vulnerable populations, in
26 which severe or deadly illness can occur. There is limited data on immunocompromised patients
27 in this outbreak, particularly on people living with HIV, who are disproportionately affected.

28 Methods: We reported seven cases of monkeypox in people living with HIV in South Florida,
29 USA. Relevant demographic, epidemiologic and clinical data were described.

30 Results: All the patients were men, identified as gay or bisexual, and were on combination
31 antiretroviral therapy (cART) for HIV. Six of the seven had CD4 counts more than 200

32 cells/mm³ (one unknown level), and one of the seven had detectable HIV viral load. Six had
33 sexual or intimate contact with asymptomatic partners prior to development of symptoms. Two
34 were hospitalized, one for proctitis and one for an increasing number of lesions. Six had
35 disseminated lesions and one had localized perianal lesions and all had 5-25 total number of
36 lesions. Five received tecovirimat with resolution of lesions in 2-14 days and all were doing well
37 at the time of the present report. Close contacts received the Jynneos vaccine which was well
38 tolerated.

39 Conclusions: Our case series described monkeypox in people living with HIV and have noted
40 atypical symptoms (lack of fever and more notable anogenital lesions) and relatively mild course
41 as described in HIV seronegative patients. We stress the importance of early detection and
42 isolation as well as vaccination to contacts, which has been well tolerated. In our case series, we
43 are unable to estimate the effectiveness of tecovirimat given the limited number of patients, but
44 all our patients had lesions that resolved within two weeks of rash onset and had no side effects
45 reported.

46
47 *Keywords:* Monkeypox; HIV; South Florida; rash; sexual contact.

52 INTRODUCTION

53 Monkeypox, a zoonotic disease caused by the monkeypox virus, results in a skin rash similar to
54 smallpox, which is endemic in several Central and West African countries [1]. There are two
55 clades of Monkeypox virus, the West African, and Central African/Congo Basin, with the latter
56 causing more severe and contagious illness [1,2].

57 Monkeypox is rarely exported from the endemic areas of Africa. In 2003, there was a zoonotic
58 outbreak in the United States of America (USA) causing 47 confirmed or suspected cases [3].

59 This outbreak was linked to the importation of Gambian giant rats, squirrels and dormice which
60 had transmitted the virus to prairie dogs that were then sold as pets. There were no confirmed
61 cases of person-to-person transmission. Imported monkeypox infections in humans following

62 travel have been sporadically reported in the United Kingdom (UK), Europe, Israel, Singapore
63 and most recently in the USA in 2021 [2, 4-8].

64 Since May 2022, a global outbreak of monkeypox has been occurring in many non-endemic
65 countries. In mid May 2022, the Massachusetts Department of Public Health (MDPH) and the
66 Centers for Disease Control and Prevention (CDC), confirmed the presence of the West African
67 clade of Monkeypox virus from a lesion swab on a Massachusetts resident [9]. Since then,
68 confirmed cases have been reported in 47 states in the USA, as well as 72 other countries, none
69 of which had endemic monkeypox with the highest number in the USA and Spain. However,
70 these numbers are likely to be underreported given lack of familiarity with this entity, poor
71 access to testing and generally self-limited course [10,11]. Cases have largely been in males,
72 especially concentrated amongst men who have sex with men (MSM) and although initially non-
73 endemic monkeypox was found in Europe, now it has spread to the Americas, Asia, and
74 Australia [11]. Recent data from a large case series of 528 patients, noted 98% of which were
75 men who identified as gay or bisexual. Cases were thought to be largely related to sexual contact
76 (95%), only 26% had known monkeypox contact and most (72%) had no foreign travel in the
77 month prior to diagnosis [12].

78 For most individuals, monkeypox is a self-limited disease with symptoms lasting from two to
79 four weeks. Severe cases of monkeypox occur more commonly among children and are related
80 to the extent of virus exposure, patient health status and nature of complications. The incubation
81 period from time of exposure to clinical illness is usually 5-13 days (range 5-21). The patients
82 present with a prodromal phase that includes fevers, chills, and myalgias followed by a
83 characteristic rash, which typically begins as macules and evolves to papules, vesicles and then
84 pustules. The lesions eventually crust over, which then dry up and fall off. However, during this
85 outbreak, some patients have presented with only genital, rectal, and/or oral lesions without the
86 initial prodrome. Additionally, other atypical symptoms include few or single lesions, skin
87 lesions in different stages of development, and isolated anal pain and bleeding [10].

88 Underlying immune deficiencies may lead to worse monkeypox outcomes. Although data in
89 immunocompromised patients with monkeypox are very limited, severe complications have been
90 seen in immunocompromised patients who have had smallpox or have received smallpox
91 vaccination with a replication-competent vaccinia virus [3]. The literature in people living with
92 HIV is scant, with some reports suggesting a more severe disease, and others describing a benign

93 course, very similar to that observed in immunocompetent patients [12, 13]. One notable
94 complication is superimposed bacterial cellulitis, which may require hospitalization [12, 14].
95 Given that people living with HIV have been disproportionately affected during the present
96 outbreak, there is a clear need for studies aiming at evaluating the clinical characteristics and
97 outcomes of monkeypox in this population. There is currently one medication, tecovirimat,
98 which is under investigational use, recommended routinely for treatment in severe disease or
99 those at high risk for disease, including immunocompromised patients. Brincidofovir and
100 cidofovir are alternatives that have been used in the treatment of smallpox but have adverse
101 effects of elevated liver enzymes, nephrotoxicity and interactions with antiretroviral therapy
102 which precludes their use. Prevention includes the use of the Jynneos, ACAM2000 and LC16
103 smallpox/monkeypox vaccines but data on effectiveness for all are limited [15, 16].

104 We report seven cases of people living with HIV who were diagnosed with monkeypox at
105 University of Miami Hospital, Jackson Memorial Hospital, and AIDS Healthcare Foundation
106 (AHF) in South Florida, USA during the period of June 13 to July 11, 2022. We described
107 relevant demographic, epidemiologic and clinical data. A table that summarizes the clinical
108 characteristics of the patients is also presented (Table 1).

110 **CASE PRESENTATIONS**

111 *Case 1*

112 A 37-year-old man with HIV on cART (CD4 262 cells/mm³, viral load undetectable) and Kaposi
113 Sarcoma on partial remission was admitted to the hospital with severe rectal pain and skin
114 pustules. Symptoms of fever, lymphadenopathy and fatigue started one week before
115 hospitalization. He has had systemic symptoms intermittently for the last three years from his
116 Kaposi Sarcoma but worsened in the week prior to his skin lesions. Three days later, he noticed a
117 pustule-like facial lesion which spread to his head, torso, extremities, scrotum and anal lesions
118 with significant rectal pain and scant blood in stools. He reported not having sex in the last two
119 months. He did not travel outside of Florida in the last 12 months but went to a concert two
120 weeks prior to symptoms. On exam, he had about 20 lesions, in various stages of development,
121 including papules, vesicles and pustules with an umbilicated center (Figure 1A). He had bilateral
122 increased size of inguinal lymphadenopathy (previous biopsy confirmed Kaposi sarcoma). He
123 had two perianal lesions with pain on palpation, clear drainage from rectum and rectal bleeding

124 (Figure 1B). Biopsy was negative for herpes simplex virus, varicella zoster virus, *Treponema*
125 *pallidum*, bacterial or fungal organisms. Swabs from the pustules were positive for Orthopox
126 PCR. He declined a rectal swab due to extreme rectal pain and was treated empirically for
127 proctitis with ceftriaxone, doxycycline and valacyclovir, with significant improvement of
128 symptoms. He developed more lesions through the first three days of his hospital course but then
129 improved with lesions becoming crusted, all prior to tecovirimat (Figure 1C).

130 *Case 2*

131 A 43-year-old man with HIV on cART (CD4 668 cells/mm³, viral load undetectable) and history
132 of multiple sexually transmitted infections was seen in the outpatient clinic for generalized
133 weakness and fatigue for two days followed by a skin rash and pain in his perianal and inguinal
134 region. The skin rash consisted of a few papules that progressed into vesicles and umbilicated
135 pustules. He reported having unprotected sex with a male about one month prior his symptoms
136 started at which time he developed the weakness and fatigue. He did not travel outside of Florida
137 within the past two months. On examination he had umbilicated pustules on his left perianus and
138 left anal verge with pustular non umbilicated lesions on the right wrist and right thigh (Figure 2).
139 He had tender left sided inguinal lymphadenopathy. Testing from lesion's swabs came back
140 positive for Orthomyxoviridae. The patient was started on tecovirimat with rapid improvement
141 of his lesions in the next 48 hours. At that time, he noted all his lesions had begun crusting. The
142 lesions had completely resolved by day seven of antiviral therapy.

143 *Case 3*

144 A 44-year-old man with HIV on cART (CD4 296 cells/mm³, viral load undetectable) and
145 alcohol abuse presented to the STI (sexually transmitted infection) clinic for evaluation and
146 treatment of monkeypox. One week prior, he developed fatigue and a rash, which started as a
147 vesicle on his chin. The following day, he went to a pool party and found more lesions on his
148 chest and legs. He went to the emergency room where samples from the lesions were taken and
149 were positive for Orthomyxoviridae. He denied any travel outside of Florida within the past two
150 months. The month before the onset of symptoms, he reported intimate contact with another man
151 at a bar, where there was naked hugging and kissing but no sexual intercourse or oral sex. He did
152 not recall any skin rash on that person. He lived with his ex-husband who was asymptomatic and
153 denied any sexual or close physical contact with him. On exam, he had multiple umbilicated
154 pustular lesions with erythematous borders scattered on his scalp, face, chest all in the same

155 stage of development except for one 2.0 cm ulcerated lesion below his right lower lip that was
156 crusted (Figure 3 A,B,C). He had tender left inguinal lymphadenopathy. No perineal or anal
157 lesions were seen. The patient received tecovirimat with resolution of lesions after two weeks.

158 *Case 4*

159 A 38-year-old man with HIV on cART (CD4 553 cells/mm³, viral load undetectable) presented
160 to the clinic for follow up after a diagnosis of monkeypox at a different facility. The patient
161 reported three days of extreme fatigue followed by scattered pustular lesions on his arms and
162 chin followed by lesions on his penis and inguinal region. He was seen approximately one week
163 after symptoms onset. He denied fever or other constitutional symptoms. He reported attending a
164 pool party three weeks before with multiple sexual encounters that day. He lived with a partner
165 who did not have any symptoms at the time of these encounters. On examination, the lesions on
166 his face were dried and crusted. He had four other umbilicated lesions, one on the distal aspect of
167 the dorsal penile shaft and the other three at the base of the penis (Figure 4A). He received
168 tecovirimat and noted that all lesions had formed scabs by day eight of treatment.

169 *Case 5*

170 A 53-year-old man with HIV on cART (CD4 634 cells/mm³, viral load undetectable) was seen
171 in the clinic for management of monkeypox. The patient is the partner of case 4 and was seen at
172 the same time. They both went to the same pool party and had multiple sexual encounters that
173 day. As in case 4, the patient reported extreme fatigue at the same time as his partner and for
174 three days preceding the skin rash. In his case, he had perianal lesions with no other lesions in
175 other parts of his body. On examination, all lesions were either crusting or already in the process
176 of scabbing/healing (Figure 4B). He had no inguinal lymphadenopathy despite the location of his
177 lesions. He received tecovirimat with resolution of lesions after day eight of therapy.

178 *Case 6*

179 A 41-year-old man with HIV on cART (CD4 505 cells/mm³, viral load 236,988 copies/ml) and
180 history of syphilis presented to the Emergency Department (ED) for rash. Three days prior, he
181 went to a party and the following day he began to experience a slight itching sensation over his
182 face. The next day he developed non-tender, fluid filled vesicles on his face. Over the next three
183 days the lesions began to enlarge and spread down to his arms, back and genitals with
184 umbilication. He returned to the ED, where he was admitted due to the increasing number of
185 lesions. He denied systemic symptoms and had only skin involvement. He traveled to the

186 Bahamas about six weeks before. He had sexual intercourse with both male and female partners,
187 with oral, anal (penetrative and receptive) and genital intercourse. His last sexual encounter was
188 on the day of the party. He also had intercourse without condoms about two weeks prior to the
189 rash. Superficial swab of lesion was positive for monkeypox virus PCR. He had negative testing
190 for gonorrhea, chlamydia and change in RPR titer. He was admitted for one day and was
191 discharged home feeling well without treatment. He was subsequently lost to follow up.

192 *Case 7*

193 A 33-year-old man with HIV on cART (unknown CD4, viral load undetectable), history of
194 syphilis and rectal gonorrhea presented to the clinic for headache, fatigue, chills, pruritic rash,
195 and rectal pain for four days. His exam was notable for pustules on his forearm, penis, upper lip
196 and on anal verge. He had sex with a male partner one week prior. He did not travel outside of
197 the country for the past three months but had contact with his mother who is from Peru. Skin
198 swab was positive for Orthopox, received tecovirimat and at his three weeks follow up, he had
199 no further signs or symptoms of monkeypox.

200
201 **DISCUSSION**

202 During the 2022 monkeypox outbreak, 22141 confirmed cases have been reported worldwide in
203 locations that have not historically reported monkeypox. As of July 29, 2022, there were 5189
204 cases confirmed in the United States, with 373 of those cases from Florida [17, 18]. Although
205 Florida has 67 political subdivisions (counties), cases are reported in only 16 of them and most
206 of the cases are spread in two areas (184 in Broward County and 96 in Dade County). Our seven
207 cases live in those two areas (four in Broward County and three in Miami-Dade) and they
208 represent the early cases identified in our state. We witnessed the rapid spread of cases locally
209 with 10 times increase in cases in only a three-week period.

210 In the current outbreak in the USA, patients with monkeypox generally report having close,
211 sustained physical contact with other people who have monkeypox. In a recent update given by
212 the CDC, most infected patients were male, with a median age of 36 years (range 20-76), and
213 99% of them reported sexual contact with other men. Most cases present with a skin rash, with
214 small and firm lesions that are circumscribed, sometimes itchy, and umbilicated in different
215 phases of development that rapidly progressed to pustules with crusting. Prodromal symptoms

216 were mild or absent and lymphadenopathies and fever were less common. Anorectal pain with
217 visualization of proctitis by exam was another finding [19].

218 There is limited information about monkeypox in people living with HIV. A study from Nigeria
219 in 2020, prior to this current outbreak, included 40 patients, of which nine had HIV (four newly
220 diagnosed, five on ART, CD4 range 20-357 cells/mm³). Compared to patients without HIV, they
221 found those with HIV were more likely to have larger skin rashes (≥ 2 cm), secondary bacterial
222 skin infection, genital ulcers, and illness duration ≥ 28 days [13]. An earlier study from Nigeria
223 in 2017-18 noted that of 122 confirmed or probable cases of monkeypox, there were seven
224 deaths (6% fatality rate), four of which had HIV infection. However, there was no mention of the
225 total number of patients with HIV or other baseline comorbidities [20]. A recent study conducted
226 by Thornhill et al. reported 528 cases of monkeypox in 16 countries between April and June of
227 2022. A total of 218 cases were in people living with HIV, of whom 99% were MSM. The
228 median CD4 count in this group was 680 cells/mm³. In the vast majority of these persons, HIV
229 infection was well controlled; 96% of patients were taking ART, and the HIV viral load was less
230 than 50 copies/mL in 95% of individuals. They found a benign course in individuals with HIV,
231 similar to those without HIV, and no deaths were reported [12]. However, following this study,
232 there have been reports of the first five monkeypox deaths outside of Africa. One was in an HIV
233 infected person in Peru, another with lymphoma on treatment and three with unknown
234 comorbidities. Historically, immunocompromised patients, pregnant women, children, especially
235 under 8 years, and patients with compromising skin integrity conditions are considered at high
236 risk for severe disease; for this reason, continued vigilance of these subpopulations is required
237 [18, 21].

238 According to the last WHO situation report in the current outbreak, among cases with reported
239 sexual orientation, 60% (1214/2025) identified as gay, bisexual, and other men who have sex
240 with men and 41% (335/827) of cases with known HIV status were positive for HIV [22]. In
241 England, the UK Health Security Agency revealed that of a total of 445 patients who underwent
242 surveillance questionnaires, 29.5% reported HIV infection, of whom 99.2% were on HIV
243 treatment [23].

244 In this paper, we reported seven cases of monkeypox in people living with HIV in the United
245 States (Table 1). All were male and receiving antiretroviral treatment with CD4 counts >200
246 cells/mm³ except for one unknown CD4 count but undetectable HIV viral load. One patient had

247 a detectable HIV viral load. There was one patient with Kaposi sarcoma (AIDS-defining illness)
248 who was the only patient that required admission to the hospital for proctitis. A second patient
249 was admitted for an increasing number of lesions but was discharged the following day. All
250 cases had mild prodromal symptoms with the main presentation of extreme fatigue days before
251 the skin rash, and only one with fever. None of the seven patients had traveled outside Florida
252 within the prior one month, suggesting the local spread of the infection. Five of the seven
253 patients reported multiple unprotected sexual encounters with other men weeks before the skin
254 rash. One patient reported close intimate contact with another male with kissing and naked
255 contact but no sexual intercourse. Only one patient reported no close sexual or intimate contact
256 nor known exposures. Of interest, the patients who had sexual and intimate skin contact did not
257 recall seeing any skin lesions on their partner, suggesting acquisition of monkeypox from
258 asymptomatic carriers with viral shed in body fluids or from oligosymptomatic individuals
259 whose lesions were overlooked [24]. In a recent study conducted in Spain, the authors tested
260 various body fluids of 12 patients with monkeypox and noted positive virus in not only skin
261 pustules but also rectal swabs (11/12), nasopharyngeal swabs (10/12), semen (7/9), urine (9/12)
262 and feces (8/12), suggesting multiple potential sources of transmission [25]. This outbreak's
263 monkeypox virus genome has noted mutations from endemic virus, therefore further studies
264 regarding the infectivity of oral, rectal, and vaginal mucosa are necessary [26].

265 All the patients in the present series had skin lesions, starting as small papules, rapidly evolving
266 into pustules. According to the WHO rash burden classification (benign, 5-25 lesions; moderate,
267 26-100 lesions; grave, 101-250 lesions; and plus grave, >250 lesions), all our patients had benign
268 burden (5-25 lesions) [3]. Six cases had disseminated lesions most starting on their face and then
269 spreading to the extremities followed by the genitals. Only one case had localized lesions in the
270 perianal area. Despite the benign rash burden in our patients, one of them experienced extreme
271 rectal pain and required hospitalization for three days. Overall, the manifestations and disease
272 severity in our case series seemed to be similar to those described in non-HIV affected
273 individuals during the current outbreak.

274 In terms of concomitant STIs, Girometti et al. reported a case series of 54 patients in the UK,
275 24% living with HIV (all of them on ART and undetectable) and found a high rate of concurrent
276 STIs. Of the 51 patients who had sexual health screening, 13 (25%) patients were positive for
277 gonorrhea and chlamydia, with a higher prevalence in individuals with HIV (7/13, 54%) than in

278 those HIV-negative (6/41, 15%) [27]. In our study, we had one patient with proctitis. Although
279 his urine gonorrhea and chlamydia PCR were negative, we could not exclude a concomitant STI
280 completely because he declined rectal testing. However, he improved on ceftriaxone and
281 doxycycline rapidly, suggesting an STI coinfection.

282 All our patients were given/offered treatment with tecovirimat given their HIV status. Five had
283 received and taken treatment with three seeing improvement and two that had already begun to
284 improve prior to treatment. Delays in treatment were due to need for confirmatory testing and
285 limited availability of medications, which at the time were stockpiled at the CDC. The
286 medication was well tolerated with no reported side effects in any of the five cases (two have not
287 yet received treatment). In the USA, tecovirimat (TPOXX®) is only approved for the treatment
288 of smallpox and is offered under an investigational new drug/compassionate use protocol to
289 patients with monkeypox at high risk of complications or presenting with severe disease. The
290 effectiveness of this medication for monkeypox has not been tested in prospective trials. The
291 clinical data is based on observational studies and anecdotal cases that suggest a shorter duration
292 of symptoms and faster healing of pox lesions [16, 28]. It is not possible to comment about the
293 benefit of tecovirimat in our case series. Although the patients improved while taking it, we are
294 uncertain if this can be attributed to the medication or the natural course of the disease.

295 The vaccine deployed for monkeypox in the USA during this current outbreak is the Jynneos
296 vaccine, a live attenuated non-replicating vaccine, which is FDA approved for the prevention of
297 smallpox and monkeypox [29]. According to the current policy in the State of Florida, the
298 vaccine is recommended for immunocompromised MSM with HIV (CD4 count <200 cells/mm³)
299 and other MSM with a recent history of sexually transmitted infections. It is also indicated as
300 post-exposure prophylaxis in close contacts to monkeypox cases within 14 days of exposure
301 [30]. Our patients' spouses and partners were evaluated, and all asymptomatic partners received
302 the vaccine with no side effects. Mild arm pain was reported by others who were vaccinated.

303

304 **CONCLUSION**

305 Monkeypox has had a resurgence of cases in the past couple of decades in endemic countries in
306 West and Central Africa but now there is a significant and rapid rise of cases in non-endemic
307 countries. We noted cases of monkeypox in persons living with HIV in the United States, in
308 whom the majority had anogenital lesions and a relatively mild disease course, very similar to

309 people without HIV. Transmission appeared to have been through sexual or intimate contact with
310 asymptomatic or oligosymptomatic partners. Information about the burden of monkeypox
311 infection in high-risk asymptomatic persons is in need, to determine if screening in persons
312 without skin lesions is warranted. We stress the importance of early detection and isolation as
313 well as vaccines for contacts, which has been well tolerated. We are unable to comment on the
314 clinical benefit of tecovirimat given the limited number of patients in this case series, but all had
315 lesions that resolved within two weeks of rash onset and had no side effects reported. More data
316 on manifestations and outcomes of monkeypox in patients with uncontrolled HIV is needed.

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320 **CONFLICT OF INTEREST**

321 The authors declare no competing conflict of interest.

322

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326

327 **AUTHORS' CONTRIBUTIONS**

328 Conceptualization, PL; literature review, LW, PL, and JAGZ; writing-original draft preparation,
329 LW, PL, and JAGZ; writing-review and editing, LB, ZH, LW, PL, and JAGZ. All authors have
330 read and agreed to the published version of the manuscript.

331

332 **INFORMED CONSENT STATEMENT**

333 In order to publish the pictures, written informed consent was obtained from the patients.

334

335 **INSTITUTIONAL REVIEW BOARD**

336 IRB approval not required per University of Miami, Florida, USA

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Table 1 - Clinical characteristics of people living with HIV diagnosed with monkeypox in the case series.

Characteristic	All patients (N=7)
Median age (range) - years	41 (33-53)
Median Abs CD4/% (range) - cells/mm ³	529/29% (262-668/14-42%)
Median HIV Viral load (range) - copies/ml	<20 (<20-236,988)
Known to be taking antiretroviral therapy (ART) - no. (%)	7 (100%)
Prodrome symptoms	
Fatigue - no. (%)	6 (86%)
Fever - no. (%)	1 (13%)
Site of lesions	
Face - no. (%)	5 (71%)
Anogenital - no. (%)	6 (86%)
Extremities - no. (%)	6 (86%)
Extracutaneous manifestations	
Rectal/perianal pain - no. (%)	3 (43%)
Lymphadenopathy - no. (%)	3 (43%)
Received monkeypox specific treatment (tecovirimat) - no. (%)	6 (86%)
Outcome	
Resolved	6 (86%)
Lost to follow up	1 (13%)

Figure 1 - Vesicular and umbilicated lesions in leg (A) and perianal region (B). Healing lesions in left foot (C).



Figure 2 - Perianal region with pustular lesions.



Figure 3 - Pustular and crusted lesions in chin (A). Pustular lesions with erythematous border in chest (B) and scalp (C).

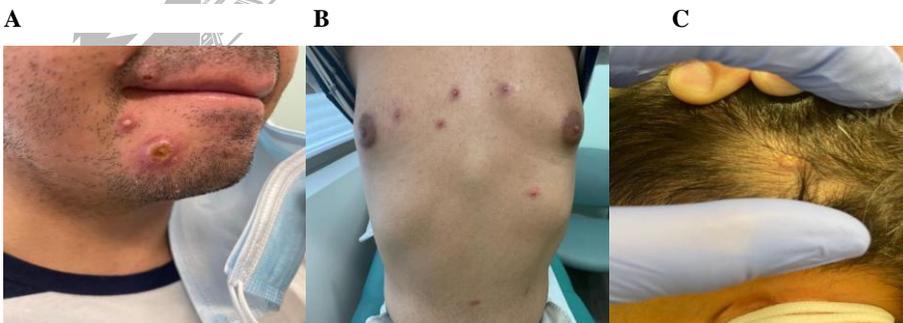


Figure 4 - Umbilicated and vesicular lesions in the dorsal penile shaft and base of the penis from Case 4 (A). Perianal lesions in scabbing/healing process from Case 5 (B).



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