

Suspected “Cowpox” in an Immunocompetent Man

Suspeita de “varíola bovina” em homem imunocompetente



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ABSTRACT

We report the case of a 22-year-old heterosexual male with no prior comorbidities, residing in Caçapava, countryside of São Paulo State, who presented with a painless papular lesion on his right middle finger associated with ipsilateral axillary lymphadenopathy, followed by a cluster of similar lesions in the right inguinal region. The clinical suspicion of cowpox was based on the patient's striking epidemiological history: he worked professionally as a milker and reported direct contact with cows that had “rashes” on their udders, in addition to having previously observed similar lesions on his coworkers' hands. No specific laboratory testing or biopsies were performed (either on the patient or the animals), a fact that prevents us from definitively confirming this clinical suspicion. However, the spontaneous resolution of the lesions helped corroborate this diagnostic hypothesis. Scientific literature research for similar cases revealed that milker's disease most commonly corresponds to the *Parapoxvirus* genus rather than the *Orthopoxvirus* genus (which includes cowpox and *mpox*, among others). Proper clinical and epidemiological knowledge regarding these zoonoses carries relevant diagnostic, therapeutic, and preventive implications.

Headings: Cowpox. Pseudocowpox virus. Poxviridae Infections. Skin diseases. Lymphadenopathy. Case report.

RESUMO

Relatamos o caso de um paciente do sexo masculino, de 22 anos, heterossexual e sem comorbidades prévias, residente em Caçapava, interior de São Paulo, o qual apresentou lesão papular indolor no quirodáctilo médio direito associada a linfadenopatia axilar ipsilateral sucedida por um agrupamento de lesões semelhantes na região inguinal direita. A suspeita clínica de varíola bovina baseou-se nos marcantes antecedentes epidemiológicos do paciente, pois trabalhava profissionalmente como ordenhador e relatava contato direto com algumas vacas que apresentavam “brotoejas” em seus úberes, além de já ter visto lesões semelhantes nas mãos de colegas de trabalho. Não foi realizado nenhum exame laboratorial específico, nem se procedeu a biópsias (nem no paciente, nem nos animais), fato que não nos permite efetivamente garantir a confirmação desta suspeita clínica. A resolução espontânea das lesões, todavia, também ajudou a corroborar esta hipótese diagnóstica. A pesquisa científica em busca de casos semelhantes na literatura médica nos permitiu aprender que a doença dos ordenhadores mais comumente corresponde ao gênero *Parapoxvirus* e não ao gênero *Orthopoxvirus* (o qual inclui a varíola bovina e o *mpox*, dentre outros), de tal forma que o conhecimento adequado do ponto de vista epidemiológico e clínico sobre estas zoonoses traz implicações diagnósticas, terapêuticas e preventivas de impacto relevante.

Descritores: Varíola bovina. Vírus da Pseudovaríola das Vacas. Infecções por Poxviridae. Dermatopatias. Linfadenopatia. Relato de caso.

INTRODUCTION

Poxviruses are a large family of complex viruses that naturally infect a diverse range of species, including primates (human and non-human), domestic animals, cattle, horses, and zoo animals [1]. When infecting humans, these zoonoses most commonly manifest as localized, self-limiting dermatological lesions (vesicles). Although typically not life-threatening, they can become severe in immunocompromised patients, children, pregnant women, and individuals with eczema [2-6].

The *Orthopoxvirus* genus includes the variola virus (“smallpox”, which was eradicated in the 1980s after causing over 300 million deaths in the 20th century alone [7]), monkeypox (whose 2022 global outbreak raised major concerns regarding emerging zoonoses [3]), cowpox (responsible for bovine pox in European countries, western Russia, and central and northern Asia [2]), and the vaccinia virus (whose cross-immunity with smallpox enabled the production of smallpox vaccines [7]). Vaccinia virus has also emerged as the endemic infectious agent of cowpox in Brazil, as demonstrated by insightful studies conducted since the 1990s [8,9].

However, occupational infections acquired through hand abrasions in individuals handling infected animals (especially dairy cattle, as well as sheep and goats) most commonly correspond to another genus of Poxviruses: the *Parapoxvirus* genus, with the pseudocowpox virus being the primary etiology of the so-called “milker’s nodules” [4,10,11]. The aim of this article is to describe a case of probable pseudocowpox in an immunocompetent man working as a milker in rural São Paulo.

CASE REPORT

A 22-year-old heterosexual male with no prior comorbidities, residing in the city of Caçapava (countryside of São Paulo State, Brazil), developed a pruritic hand lesion associated with ipsilateral axillary lymphadenopathy. The patient reported that approximately 10 days prior, an initial 3 mm ulcer appeared on the tip of a right-hand finger, displaying well-defined, raised, and indurated borders, a depressed center, and a necrotic base, accompanied by a smaller satellite vesicular lesion—both painless but pruritic. There was no decline in general health condition, nor systemic symptoms such as fever, adynamia, headache, or myalgia. On

physical examination, he presented a hypochromic papule with central ulceration on the right middle finger alongside a smaller, intact vesicle (Figure 1), as well as several palpable, mobile, and tender lymph nodes (approximately 1 cm in diameter) in the right axilla.



Figure 1: A 3 mm ulcer on the right middle finger (primary lesion) showing well-defined raised borders, a depressed center, and a necrotic base, accompanied by a smaller satellite vesicular lesion.

Epidemiologically, the patient worked as a milker and reported recently handling cows with “rashes” on their udders, in addition to having seen similar lesions on his coworkers’ hands. He denied knowing of similar conditions among family members, including his wife. Empiric antibiotic therapy (amoxicillin-clavulanate) was initially prescribed, but no regression of the cutaneous lesions or axillary lymph nodes was observed over the following week. On the contrary, three days later, a cluster of similar ulcers appeared in the right inguinal region (Figure 2), which were likewise painless and pruritic, without satellite lymphadenopathy.



Figure 2: Raised papular lesions with a depressed, darkened center surrounded by a mildly erythematous area in the right inguinal region (evolutionary clinical picture documented one week later).

No ancillary tests were obtained other than a complete blood count (leukocyte count of $7,500/\text{mm}^3$, with 1% band neutrophils, 56% segmented neutrophils, and 28% lymphocytes), and no biopsies were performed. Nevertheless, progressive reduction in the size of all lesions and the axillary lymphadenopathy was observed starting from the third week, with complete resolution after approximately three months, without further findings or clinical complications. The clinical diagnosis of pseudocowpox was based on the physical examination and striking epidemiological factors, supported by a targeted literature review of similar case reports.

DISCUSSION

Milker's disease is a zoonosis caused by the species *Parapoxvirus pseudocowpox*, a DNA virus belonging to the Poxviridae family that is usually transmitted to humans through contact with lesions on infected cow udders [4,6,10,11]. In cattle, the lesions resemble those of other severe conditions, such as vesicular stomatitis and foot-and-mouth disease, requiring laboratory confirmation through polymerase chain reaction (PCR), electron microscopy, viral isolation,

and serological tests (although the latter do not always differentiate between species) [6,9].

In immunocompetent humans, lesions typically affect the fingers after an incubation period of a few days and characteristically evolve through distinct morphological stages: maculopapular, vesicular, targetoid, pustular, and crusting [6,10,11], resolving with spontaneous healing over 6 to 12 weeks without scarring [4,6,10,11]. Secondary bacterial infections represent the main described complications, alongside erythema multiforme and lymphangitis [10-12]. The incidence of regional lymphadenopathy (usually axillary, as in the present case) is estimated at up to 20% of cases, typically appearing between the 2nd and 4th weeks [8,6,10,11]. Conversely, in immunocompromised patients, the inability of the cellular immune response to limit pseudocowpox replication tends to foster complications, such as exuberant exophytic tumors, chronic ulcerations, and disseminated cutaneous spread mimicking malignancies like squamous cell carcinoma and Kaposi's sarcoma, among others [4-6].

Although the primary site occurs almost exclusively on the fingers and hands (sites of microtrauma during milking), autoinoculation via scratching or handling the active lesion can transfer the virus to other body regions, as occurred in our patient's inguinocrural area. This mechanism is well documented, including cases of lesion propagation from fingers to the face and eyes [13,14]. This underscores the importance of advising patients on hand hygiene and avoiding contact with mucous membranes (including those of other individuals) and other body sites until complete resolution. However, this autoinoculation should be distinguished from secondary immunological eruptions occurring 6 to 17 days after the primary lesion: some patients develop distant urticarial rashes or erythema multiforme (including on the trunk and face), which represent sterile hypersensitivity reactions (free of viral particles) [10,13,14].

The diagnosis of milker's disease is generally based almost exclusively on lesion morphology and location, clinical course, and, above all, epidemiology [6,10,11]. Differential diagnosis primarily involves viral diseases caused by other *Parapoxviruses* (among which contagious ecthyma caused by the Orf virus is clinically indistinguishable, except for its epidemiological link to sheep and goats rather than cattle [6,11,13-15]) and the aforementioned zoonotic *Orthopoxviruses*. "True" cowpox caused by *Orthopoxviruses* cowpox and vaccinia differs from pseudocowpox by causing deeper, more painful, necrotic ulcerative lesions accompanied by pro-

minent systemic symptoms [1,2,8]. Although belonging to the same family, *Orthopoxvirus* monkeypox exhibits a distinct epidemiology; meanwhile, mpox is a systemic disease characterized by intense prodromal fever, asthenia, and myalgia [3]. Unlike focal nodules restricted to the hands, its lesions are well-circumscribed, typically progress synchronously, and frequently affect mucous membranes (oral and anogenital) and extremities in a disseminated pattern [3].

Other potential differential diagnoses include cutaneous anthrax (*Bacillus anthracis*) and tularemia (both extremely rare in Brazil), pyogenic granuloma, mycobacterial infections (tuberculous and non-tuberculous), and cat-scratch disease [4,6,10,11]. Classical cutaneous sporotrichosis may cause diagnostic confusion as it frequently presents in a nodular lymphangitic form (sporotrichoid pattern), with ascending nodes along the lymphatic drainage of the affected limb [16]—a pattern absent in pseudocowpox. Furthermore, while pseudocowpox is strictly linked to handling bovine udders and teats, sporotrichosis is associated with cat scratches/bites or soil and plant handling [16]. In such cases, fungal culture (or PCR techniques) from skin samples can confirm *Sporothrix* sp., whereas pseudocowpox displays cytoplasmic inclusion bodies on histological examination [6,10-12,16-18].

Real-time PCR (RT-PCR) can be useful if biopsy is inconclusive [6,8,10] and allows differentiation between *Orthopoxvirus* and *Parapoxvirus* [1,6,17]. However, these molecular tests have very limited availability in Brazil [6,10], in both the public and private sectors. The fact remains that, because it most frequently affects milkers on small farms far from major urban centers, most pseudocowpox cases are neither laboratory-confirmed nor formally notified. Interhuman transmission of *Parapoxviruses* is extremely rare or non-existent [4,6,10,11], whereas *Orthopoxvirus* infections spread through close skin-to-skin contact, respiratory droplets, sexual contact, and contaminated fomites [2,3,8]. Healthcare professionals should be aware, however, that both diseases can be contracted not only from cattle and livestock, but also from accidental hosts like primates, dogs, and cats, as well as natural rodent reservoirs [1-4,6,8,10,15].

In the case reported here, the initial prescription of empirical antibiotics reflected clinical uncertainty that contrasted with the obvious epidemiological link, reiterating that the well-described underdiagnosis of this occupational dermatosis frequently leads to unnecessary isolation protocols and/or systemic treatments [6,10,11,18]. Specific antivirals or immunoglobulins are

not indicated for immunocompetent patients, leaving only the rational use of topical antiseptics and protective dressings when necessary [6,10,11].

In clinical practice, precise molecular differentiation between the two genera does not significantly override clinical findings in individual patient care. However, it emerges as strategic and essential for epidemiological surveillance and economic impact within the veterinary context: the inadvertent identification of an *Orthopoxvirus* can trigger false international public health emergency alarms due to highly transmissible zoonotic outbreaks, as well as lead to mandatory herd quarantines and inappropriate trade restrictions [6,9,10]. It is also important to note the co-infection of *Parapoxvirus pseudocowpox* and *Orthopoxvirus vaccinia* in rural Brazil [8,9], with cowpox cases commonly linked to non-technified farms that facilitate viral persistence in the environment. Therefore, during an outbreak, laboratory diagnosis in animals (via PCR) becomes a priority [9].

CONCLUSION

Milker's disease should be considered in the differential diagnosis of nodular or ulcerative lesions in workers with occupational exposure to cattle, particularly when there is contact with animals presenting udder lesions. The occurrence of subsequent lesions distant from the primary inoculation site may represent autoinoculation. Early recognition of the disease can prevent unnecessary antimicrobial treatments and enable appropriate hygiene measures to prevent transmission to other body areas. Finally, the indirect public health and livestock industry implications of an inaccurate clinical diagnosis cannot be underestimated.

“This case report deserved an official declaration of acknowledgement and ethical approval by its institution of origin and was peer-reviewed before publication, whilst the authors declare no fundings nor any conflicts of interest concerning this paper. It is noteworthy that case reports provide a valuable learning resource for the scientific community but should not be used in isolation to guide diagnostic or treatment choices in practical care or health policies. This Open Access article is distributed under the terms of the Creative Commons Attribution License (CC-BY), which allows immediate and free access to the work and permits users to read, download, copy, distribute, print, search, link and crawl it for indexing, or use it for any other lawful purpose without asking prior permission from the publisher or the author, provided the original work and authorship are properly cited.”

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