

CASE REPORT

**VULVAR INFECTION AND POSSIBLE HUMAN-TO-HUMAN TRANSMISSION
OF BOVINE POXVIRUS DISEASE**

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ABSTRACT

In a dairy cattle farm, father and son developed successively a vesicopustular infection, with lesions in the hands and wrists, after contact with cows with vesicular lesions on the udder. After sexual contact with her husband, the mother showed a severe vesicular vulvar infection, which healed in about three weeks, leaving no scars. All family members showed high levels of antibodies in a plaque reduction neutralization test, using as antigen a locally isolated poxvirus strain, identified as a vaccinia-like virus by sequencing techniques. These data reconfirm that vaccinia-like viruses are circulating in Brazil and that person-to-person transmission may occur, without any relation to vaccinations against smallpox.

INTRODUCTION

The *Poxviridae* virus family includes an ancient group of viruses, which infects humans, vertebrate and insects. In vertebrates, these viruses cause, mainly, vesicular/pustular infections of different degrees of severity (Schatzmayr & Costa 2005). Some of the human pathogenic poxvirus infections are zoonoses.

Orthopoxvirus is the most important genus in relation to human infections, including the smallpox virus, eradicated as a human disease in 1977 and the vaccinia virus, with different strains that were used in vaccines to prevent smallpox.

Orthopoxvirus infections after the discontinuation of the vaccination against smallpox have been observed in the state of Rio de Janeiro (Damaso et al. 2000, Schatzmayr et al. 2000), in dairy cattle and in humans in close contact with them. Over the

years, poxvirus strains isolated in the state were characterized as vaccine-like viruses similar to the vaccinia-IOC strain, which was used in the past for vaccine preparation (Damaso et al. 2000). Other orthopoxvirus strains isolated in the southeastern region of the country (De Souza et al. 2003, Nagasse-Sugahara et al. 2004, Lobato et al. 2005) were confirmed as vaccinia-like poxviruses.

The orthopoxviruses exhibit a tropism for epithelial cells and, in general, have the tendency to produce cutaneous lesions. In most cases, the lesions are characterized by progressive stages of macules, papules and vesicles. The initial opalescent vesicular fluid becomes opaque, turbid and finally turns into a pustule. The absorption of the fluid promotes the formation of a scab and the healing of the lesion. Among the members of the orthopoxviruses, the most deadly virus for humans is variola major, the agent of smallpox, but this virus now is only known to exist in two World Health Organization (WHO) approved repositories, at the Centers for Disease Control and Prevention (CDC), Atlanta, USA, and at the Vector Laboratory, Novosibirsk, Russia.

This article describes female genital infection and most probably a human-to-human transmission of a bovine poxvirus disease.

A family of three were infected by poxvirus: the husband (BDV, 47 years), wife (AJV, 40 years) and son (BLJV, 17 years), who work on a farm, milking cows by unprotected hand in Paraíba valley (Brazil). On 11 October 2008, BDV began with symptoms of macula, papule and pustules on his hands and wrists. He received the usual treatment with symptomatic medicine.

In order to not reduce milk production, his son helped him and showed the same lesions after one week (18 Oct 2008) and his wife had vulvar pustules two weeks after the

beginning of her husband's disease (25 Oct 2008). The couple had sexual relations after the husband's hands lesions were evident.

AJV went to the Gynecology and Obstetrics Emergency Health Service of the University Hospital of Taubaté during the pustular stage (25 Oct 2008). Antibiotics were given for secondary infection and analgesics. She had gentian violet (1% solution in water) treatment for the vulvar pustules (Figure 1).



Figure 1. Vulvar lesions of poxvirus.

AJV was sent for an appointment in the Vulvar Pathology Ambulatory Clinic and on genital examination exhibited hyperemia, edema, many ulcers in the entire vulvar area and bilateral inguinal adenopathy. The swollen area was acutely sore when touched. There were no signs of secondary infection at that time. Vaginal examination was not possible because of her aching and a synechia in the middle of labia minor. Vagitrene (R) vaginal cream (*Triticum vulgare* aquosum extractum) was prescribed for topical use, which has a cicatrizing effect on vulvar lesions. She returned in December (23 Dec 2008) fully

recovered, with no scars observed. Serologies was negative for sexually transmitted diseases, including AIDS, syphilis and hepatitis B.

In January 2009, blood samples of the family were collected and sent to the Laboratory of Morphology and Viral Morphogenesis, Instituto Oswaldo Cruz. All sera were positive, with high levels of orthopoxvirus antibodies. For the serology a plaque reduction neutralization test has been applied to the sera, using as antigen the *Orthopoxvirus* strain Cantagalo/IOC, as already described (Costa et al. 2007).

DISCUSSION

Infection caused by orthopoxviruses in humans and animals have been described in the state of Rio de Janeiro in the past (Silva & Moraes 1961, Mesquita & Schatzmayr 1969). Smallpox vaccination in Brazil during the smallpox eradication campaign was carried out in the rural areas on a farm-by-farm system and careless handling of flasks containing the smallpox live vaccine, with high virus titers, was usual. These procedures most probably allowed the dissemination of the vaccinia virus in nature, probably with more than one introduction. Smallpox vaccination was discontinued in the country in the 1970s, but several studies confirm that vaccinia-like viruses are circulating in nature, sustaining and generating new human and animal infections (Silva et al. 2008). A recent review emphasized the capacity of orthopoxviruses to adapt themselves to new animal species and also confirm the presence of vaccinia-like cases in Brazil, characterizing a zoonosis in expansion (Regnery 2007).

Vulvar infections caused by vaccinia virus transmitted from vaccinees to family members (Humphrey 1963, McLaughlin et al. 2007) as well as infections acquired in hospitals (Toscano & Angela 1953) have been described.

In a literature revision, published in 1963, Humphrey found 70 cases of vulvar vaccinia related to vaccinations, including the 24 cases occurred in an infirmary, after contact, with an infected catheter, described by Toscano & Angela in 1953.

One case of vulvar infection with cow-pox occurred after direct contact with cows has been also described (Mittal et al. 1993).

Our cases however, are the first description in the country of person-to person transmission of a poxvirus, starting from an animal infection occurred in natural conditions, not related to vaccinations, reconfirming that vaccinia-like virus are circulating in Brazil (Schatzmayr et al. 2000)

A few zoonoses may be transferred through casual contact, but others are much more readily transferred by activities that expose humans to the semen, vaginal fluids, urine, saliva, feces and blood of animals. Many farms in the state involved in milk production are family enterprises, have a limited numbers of animals and less than optimal hygienic conditions (Simonetti et al. 2007). Gloves could avoid this contact but they are not usually used.

The poxvirus in AJV was possibly transmitted by direct contact of pustules in the husband's hands or by her own hands. She had no lesions on her hands; only in the vulva.

Since the smallpox vaccination has been interrupted in our country, about 45 years ago, human poxvirus cases have been observed only in workers in direct contact with animals with lesions, but no human-to-human transmission had been confirmed. Most

patients had lesions only on the hands and fingers, but lesions on the face were also recorded. Almost all patients could not perform their normal activities for at least one week during their illness. In the patients, pain in the lesions, fever, regional ganglion inflammation, headache and prostration were described. The clinical course lasted about 3 weeks, with an incubation period after first contact with infected animals of 5 to 7 days (Costa et al. 2007). There is no specific treatment in human cases because the disease is normally self-limited, just local hygiene and symptomatic medicines (Schatzmayr et al. 2000; Schupp et al. 2001).

The implications for zoonotic contact of each emerging disease should be carefully assessed by practitioners. These cases show the necessity of mandatory notification of orthopoxviruses in cattle in regions where this disease is present, so that proper orientation can be given to medical professionals who work with farmers. Furthermore, as shown in this paper, there is the possibility of human-to-human disease transfer, which is a concern in terms of public health.

REFERENCES

Costa RVC, Simonetti BR, Abreu DC, Simonetti JP, Gonçalves MCR, Silva MEV, Brust LAC, Barth OM, Schatzmayr HG. 2007. Animal infections by vaccinia-like viruses in the state of Rio de Janeiro: 2- Paraíba river valley. *Virus Rev. & Res.* 12: 37-42.

Damaso CRA, Esposito JJ, Condit RC, Moutssatché N 2000. An emergent poxvirus from humans and cattle in Rio de Janeiro state: Cantagalo virus may derive from Brazilian smallpox vaccine. *Virology* 277: 439-449.

de Souza Trindade G, da Fonseca FG, Marques JT, Nogueira ML, Mendes LC, Borges AS, Peiro JR, Pittuco AM, Bonjardin CA, Ferreira PC, Kroon EG 2003. Araçatuba virus: a vaccinia like virus associated with infection in humans and cattle. *Emerg. Infect. Dis.* 9: 155-160.

Humphrey DC 1963. Localized accidental vaccinia of the vulva: report of three cases and a review of the world literature. *Am. Obstet. Gynecol.* 86: 460-469.

Lobato ZIP, Trindade GS, Frois MCM, Ribeiro EBT, Dias GRC, Teixeira BM, Lima GMF, Almeida GMF, Kroon EG 2005. Surto de varíola bovina causada pelo vírus Vaccinia na região da Zona da Mata Mineira. *Arq. Bras. Med. Zootec.* 57: 423-429.

McLaughlin J, Schmidt T, Westcott M, Baumbach J, Lofgren JP, Gerber S, Panares R, Staggs W, Collins L, Tong S, Li Y, Mar E, Ruone S, LaMonte-Fowlkes MA, Anderson L, Reynolds M, Trindade G, Olson V, Damon A, Fagan R, Lederman E 2007. Vulvar vaccinia infection after sexual contact with a military smallpox vaccinee – Alaska, 2006. *MMWR/CDC* 56: 417-419.

Mesquita JA, Schatzmayr HG 1969. Estudos laboratoriais de infecções humanas e de bovinos com vírus do grupo Pox. *Rev. Soc. Bras. Med. Trop.* 3: 171-175.

Mittal RR, Jain C, Gupta V, Kaur S 1993. Cowpox of vulva. *Indian J. Dermatol. Venereol. Leprol.* 59: 138-139.

Nagasse-Shugara TK, Kisielius JJ, Ueda-Ito M et al. 2004. Human vaccinia-like virus outbreaks in São Paulo and Goiás States, Brasil: virus detection, isolation and identification. *Rev. Inst. Med. Trop. São Paulo* 46: 315-322.

Regnary RL 2007. Poxvirus and the passive quest for novel hosts. *Curr. Top. Microbiol. Immunol.* 315: 345-361.

Schatzmayr HG, Costa EA 2005. Poxvirus. In: JR Coura (ed.). *Dinâmica das Doenças Infecciosas e Parasitárias*. Editora Guanabara, Rio de Janeiro, Capter 169, p. 1936-1944.

Schatzmayr HG, Lemos ER, Mazur C, Schubach A, Majerowicz S, Rozental T, Schubach MC, Bustamente MC, Barth OM 2000. Detection of poxvirus in cattle associated with human cases in the state of Rio de Janeiro: preliminary report. *Mem. Inst. Oswaldo Cruz* 95: 625-627.

Silva AC, Reis BB, Ricci Junior JER, Fernandes FS, Corrêa JF, Schatzmayr HG 2008. Infecção em humanos por varíola bovina na microrregião de Itajubá, estado de Minas Gerais: relato de caso. *Rev. Soc. Bras. Med. Trop.* 41: 507-511.

Silva PL, Moraes LT 1961. Nota sobre a ocorrência da varíola bovina no estado do Rio de Janeiro. I. Estudo da doença no Município de Três Rios. *Veterinária (RJ)* 14: 31-35.

Simonetti BR, Abreu DC, Simonetti JP, Gonçalves MCR, Silva MEV, Barth OM, Schatzmayr HG 2007 Animal infections by vaccinia-like viruses in the state of Rio de Janeiro: 1- Northwestern region. *Virus Rev. & Res.* 12: 32-36.

Schupp P, Pfeffer M, Meyer H, Burck G, Kömel K, Neumann C 2001. Cowpox virus in a 12 year-old-boy: rapid identification by an orthopoxvirus-specific polymerase chain reaction. *British J. Dermatology* 145: 150.

Toscano F, Angela G 1953. Considerazioni su di una epidemia di vaccinosi vulvare da cateterismo. *Minerva Pediatr.* 5: 987-990.