Feline Orthopoxvirus Infection - Case Report

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KEY WORDS

Cowpox, histology, immunohistochemistry (IHC), electron microscopy, cat.

SUMMARY

A ten year old cat was presented due to a bite-like lesion on the hind leg. Skin biopsies revealed ulcerative lesions with intracytoplasmic inclusion bodies typical of poxvirus infection. By means of electron microscopy viral particles were demonstrated, being morphologically consistent with orthopoxvirus. Additionally orthopoxvirus antigen was detected by immunohistochemical methods within keratinocytes of the epidermis and within the epithelium of hair root sheaths. Cowpox is the only orthopoxvirus currently known to infect cats and therefore is the most likely cause of disease in this case.

INTRODUCTION

Poxviruses represent a large family of double-stranded DNA viruses and infect humans as well as animals producing characteristic vesicular skin lesions. The genus Orthopoxvirus is a member of the poxvirus family and includes several species of either medical or veterinary interest, the most important being smallpox virus, cowpox virus, vaccinia virus, monkeypox virus and infectious ectromelia. Cowpox virus is known to infect cats since many years[13]. Nowadays cats seem to be the most frequently recognized host of Cowpox virus and are reported from many European countries[2,4,8,14].

However, it is still a rare infection in cats, but should be kept in mind because of its zoonotic potential. No record of a confirmed or suspected case of orthopoxvirus is registered in the database of our institute, and to our knowledge no orthopoxvirus infection was reported in Switzerland until now although it was reported in at least two of the neighbouring countries[4,3].

CASE DESCRIPTION

A 10 year old male castrated cat (domestic short hair) was presented to the veterinarian due to a bite-like lesion on the left hind leg. After two weeks of treatment with antibiotics and corticosteroid containing ointment, the animal developed multiple ulcerative skin lesions which were disseminated all over the body. The ulcers were variable in diameter (0.5 to 2 cm), covered with thick crusts, round-shaped and sharply demarcated. No other signs of systemic illness were present. A skin biopsy was carried out. One week later the cat was euthanized due to progressive skin lesions (Fig. 1) not responding to treatment. The histological examination of haematoxylin and eosin-stained sections of formalin-fixed and paraffin-embedded skin biopsies revealed lesions typical for poxvirus infection. The epidermis was extensively ulcerated and covered by a thick serocellular crust. The intact epidermis at the margin of the ulcerated area was hyperplastic and mild to moderate ballooning degeneration of epidermal cells was evident. Large, homogenous, eosinophilic intracytoplasmic inclusion bodies were seen in these areas within cells of the stratum spinosum (Fig. 2) as well as in epithelial cells of outer hair root sheaths. A severe, diffuse, primarily neutrophilic inflammation was present at the base of the ulcers and in the dermis, sometimes even reaching the subcutaneous tissue. Most of the hair follicles within these areas were ruptured and furuncles were formed. Additional skin specimens obtained after euthanasia of the cat one week later revealed lesions consistent with chronic ulcerative pyoderma but no inclusion bodies were present anymore. No additional lesions were seen in the internal organs that were examined (heart, lung, liver). Immunohistochemistry was performed using a monoclonal antibody (kindly provided by C.P. Czerny of the Institute for Medical Microbiology, Infectious and Epidemic Diseases, Ludwig-Maximilians-University, Munich) directed against the epitope A1 of the orthopoxvirus fusion protein. The immunohistochemical method

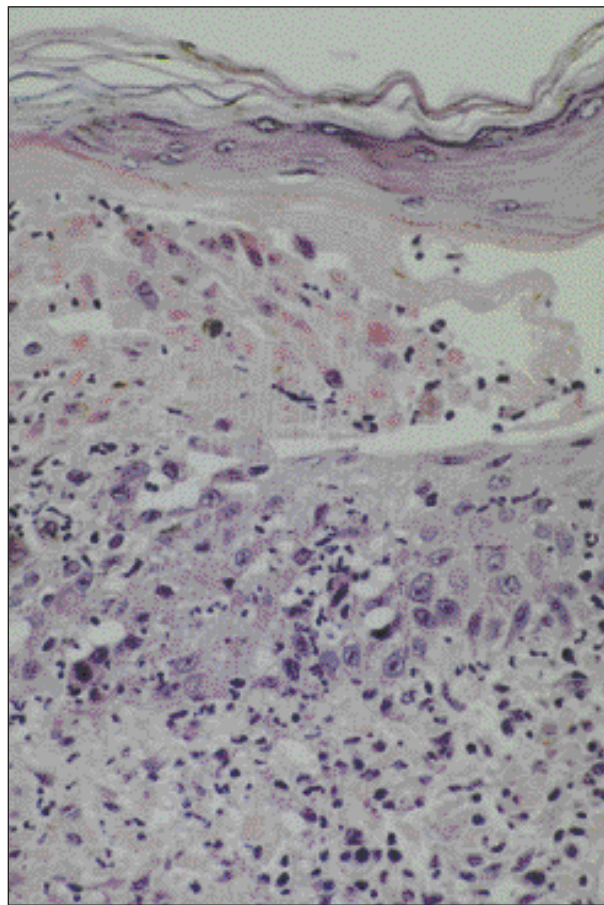Figure 1: Hind limb: extensive ulcerative dermatitis on the left hind leg.

Figure 2: Photomicrograph of H&E stained skin biopsy section: hyperplastic epidermis with an intraepidermal vesicle containing abundant eosinophilic intracytoplasmic inclusions in keratinocytes, exocytosis of neutrophils, and diffuse mixed inflammatory infiltrates in the superficial dermis.

applied was the EnVision method (Dako EnVision™) as described by the manufacturer. The primary antibody was diluted 1 in 200 in phosphate-buffered saline (PBS) and was incubated at 37°C for 1 hour. Aminoethyl-Carbazole substrate (Zymed laboratories, San Francisco) was used as chromogen. Keratinocytes of the epidermis and epithelial cells of the hair follicles (Fig. 3) within the lesion were positively labelled. For electron microscopy, formalin-fixed samples of the skin were postfixed in glutaraldehyde and osmium tetroxide and embedded in Epon. Ultrathin sections were stained with uranyl acetate and lead citrate. Inclusion bodies within the stratum spinosum were found to consist of round to brick-shaped, enveloped virions, measuring approximately 260-300 nm x 150-190 nm, that were embedded in finely fibrillar material (Fig. 4).

DISCUSSION

In the presented case characteristic histopathologic skin lesions as well as the presence of inclusion bodies typical of poxvirus infection were observed.

Immunohistochemically a positive reaction for orthopox antigen was detected and in addition electron microscopy revealed viral particles morphologically typical of orthopoxvirus. Since cowpox is the only orthopoxvirus currently known to infect cats, the presented case is most likely a case of cowpox infection in a cat.

The geographic range of cowpox virus is limited to Europe and the western parts of the former USSR[5]. Despite its name this virus is rarely isolated from cattle, but most commonly from cats. It has also been found in various zoo animals such as cheetahs, lions, panthers, elephants and rhinoceroses as well as from rats and gerbils[2]. Occasionally dogs[3] are infected. The cat seems not to be the reservoir host, but is an accidental host as humans are. Based on serological and virus isolation data, wild rodents are thought to be the natural reservoir[9,11,12,15] although this has not yet been confirmed. Cats are thought to become infected by hunting rodents. The increased disease rate observed during autumn corresponds well with peak rodent populations during that season. Virus entry
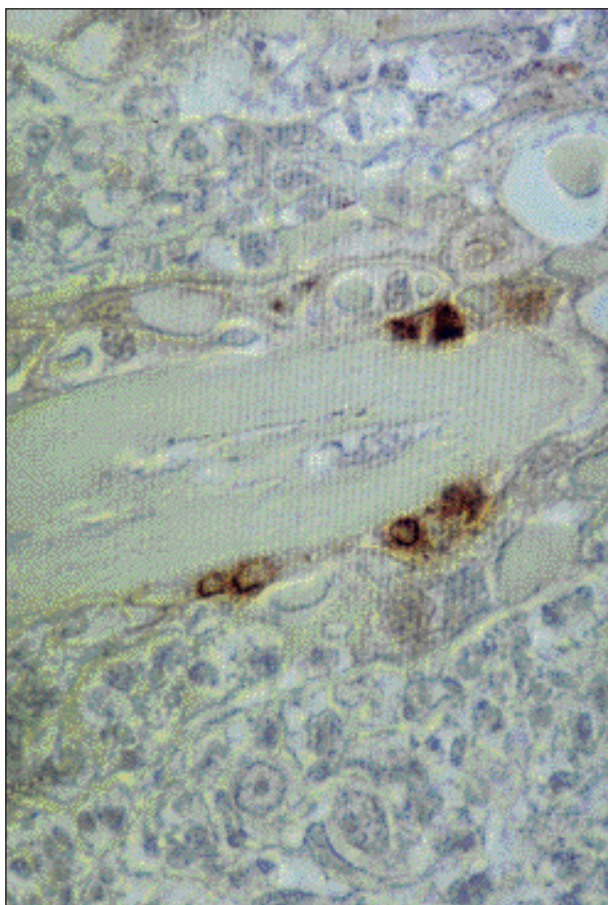
Figure 3: Immunohistochemical staining of a histological section of a hair follicle, EnVision method (Dako EnVision™): scattered keratinocytes of the hair root sheath show a strong positive staining for orthopoxvirusantigen.
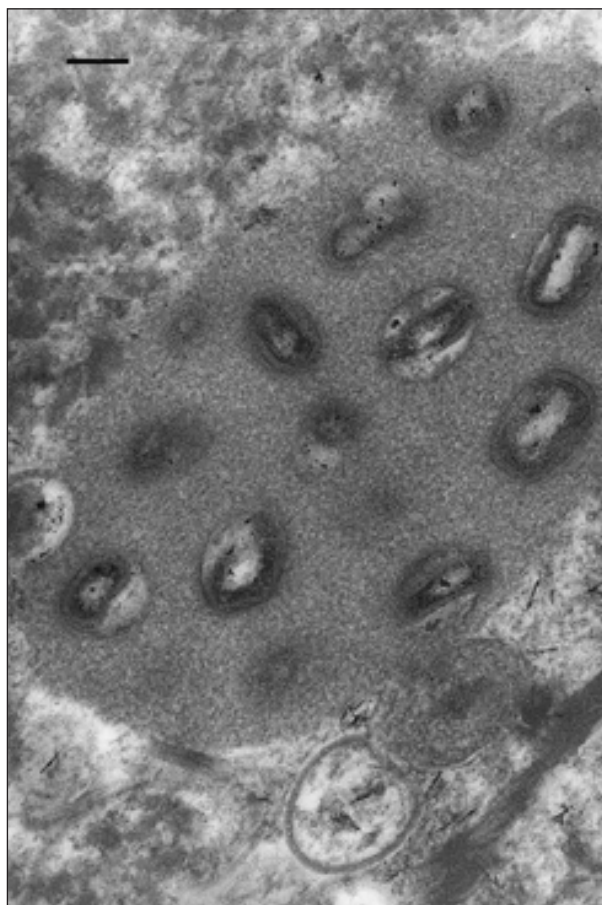

Figure 4: Epidermis (Keratinocyte): Enveloped brick-shaped orthopoxvirus particles (approximately 280 nm x 170 nm) within finely fibrillar material. Electron micrograph, bar = 130nm.

seems to occur at the site of bites or scratches. Usually infected cats have a single primary skin lesion of variable appearance most often located on the head, neck or forelimb. These are described as small erythematous macules of gradually increasing size which become soon ulcerated and scabbed. Widespread secondary lesions develop a few weeks later. Pruritus is rarely observed and most cats are only mildly pyrexic, inappetent and depressed. Some cats also develop ulcerative lesions in the mouth and mild upper respiratory tract infection may occur, but normally the infection is benign and most animals recover without therapy. However, cases of systemic infections with severe clinical signs may occur, and severe necrotizing pneumonia due to cowpox infection has been reported in cats[8] as well as in wild Felidae in zoos[10]. Such an aggravated clinical course has been associated with underlying immunosuppression, for example infections with feline leukemia virus or treatment with corticosteroids, or with secondary bacterial infections[2]. In our case the treatment with corticosteroid containing ointment is most likely the reason for the progressive clinical course. Because of the variable appearance of the primary lesions, cowpox infection is often not suspected in the early stage of the disease. Common differential diagnoses are bite wounds, lesions of the eosinophilic granuloma complex and tumors. Laboratory tests are often required because of the difficulties in establishing a correct clinical diagnosis. Histopathological evaluation of skin biopsies is often useful in reaching a diagnosis because of the characteristic skin lesions. Immunohistochemical techniques which are relatively easy to perform and work on formalin fixed and paraffin embedded tissue may help identifying orthopoxvirus antigen within the tissue. In addition electron microscopy allows a diagnosis of orthopoxvirus infection. Other diagnostic tools to confirm the presence of orthopoxvirus are virus isolation in tissue or cell culture. This is usually only successful when fresh lesions are present and was not attempted in our case because there was not enough material. As another diagnostic aid serum antibody tests are available[2]. For further characterisation of the virus polymerase chain reaction is used.

Although cowpox virus infection is uncommon in cats and cows, its zoonotic potential must be kept in mind. Human cowpox infection is frequently linked to diseased cats and cat-to-man-infection has been documented[1,6], whereas rodents as source of infection were only rarely mentioned[1]. However, human cowpox is quite rare and this may be related to a low infectivity of the cowpox virus for humans[1]. On the other hand there might be a rise in susceptible individuals and an increased incidence of human and animal cowpox infection because of the cessation of smallpox vaccination[7,16]. But based on epidemiologic data from England there is no clear evidence for an increased incidence of human cowpox infection and in addition the authors indicate that vaccination against smallpox provide only limited protection against cowpox[1]. But without doubt immunosuppressed humans are at great risk and infections in these patients can be life-threatening and may be even fatal[7]. Because cats are the major source of infections rapid establishment of a correct diagnosis in suspected cases of cowpox virus infection is of great importance.

REFERENCES

1. BAXBY D, BENNETT M, GETTY B, 1994: Human cowpox 1969-93: a review based on 54 cases. Br J Dermatol, 131(5), 598-607.
2. BENNETT M, GASKELL CJ, BAXBY D, GASKELL RM, KELLY DF, NAIDOO J, 1990: Feline cowpox virus infection. J Small Anim Pract, 31, 167-173.
3. BOMHARD D, PFLEGHAAR S, MAHNEL H, SCHNEEKLOTH-DÜCKER I, 1991: Fallbericht: Katzenpockeninfektion als Zoonose für Hund und Mensch. Kleintierpraxis, 36, 511-513.
4. CANESE MG, LAVAZZA A, MASSONE A, GALEANO F, BODLINI M, 1997: Feline Poxvirus infection. A case report. Schweiz Arch Tierheil, 139, 454-457.
5. CHANTREY J, MEYER H, BAXBY D, BEGON M, BOWN KJ, HAZEL SM, JONES T, MONT-GOMERY WI, BENNETT M, 1999: Cowpox: reservoir hosts and geographic range. Epidemiol Infect, 122(3), 455-460.
6. CONRAD A, CZERNY CP, KAPP A, KIEHL P, 1997: Lokalisierte Infektion mit dem Kuhpocken-/Katzenpockenvirus. Aktuelles zur Epidemiologie, Diagnostik und Therapie. Hautarzt, 48(12), 918-922.
7. EIS-HÜBINGER AM, GERRITZEN A, SCHNEWEIS K, PFEIFF B, PULLMANN H, MAYR A, CZERNY CP, 1990: Fatal cowpox-like virus infection transmitted by cat [letter]. Lancet, 336(8719), 880.
8. HINRICHS U, VAN DE POEL H, VAN DEN INGH TSGAM, 1999: Necrotizing pneumonia in a cat caused by an orthopox virus. J Comp Path, 121, 191-196.
9. KAPLAN C, HEALING TD, EVANS N, HEALING L, PRIOR A, 1980: Evidence of infection by viruses in small British field rodents. J Hyg (Lond), 84(2), 285-294.
10. MARENNIKOVA SS, MALTSEVA NN, KORNEEVA VI, GARANINA N, 1977: Outbreak of pox disease among carnivora (felidae) and edentata. J Infect Dis, 135(3) 358-366.
11. MARENNIKOVA SS, SHELUKHINA EM, EFREMOVA EV, 1984: New outlook on the biology of cowpox virus. Acta Virol, 28(5), 437-444.
12. MÜLLER T, HENNING K, KRAMER M, CZERNY CP, MEYER H, ZIEDLER K, 1996: Seroprevalence of orthopox virus specific antibodies in red foxes (Vulpes vulpes) in the Federal State Brandenburg, Germany. J Wildl Dis, 32(2), 348-353.
13. THOMSETT LR, BAXBY D, DENHAM EMH, 1978: Cowpox in the domestic cat [letter]. Vet Rec, 103(25), 567.
14. TRYLAND M, MYRMEL H, HOLTET L, HAUKENES G, TRAAVIK T, 1998: Clinical cowpox cases in Norway. Scand J Infect Dis, 30(3), 301-303.
15. TRYLAND M, SANDVIK T, MEHL R, BENNETT M, TRAAVIK T, OLSVIK O, 1998: Serosurvey for orthopoxviruses in rodents and shrews from Norway. Journal of Wildlife Diseases, 34(2), 240-250.
16. VESTEY JP, YIRRELL DL, NORVAL M, 1991: What is human catpox/cowpox infection? Int J Dermatol, 30(10), 696-698.