GUIDELINE for Poxvirus infections in cats

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The Cowpox in cats guideline was first published in the J Feline Med Surg 2013; 15: 557-559; the present guidelines were updated by K. Möstl et al.

Key points

- In cats, *Orthopoxvirus* infections are repeatedly reported, usually caused by cowpox virus.
- Cowpox virus has a wide host spectrum including man (zoonosis!) and occurs predominantly in small rodents.
- Cats with rodent contact are at risk of infection.
- Skin lesions are predominantly found on the head and paws. They usually heal spontaneously, in severe cases progressive proliferative ulcerations ensue.
- In kittens and immunosuppressed cats, generalized cowpox infections frequently take a fatal course.
- Corticosteroids enhance systemic spread of the virus and are contraindicated.
- Biopsy and/or scab material is suitable for diagnosis.
- Owners of affected cats (as well as of affected pet rats) must be informed about the zoonotic risk.
- Monkeypox virus, another *Orthopoxvirus*, also has a wide host spectrum, but has not yet been reported in cats (see addendum). On 28 November 2022 the WHO recommended to adopt “mpox” as the new synonym in English for the disease. Mpox should become a preferred term, replacing monkeypox, after a transition period of one year (WHO 28-11-2022).

Agent properties

Poxviruses are amongst the largest animal viruses. They induce “viroplasma” zones in the cytoplasm of infected cells, which appear as inclusion bodies by light microscopy. The *Orthopoxvirus* genus (subfamily *Chordopoxvirinae*) includes, amongst others, the species variola (smallpox) virus, with humans as the only susceptible hosts, and cowpox virus, the most important poxvirus in cats. A fatal infection of a cat with another *Orthopoxvirus*, distantly related to cowpox virus, and more closely related to ectromelia virus, was reported by Lanave et al. (2018). The monkeypox virus is also a member of this genus, which has a wide host spectrum, but it has not yet been reported in cats (see addendum).

The enveloped poxvirus is rather resistant to physical effects but very susceptible to chemical inactivation. Therefore, poxviruses can persist in the environment for a long time, if they are not exposed to any chemical treatment. So protected viral infectivity can be maintained for months. For disinfection, almost all disinfectants are efficacious. Alcohol, sodium hydroxide solution, sodium hypochlorite, quaternary ammonium compounds, chloramine T, iodine, as well as detergents (sodium deoxycholate, Nonidet P40) and in general all disinfectants which were tested for their efficacy (such as DVG-listed or VAH-listed commercial products) are recommended. It is important to clean the surface to be disinfected thoroughly before applying the disinfectant, as in the dry scabs the virion is covered and protected by proteins from crust material (Gaskell et al., 1987). Heating to >80°C leads to rapid inactivation.

Epidemiology

Poxviruses are ubiquitous amongst mammals. “Cowpox” is a misnomer, the virus occurs as an inapparent infection predominantly in small rodents, which are considered the natural reservoir (Bennett and Baxby, 1996). The host spectrum is wide. In addition to bovines, infections have been seen in exotic felids (after having been fed laboratory rats), anteaters, elephants, rhinoceroses, okapis and cheetahs in zoos in Europe (Marennikova et al., 1977; Baxby et al., 1982).

In domestic cats, the infection occurs sporadically, usually after contact with rodents, frequently in late summer to autumn. Rosone et al. (2021) performed a sero-epidemiolocal study in stray cats in the region of Rome and also in different wild and exotic felids in Central Italy and did not find evidence for *Orthopoxvirus* infections. However, in Germany in areas with previous reports of cowpox virus infections in cats 17% of outdoor cats exhibited antibodies against *Orthopoxviruses* (Appl et al., 2013). Transmission between cats has been reported rarely (Bennett and Baxby, 1996; Appl et al., 2013).

Pathogenesis and immunity

After local replication at the site of infection, the virus causes a generalised infection with viraemic spread and multiple skin lesions. Virus has been isolated from the thoracic and peritoneal cavities.

Neutralising and haemagglutination-inhibiting antibodies appear approximately two weeks after infection.

Clinical signs

In most cases, contacts with wild rodents (rats) or hunting are reported anamnestically. Infection usually starts with head lesions inflicted by the struggling rodent and then spreads to other body parts, notably paws and ears (Fig. 1) following viraemia and during grooming. Focal or multifocal crusting dermatitis develops (Fig. 2) with possible spontaneous cure. However, often itching and poorly resolving ulcers (diameter 3 – 15 mm) with hard margins are noted (Gaskell et al., 1987). Lesions are predominantly found on the face and paws; in severe cases, progressive proliferative deep ulcerations ensue. The animals appear healthy if lesions are not superinfected by bacteria, but Appl et al. (2013) also reported lymphadenopathy, inappetence, lethargy, pyrexia and respiratory signs in some cats.

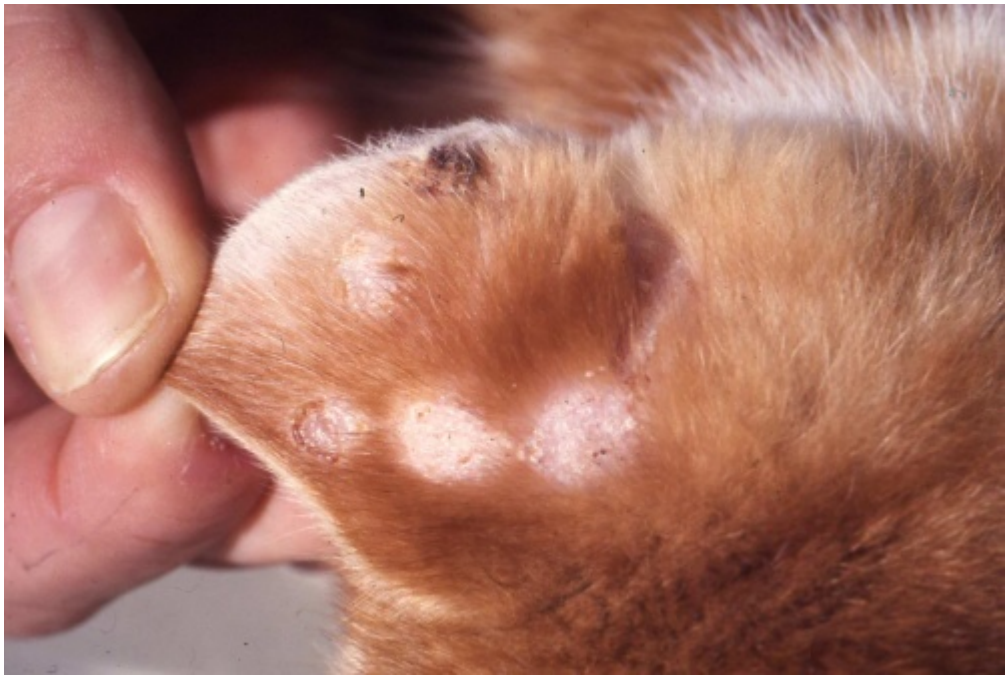

Fig. 1. Cowpox virus induced lesions. Note: gloves should be worn when examining a cat with suspected cowpox! © Marian C. Horzinek

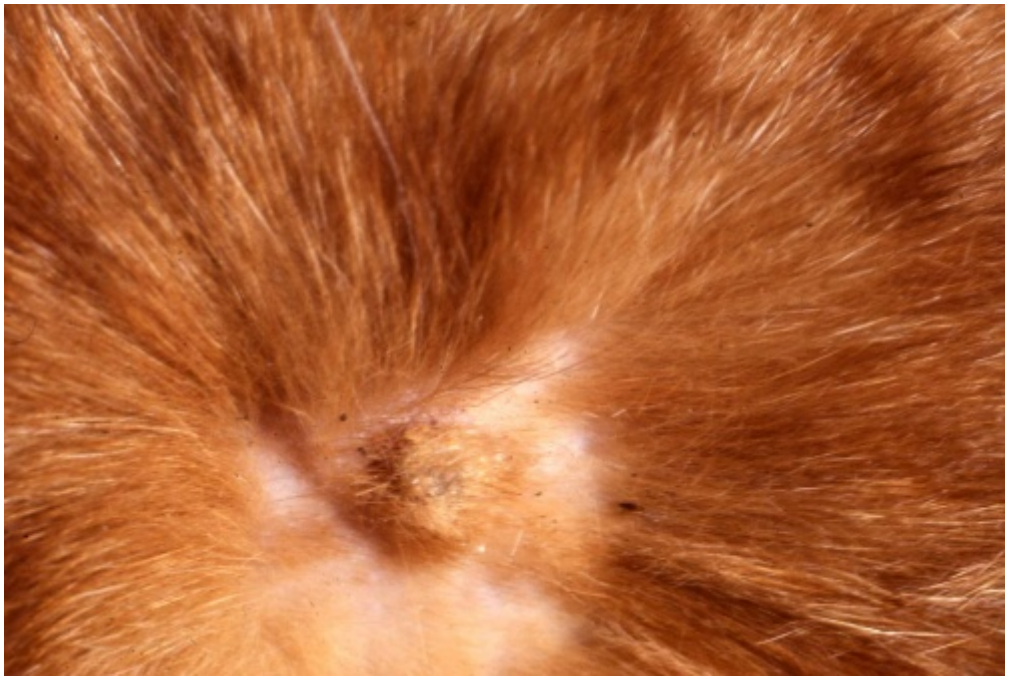

Fig. 2. Skin lesions covered by crusts. (C) Marian C. Horzinek

Ludwig et al. (2016) reported a case of ulcerative pododermatitis and disseminated erosive lesions on a forelimb of an 11-year-old cat. The affected forelimb presented painful and severe erythematous swelling with an ulcerated, sanguineous and purulent palmar surface. Before diagnosis of cowpox virus infection by PCR, unsuccessful antibiotic and anti-inflammatory treatment had been performed. The cowpox virus detected was sequenced and clustered with other European isolates.

Sometimes the mucosae of the pharynx and oesophagus are affected. Pneumonia, at times with exudative pleuritis and atelectasis, has been described (Schöniger et al., 2007; Schulze et al., 2007; Herder et al., 2011). McInerney et al. (2015) reported five cases of pneumonia, of which three had pleural effusions and two had mixed infections (feline herpesvirus, *Bordetella bronchiseptica* and *Mycoplasma* spp). Four cats also presented with skin lesions.

Smith and Sloan (2017) described a fatal necrotising bronchopneumonia in a 2.5-year-old cat that exhibited fever, dyspnoea and tachypnoea, but did not show any skin lesions. This case shows the importance to consider cowpox virus infection in cats with bronchopneumonia, especially if lung lobe consolidation is observed, even in the absence of skin lesions.

Breheny et al. (2017) reported two unusual cases of cowpox virus infection. The first presented with inspiratory dyspnoea and stridor; laryngeal oedema and a 1 cm paralaryngeal mass were identified (without any other abnormalities). The second case displayed non-specific clinical signs, multiple nodular lesions and ulcerations, and central neurological signs at the terminal stage.

Another case of unusual clinical presentation and atypical morphological manifestation of cowpox virus infection was reported by Jungwirth et al. (2018) in Germany. Five cats that presented within 4 weeks to the same veterinary clinic displayed lameness and skin lesions affecting the hindlimbs, with severe oedematous, hyperaemic swellings as well as plaque-like lesions or erosions. Typical pox lesions of the forelimbs or head were lacking or sparse. Cowpox virus infection was confirmed in all five cats and gene sequences in four of them were identical, which could indicate hospital-acquired transmission.

Diagnosis

Biopsies from skin lesions or dried scab material (without transport medium) are used for diagnosis. Cells from biopsy material, taken from the marginal zones of inflammation contain homogeneously dense, intracytoplasmic eosinophilic bodies.

Polymerase chain reaction is the main method used for detection of cowpox viral DNA and allows also subsequent genetic and phylogenetic analyses.

For virus isolation (using embryonated eggs or cell culture) scab material can be shipped dry (cooling is not necessary) or small quantities of exudate can be dried onto cover slips for shipping to the laboratory. McInerney et al. (2015) isolated cowpox virus from

bronchoalveolar lavage fluid, oropharyngeal swabs or pleural fluid from cats with pneumonia. They also found typical inclusion bodies in fine needle aspirates from the lung.

Using negative-stain electron microscopy, evidence of brick-shaped virions is sufficient for diagnosis (Fig. 3).

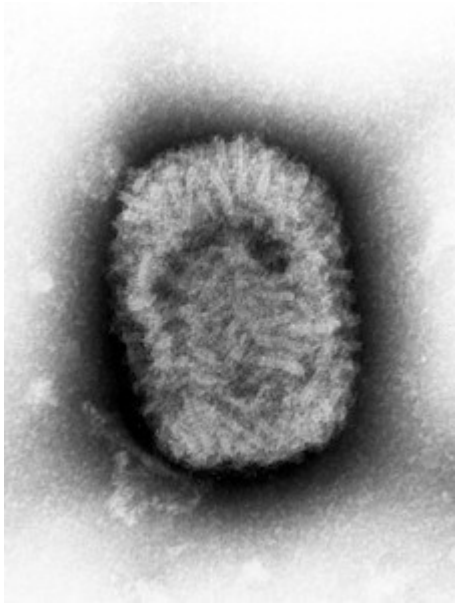

Fig. 3. Negatively stained orthopox virion; surface structure and brick-shaped outline are diagnostic. Courtesy Fred A. Murphy

Paired serum samples can be used for retrospective diagnosis. Evidence of increasing titres of antibodies in paired serum samples (seroconversion) from animals with characteristic lesions is strongly indicative of recent infection (Gaskell et al., 1987).

Treatment

To prevent secondary bacterial infections, therapy should focus on cleaning and treating the ulcerated areas and broad-spectrum antibiotics may be needed if there is evidence of bacterial infection, as well as general supportive therapy. The use of corticosteroids must be avoided (Gaskell et al., 1983; 1987). McInerney et al. (2015) reported improvement of the condition after treatment with interferon omega in two of four cats with pneumonia. Further studies, including control groups, are needed to confirm the effectiveness of interferon omega therapy.

Prognosis

The prognosis is good, as solitary superficial lesions usually heal spontaneously within 4 to 5 weeks in well-fed animals (Gaskell et al., 1987). It is poor in kittens, cats undergoing treatment with corticosteroids, cats with systemic immunosuppression, e.g., due to feline immunodeficiency virus infection, and generally when the lungs are affected. In these cases, severe generalised cowpox infections with even fatal outcome occur (Brown et al., 1989).

Vaccination

There are no vaccines available for use in animals.

Zoonotic risk

Cowpox is a zoonosis. Human cases caused by cowpox virus transmitted from cats (e.g., Willemse and Egberink, 1985; Van Reempts et al., 2022) and from pet rats (e.g., in France and Germany; Ninove et al., 2009; Vogel et al., 2012) have been reported. In most cases

skin lesions surrounded by oedema and erythema, as well as local lymphadenopathy, occurred in the people although a fatal outcome can occur in immunosuppressed individuals (Czerny et al., 1991). Cases of rare ocular infections resulting in severe conjunctival necrosis and marked orbital inflammation (Kiernan and Koutroumanos, 2021) and necrosis of the upper eyelid, keratitis and leucomatous opacity (Krankowska et al., 2021), respectively have been reported.

Owners of affected cats and pet rats must be alerted of the zoonotic risk. When handling cats suspected to be infected with cowpox virus (suggestive skin disease) it is important that the veterinary staff observes good infection control, taking protective measures such as wearing protective gloves and adopting proper hand hygiene, as cases were reported in veterinary assistants (Bonnekoh et al., 2008; Eder et al., 2017; Dugan, 2019) and students (Glatz et al., 2010). Animal sources of cowpox virus infection for humans must be kept in mind, especially as human populations are now vulnerable since the discontinuation of smallpox vaccination (Willemse and Egberink, 1985; Eder et al., 2017).

Addendum: Monkeypox virus

Monkeypox virus received careful attention because of its recent spread in the human population. It is a member of the same genus but is distinct from cowpox virus. Monkeypox virus was first detected in lab monkeys (Von Magnus et al., 1959) and is endemic in Central and West Africa. It has a wide host spectrum that includes humans, as well as various rodents, squirrels, non-human primates, prairie dogs, pigs, rabbits and other species. The US Centers for Disease Control and Prevention (CDC) state that all mammals should be considered susceptible to monkeypox virus as a precaution, but that it is unknown whether cats can be infected (CDC, 2022). The natural reservoir has not been confirmed, but rodents seem the most likely species. Monkeypox is a zoonosis, which can be transmitted from animals to humans. In May 2022, there was an unexpected finding, with many cases of human monkeypox virus infections being reported in non-endemic areas (Europe, North America, South America, Asia, Australia), as a result of virus being transmitted between humans. It is not known at present (December 2022) whether infected owners could transmit the virus to their pets, but it is important to evaluate the risk that pets (including cats) that are exposed to monkeypox virus could become infected and then transmit infection to humans, such as their owners or veterinarians. The risk is considered small following a qualitative assessment by the Human Animal Infections Risk Surveillance (HAIRS) group, but it cannot be excluded (HAIRS group, 2022). As of May 23, 2022 the European Centre for Disease Prevention and Control (ECDC) reported that the European Food Safety Authority (EFSA) was not aware of any reports of infections in animals (pets or wild animals) in the EU (ECDC, 2022). Shepherd et al. (2022) reported results of a surveillance of 154 dogs/cats from households with confirmed human cases of monkeypox virus infection during the time period from June to mid-September 2022 in the UK. No animals with clinical signs of monkeypox were reported. However, on August 10, 2022 a case of a human-to-dog transmission was reported in France (Seang et al., 2022), although Sykes (2022) considered that there was insufficient evidence that the dog was infected with monkeypox virus. There was no serological response that would have confirmed infection, and it was argued that contaminating DNA could have been detected causing a positive test result.

To reduce any risks of cross-species transmission as far as possible, in cases of monkeypox virus infection, contact between humans and pets should be reduced (Weese, 2022) and the usual hygienic measures should be taken. In case of suspected monkeypox virus infection in humans or animals, human and veterinary medical advice should be sought, respectively.

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