

CASE REPORT

Cowpox virus infection in a child after contact with a domestic cat: a case report

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SUMMARY

Human cowpox represents a seldom diagnosed zoonosis but this diagnosis should be considered more frequently as the number of cases has increased in recent years. We describe a case of cowpox in an 11-year-old boy following regular direct daily contact with a domestic cat. The 11-year-old patient, an otherwise healthy boy, demonstrated skin ulceration located at his chin, with enlargement of regional lymph nodes and fever reaching 39°C. The diagnosis of cowpox was made on the basis of PCR involving DNA isolated from a scab covering the skin lesion.

Application of PCR involving DNA isolated from the scab covering the lesion with parallel use of OPXV-specific (ORF F4L) and CPXV-specific (ORF B9R) oligonucleotide primer sequences is recommended for rapid laboratory confirmation of the diagnosis.

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INTRODUCTION

According to the current taxonomy, cowpox virus (CPXV) is a member of the genus Orthopoxvirus (OPXV) in the subfamily Chordopoxvirinae of the Poxviridae family. Viruses of the family manifest a linear double-stranded DNA genome and a complex virion structure (Gubser *et al.*, 2004). Except for variola virus (VARV), representing an obligatory human pathogen, the natural reservoir of orthopoxviruses involves animals (vertebrates) (McFadden, 2005). Wild rodents, especially voles and wood mice, are considered to provide a natural reservoir of CPXV, and its transmission to humans is mediated mostly by direct contact with domestic cats but also with pet rats (Baxby *et al.*, 1994; Baxby *et al.*, 1997; Campe *et al.*, 2009; Ninove *et al.*, 2009). Moreover, recent data indicate that the spread of CPXV in the animal population may be promoted by indirect transmission through virus-infected food production animals (Reperant *et al.*, 2016).

Human cowpox represents a seldom diagnosed zoonosis so awareness of its manifestations should be improved among physicians. Therefore, publication of single cases can provide important illustrative information on the disease, the clinical pattern and laboratory diagnosis.

CASE REPORT

The patient was a 11-year-old boy with no significant medical history, admitted to the Department of Dermatology,

Poznań University of Medical Sciences in the first days of November, 2015 due to a skin lesion located at the chin, with enlargement of the surrounding lymph nodes and fever. Two weeks earlier, he had noticed a single red, infiltrating nodule on his chin. During the next two weeks the boy manifested a subfebrile condition (his body temperature ranged between 37 and 37.5°C) and flu-like symptoms. In the period the lesion evolved into necrotic ulcer of 2 cm in size, with an undermined, roller-shaped margin, surrounded by satellite papule and an erythematous infiltrated area. The ulcer was covered by a developing thin black scab (*Figure 1*). The lesion was painless. Submental, submandibular and cervical lymph nodes were enlarged and painful but no additional systemic features developed. Before hospitalization the patient was subjected to therapy with the amoxicillin/clavulanate, but no improvement followed. On the day of admission to our Department, fever in the patient reached 39°C and in the few subsequent days it ranged between 37° and 38.5°C. Treatment with co-trimoxazole was followed by complete scab detachment.

The patient had no history of tick bite or any other skin injury in the affected region. Nevertheless, for a few months the boy maintained direct, regular contact with a house cat, which he pressed against his chin. In addition, over a week before the boy manifested morbid symptoms his parents detected a small, suppurative lesion on head skin of the cat. The observed skin lesion caused isolation of the cat in a closet, from which the animal escaped and was not found.

Laboratory investigations revealed a white blood cell count of 7,400 cells/μl with moderate monocytosis (14.2%), normal C-reactive protein (<5 mg/l), as well as procalcitonin (<0.5 ng/ml), normal results of electrolytes, coagulation tests and liver function tests. Material from smears sampled from the ulceration was analyzed in di-

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Figure 1 - 11-year-old boy with cowpox lesion. An ulcerated inflammatory lesion located on the chin after direct contact with a domestic cat. A) Note the black scab on the top of the lesion. B) Skin lesion after scab detachment.

rect preparations stained according to Gram and using a culture. In the direct preparations no Gram-stained bacilli were seen. Results of bacterial culture, including *Bacillus anthracis*, were all negative. Two punch biopsies were taken from the rim of the ulcer for histological studies by light microscopy. Haematoxylin and eosin (H&E)-stained sections showed a full thickness necrosis of the epidermis and dermis. The necrotic epithelial structures contained a single to multiple eosinophilic intracytoplasmic inclusion bodies (Figure 2). In addition, using Warthin-Starry's silver staining no bacterial presence could be demonstrated in the sampled material. In order to perform PCR, DNA was isolated from the scab covering the lesion using Swab kit (A&A Biotechnology). *Bartonella henselae*-specific PCR, targeted on riboflavin synthase gene was negative. For detection of CPXV PCR test was performed according to Shchelkunov *et al.* (2005) with parallel use of OPXV-specific (ORF F4L) and CPXV-specific (ORF B9R) oligonucleotide primer sequences. The result permitted us to rapidly and reliably diagnose human cowpox.

In the second week of hospital stay an improvement was noted; the temperature was normal, the rash disappeared, the enlargement of lymph nodes was reduced. However,

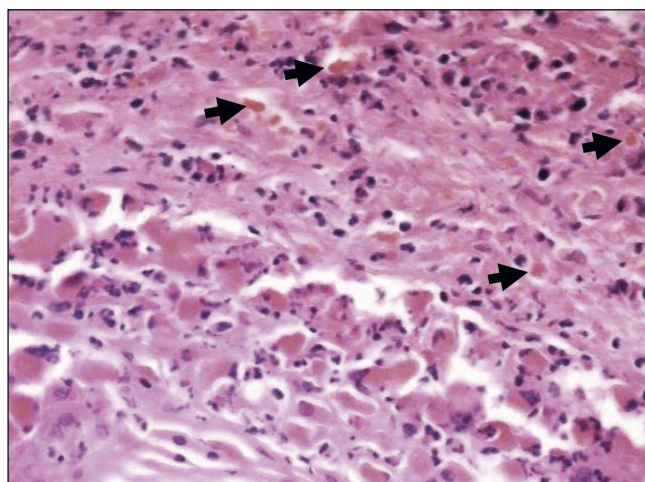


Figure 2 - Morphology of the skin lesion. Necrosis of the epithelial structures with visible eosinophilic intracytoplasmic inclusion bodies, characteristic of poxviral infections (H&E).

a complete recovery with total regression of lymph node enlargement and skin ulceration healing was observed within two months.

DISCUSSION

The presented case of a localized skin lesion accompanied by lymphadenopathy in a young boy and his regular direct contact with a house cat justified suspicion of zoonosis, mainly cat-scratch disease (CSD), cutaneous anthrax (CA) or cowpox (CPX).

It is well known that cat saliva may transmit *B. henselae*, the bacterial species causing CSD. The species, thought to represent a re-emerging human and veterinary pathogen, is widespread all over the world. In Poland it is manifested in over 10% cats (Podsiadly *et al.*, 2007). Nevertheless, in skin lesions histology failed to demonstrate CSD granulomas with typical Langhans giant cells. Also in sections stained with the Warthin-Starry's silver impregnation such bacteria could not be visualized (Rolain *et al.*, 2006). In addition no DNA of *B. henselae* could be demonstrated. Thus, results of the studies conducted ruled out the suspicion of CSD.

In turn, anthrax is induced by another bacterial species, *Bacillus anthracis*, producing highly resistant endospores, which in the natural environment, mainly in the soil, may remain infective for years (Mock *et al.*, 2001). Anthrax of animals is manifested throughout the world, and has been sporadically detected in the past 30 years in Poland (Mizak, 2004; Sadkowska-Todys *et al.*, 2015). Considering the clinical signs manifested in the presented case, a diagnosis of CA had to be considered (Lewis-Jones *et al.*, 1993). Infection of the boy could follow direct contact with the cat's fur contaminated with soil containing *B. anthracis* endospores. Negative results of bacteriological studies ruled out the suspicion of CA in the patient.

Human cowpox is a viral zoonosis, induced by CPXV, acquired after direct skin contact with infected animals. In cats, infections seem to be increasingly frequent (Chantrey *et al.*, 1999), and may be linked to climatic alterations and also to the increase in the rodent burden (Hobi *et al.*, 2015). Early diagnosis is essential for differentiating cowpox lesion from skin reactions with similar signs and symptoms, such as drug-associated eruption, secondary syphilis, scabies, insect bite, impetigo, and molluscum contagiosum. The grounds for diagnosis of the disease in

the present case was provided by detection of DNA CPXV in the analyzed samples of the scab isolated from skin lesions, using genus- and species-specific PCR. PCR assay with no additional procedures (endonuclease digestion) identified CPXV and thus this approach is simpler than other PCR methods for detection of CPXV and easier in interpretation of the obtained results. A variety of diagnostic strategies are available for detection of orthopoxviruses. However, in clinical practice rapid, direct identification tests are significant and, therefore, electron microscopy and PCR techniques are particularly suitable in diagnosis of orthopoxviruses infections (Kurth *et al.*, 2007). Negative stain electron microscopy allows for a rapid detection of poxvirus virions, providing clinically and epidemiologically important information. However, this technique provides no ground for determination of genus and specificity of human-pathogenic viruses from Poxviridae family (Kurth *et al.*, 2007). Therefore, early diagnosis of orthopoxvirus infections involves genus- and species-specific PCR test (Shchelkunov *et al.*, 2005; Kurth *et al.*, 2011). For a rapid confirmation of the diagnosis detection of species-specific antigen for orthopoxviruses might be particularly suitable (Schulze *et al.*, 2007). However, potential for serological studies is significantly restricted due to the lack of commercial diagnostic tests for detection of ortho/ cowpox infection. In turn, results obtained using home-made tests may be unreliable. Currently, it is well known that viruses of Orthopoxvirus genus are genetically and antigenically strictly related to each other, with a resulting pronounced immunological cross-reactivity (Kennedy *et al.*, 2009). Therefore, Jenner's vaccines, containing the first CPXV and, subsequently, vaccinia virus (VACV), after nearly two centuries of their prophylactic use resulted in 1977 in the successful world eradication of smallpox, the common and highly lethal disease induced by VARV (Fenner *et al.*, 1988). Therefore, beginning in 1980 a discontinuation started of the population-based vaccination programs. In turn, 20 years later the number of reported cases of human cowpox, particularly in children and adolescents has begun to increase (Wolfs *et al.*, 2002; Glatz *et al.*, 2010; Favier *et al.*, 2011; Ducournau *et al.*, 2013; Śżiujz *et al.*, 2015). The presented data indicate that the risk of CPXV infection has increased since the cessation of smallpox vaccination and the consequent decrease in orthopoxvirus immunity. Such a conclusion seems to be confirmed also by observation on smallpox-vaccinated people who, despite close contact with infected cats, showed no evidence of poxvirus disease (Bennett *et al.*, 1986). Human cowpox is clinically manifested as a localized dermal lesion with local lymphadenopathy, healing in 6-8 weeks but severe cases may take up to 12 weeks to heal (Baxby *et al.*, 1997). In immunodeficient individuals development of fatal generalized infection has also been described (Czerny *et al.*, 1991; Gazzani *et al.* 2016). In view of the present data, human CPXV infection represents a zoonotic, re-emerging disease, which should be covered by epidemiological supervision. Thus, this report described a clinical case of human cowpox, discussing diagnostic difficulties and indicating the significance of species-specific PCR in rapid diagnosis of the zoonosis.

Conflict of interest to declare

None.

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