Proliferative necrotizing otitis externa in two young cats

Proliferatieve en necrotiserende otitis externa bij twee jonge katten

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ABSTRACT

In this paper, proliferative necrotizing otitis externa is described in two young cats. The lesions were characterized by proliferative, erosive to ulcerative dermatitis with necrosis affecting the medial aspect of the pinna, the entrance of the ear canal and the periaural skin of both ears. The lesions developed rapidly and were covered by adherent crusts.

Histopathology of the lesions was characterized by severe epidermal hyperplasia, with parakeratotic hyperkeratosis, scattered apoptotic keratinocytes in the epidermis and superficial hair follicle epithelium, and serocellular crusts. In both cases, regression of the lesions appeared after systemic and topical immunomodulatory therapy.

SAMENVATTING

In dit artikel wordt proliferatieve necrotiserende otitis externa beschreven bij twee jonge katten. De symptomen werden gekenmerkt door proliferatieve, erosieve, ulceratieve dermatitis met necrose van de gehoorgang en de periaurale huid van beide oren. Histopathologisch was ernstige epidermale hyperplasie aanwezig, met parakeratotische hyperkeratose en verspreid aanwezige apoptotische keratinocyten in de epidermis en het oppervlakkige deel van de haarfollikels, met korstvorming. In beide gevallen verdwenen de laesies na behandeling met systemische en topicale immuunmodulerende therapie.

INTRODUCTION

Proliferative necrotizing otitis externa (PNOE) is a rare condition in young cats and was first described in 1998 as a disease affecting kittens between two and six months of age (Power, 1998). Since then, PNOE has been scarcely reported in the literature (Gross, 2005; Mauldin, 2007; Stevens and Lindner, 2012; Noli et al., 2020; Panzuti, 2021). It has been demonstrated to affect cats from two months to fourteen years of age, and mostly occurring at the age of four (Muller-Kirk, 2013; Momota et al., 2017). In a case series by Muller-Kirk (2013), males appeared to be predisposed. The disorder is characterized by plaque-like proliferative lesions of the upper part of the vertical ear canal and the lower medial part of the pinna. The proliferative lesions occlude the ear canal in most cases, causing otoscopic examination to be seldom possible. Necrosis and secondary infection can cause a striking odor, and occasionally, purulent discharge is seen. In two similar reports, extra-auricular lesions of the eyelids, the face, the abdomen, axilla and groin were described (MacAuliffe, 2020; Panzuti, 2021). Up till now, the pathogenesis is not well understood. Lesions exhibit T-cell-mediated keratinocyte apoptosis (Vidémont et al., 2010). In cases without spontaneous regression, immunomodulating medication, such as corticosteroids, ciclosporine and tacrolimus have been used (Mauldin, 2007; Momota, 2017; Panzuti, 2021) .

CASE DESCRIPTIONS

Case 1

A six-month-old, castrated, male domestic shorthair cat developed erythematous, well-circumscribed

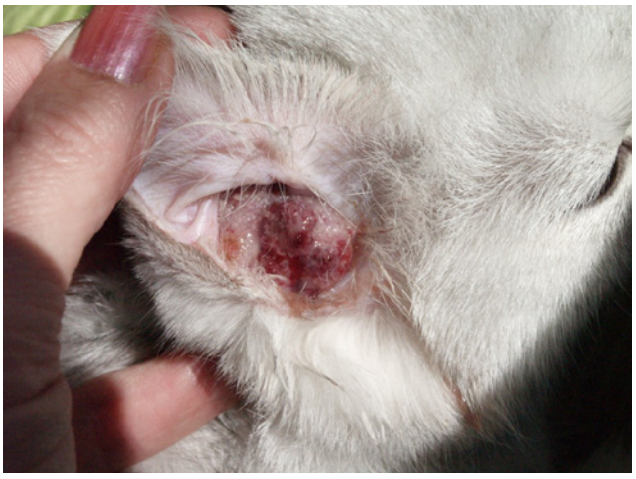

Figure 1. Proliferative lesions of the external ear canal and pinna (case 1).

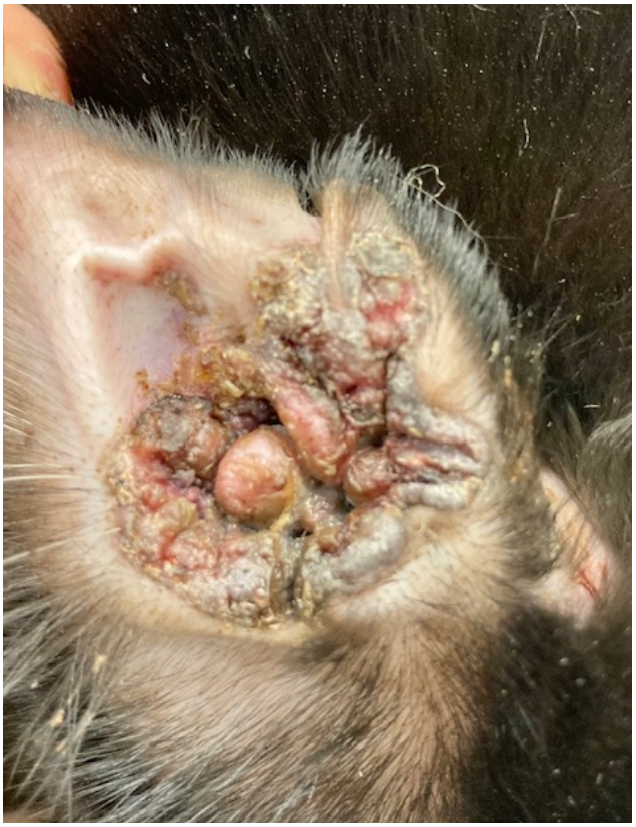

Figure 2. Proliferative and necrotizing lesions of the external ear canal and pinna, with necrotic debris and exudate (case 2).

bilateral proliferative lesions of the medial basis of the pinna and the entrance of the ear canal, with crusts and some yellow exudate (Figure 1). The owner had first noticed the lesions approximately ten days before presentation. The cat was otherwise healthy, received no medication and had routinely been vaccinated at nine and twelve weeks of age against panleukopenia-virus, feline herpes and calicivirus. The referring veterinarian prescribed dexamethasone (Dexacortone®, LeVet/Dechra, Oudewater, the Netherlands) 0.1 mg/kg/day during four days prior to referral. No other skin lesions were present and the cat was otherwise healthy. At examination, the cat was sedated, and samples were taken for histopathology (three punch biopsies of 4 mm) and bacterial culture. While waiting for the lab results, the dexamethasone treatment was continued at a higher dosage (0.2 mg/kg/day) and a ciclosporine ointment (Optimmune®, MSD/Intervet, Boxmeer, the Netherlands) was prescribed for topical treatment.

The bacterial culture revealed many *Pasteurella* multocida and a mixed culture of three other bacterial species. The *Pasteurella* strain was susceptible to all ten tested antibiotics. No yeasts or fungi were cultured.

Fifteen days after the examination, the lesions had nearly completely disappeared. The cat had eventually only been treated with oral dexametheasone, because the prescribed topical ointment was not used by the owners. The pruritus and foul-smelling suppurative discharge had resolved. No relapse was seen at least six months after the diagnosis.

Case 2

A five-months-old, female British Shorthair kitten with extensive soft tissue proliferation in both external ear canals was referred for surgical treatment (total ear canal ablation). The owner, who had owned the cat for two months by then, first noted the proliferative lesions two weeks prior to referral. Mild pruritus and a suspected deafness were noticed by the owner. There were no signs of rhinitis or other upper respiratory diseases. The cat had routinely been vaccinated like the cat in case 1 and did not receive medication. The siblings of the kitten (one male and one female) did not show abnormalities.

On clinical examination, the kitten appeared in good health. Deafness could not be excluded but was difficult to investigate. The entrance of both ear canals was occluded by irregular, erythematous plaques (Figure 2). Samples for bacterial culture and two 4 mm-punch biopsies for histopathological examination were taken. Following the biopsy, the animal was treated with 12.5 mg/kg twice a day amoxycillin-clavulanic acid (Synulox®, Zoetis, Capelle aan de IJssel, the Netherlands) for ten days.

The bacterial culture revealed coagulase negative *Staphylococcus sp*. and a mixed culture of two other bacterial species. No yeasts or fungi were cultured. The *Staphylococcus* strain was susceptible to all ten tested antibiotics including amoxycillin-clavulanic acid.

Ten days after examination, the diagnosis of PNOE was made and based on the clinical features and the histopathological results. Topical application of ciclosporine ointment (Optimune ®, MSD/Intervet, Boxmeer, the Netherlands) three times a day was started as initial therapy. As no improvement had occurred after two weeks, systemic ciclosporine treatment was started (5 mg/kg/day, Sporimune ®, AST/

Dechra, Oudewater, the Netherlands) and continued for three weeks. The lesions quickly regressed and clinically resolved within a week after starting the oral therapy. No side effects occurred. The mild pruritus disappeared. After five months, mild recurrence was observed, characterized by pruritus and mild proliferative lesions. Oral ciclosporine was prescribed again at the same dose for five days. The clinical signs quickly resolved once more, and no further recurrence was observed in the following years. The possible symptoms of deafness had vanished. The cat had a litter two years later; the kittens did not show any symptoms of PNOE. As the histopathology slide of the skin biopsies was not available anymore, only the histopathology report could be used.

HISTOPATHOLOGY

Histopathological examination of the aural plaques in both cases showed similar histopathological features pathognomonic for PNOE. Moderate to severe epidermal hyperplasia due to acanthosis with orthokeratotic to parakeratotic keratosis involving both the epidermis and the infundibular part of the hair follicles was present. Serocellular crusts containing keratin, nuclear debris, neutrophils and occasional bacteria were present at the surface in case 1 (Figures 3 and 4), comparable with the described superficial exudative inflammation in the histopathology report of case 2. In the epidermis and upper hair follicle epithelium, scattered to locally confluent hypereosinophilic shrunken keratinocytes with karyopyknosis were present in both cases, consistent with apoptosis (Figures 5 and 6). The apoptotic keratinocytes were present at different levels of the epidermis, but mainly adjacent to the epidermal keratin layer or surrounding the follicular lumen. Satellitosis (lymphocytes encircling apoptotic keratinocytes) was absent. The keratinocytes showed intracellular edema characterized by swelling and cytoplasmic pallor (not shown); mild exocytosis of neutrophils into the epidermis and hair follicle epithelium (Figures 5 and 6). In the superficial dermis, increased numbers of mast cells, eosinophils and neutrophils were present, with fewer lymphocytes, plasma cells, macrophages in the second case. A Periodic Acid-Schiff (PASS) stain did not reveal any fungi, yeast or mites in both cases.

DISCUSSION

Proliferative necrotizing otitis externa is a highly characteristic disease of uncertain etiology predominantly affecting kittens, but also occurs in adult cats. The clinical features, macroscopical and histopathological findings in the two cases presented here were consistent with PNOE, and match previous descriptions in the literature.

The clinical features are characterized by striking, tightly adherent serocellular crusts affecting the medial pinna and external ear canal, with a tendence to bilateral symmetry. The crusts are often golden to dark brown, reflecting the marked hyperkeratosis, parakeratosis and variable exudative inflammation. Both cases showed dramatic proliferative lesions in the external ear canal and pinnae, but only the lesions in case 1 were yellow-brown; the lesions in case 2 were pale white to pink with hemorrhage. This hemorrhage was present before biopsies were taken.

The pathogenesis is unknown, although in a recent study, a T-cell-mediated keratinocyte apoptosis has been demonstrated (High et al., 2020). The histopathology is characterized by marked epidermal hyperplasia extending to the infundibular part of the hair follicles and scattered to locally confluent shrunken eosinophilic keratinocytes morphologically compatible with

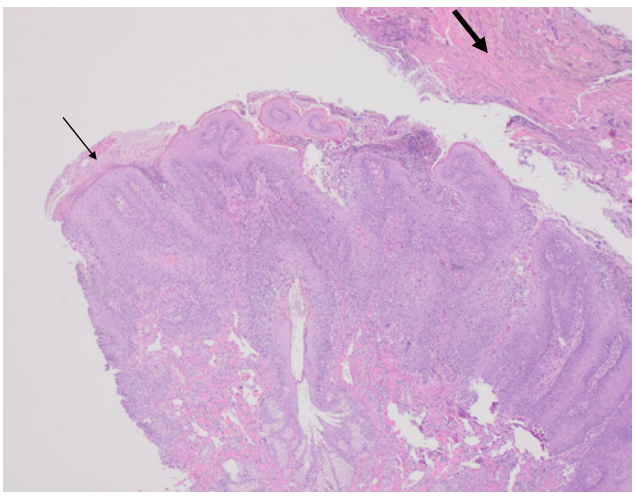

Figure 3. Overview of epidermal hyperplasia, with hyperkeratosis (thin arrow) and formation of a thick crust (broad arrow) containing keratin and nuclear debris (case 1). HE stain, 40x.

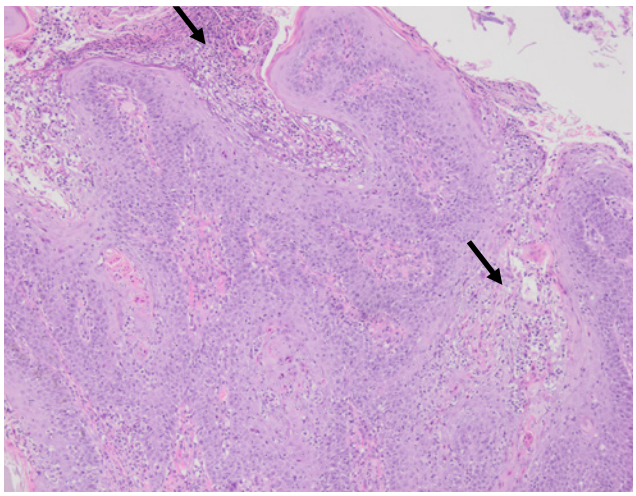

Figure 4. Epidermal hyperplasia due to acanthosis; at the surface and in the lumen of hair follicles, exudate consisting of nuclear debris and neutrophils (arrows) is present (case 1). HE stain, 100x.

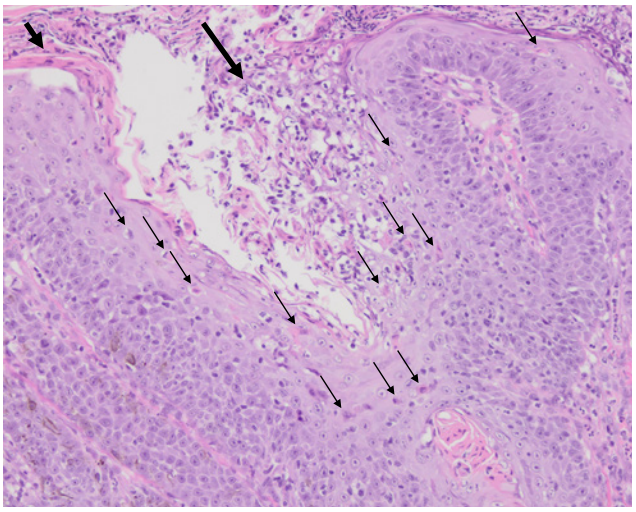

Figure 5. Scattered and occasionally clustered hypereosinophilic keratinocytes with shrunken nuclei within the epidermis and hair follicle epithelium, consistent with apoptosis (thin arrows); parakeratotic hyperkeratosis (short broad arrow) and neutrophilic superficial inflammation (long broad arrow) (case 2). HE stain, 200x.

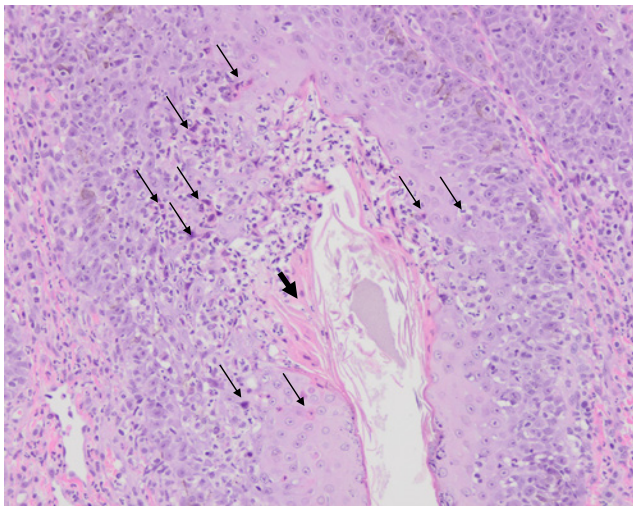

Figure 6. Scattered apoptotic keratinocytes (thin arrows) within the infundibular hair follicle epithelium, with keratosis of the hair follicle epithelium (broad arrow) (case 2). HE stain, 200x.

keratinocyte apoptosis. The histologic appearance resembles hyperkeratotic erythema multiforme in dogs (HKEM), where erosive and hyperkera-totic lesions are linked to analogous cytotoxic attack on keratinocytes by T-cells. Whereas the prognosis of HKEM is rather guarded to poor, that of PNOE is good in all described cases (High et al., 2020).

The absence of satellitosis (lymphocytes encircling apoptotic keratinocytes), the degree of epidermal hyperplasia, neutrophilic crusting and parakeratotic hyperkeratosis as well as the presence of eosinophils in PNOE are not consistent with hyperkeratotic erythema multiforme (Gross, 2005). Furthermore, the condition is clinically and histopathologically striking.

Ciclosporine and/or glucocorticosteroids are known to decrease the lesions and the intensity of pruritus, although not every case resolves with these treatments. Based on the response to ciclosporin, corticosteroids and tacrolimus, an immune-mediated basis for the disease is likely. Both cyclosporine and tacrolimus act via very similar mechanisms to suppress T-cell activation. It has been reported that the condition spontaneously resolves in many cases. However, this may take for over twelve months. Treatment that aids the resolution of the clinical condition is beneficial, especially as secondary bacterial infection can occur. (Mauldin, 2007; Momota, 2017; Noli, 2020; Panzuti, 2021).

Spontaneous regression cannot be completely excluded in the present cases; however, the partial recurrence and quick clinical response to ciclosporine in case 2 suggested that the installed therapy had a beneficial effect in controlling the disease.

The fast remission in case 1 was striking. The cat had only received dexamethasone orally for a short period of nineteen days. No antibiotics were used. Both cats were routinely vaccinated against feline panleukopenia virus (FPLV), feline herpes virus (FHV) and feline calicivirus (FCV) at six and nine weeks of age. The feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) status were unknown in both cats. Currently, there is no indication of any infectious cause of the disease. In a study by Kirk-Muller (2001), PCR for feline herpesvirus type 1 was negative in five cats, as was papillomavirus immunohistochemistry in a report by Gross (2005). In hindsight, the use of antibiotics in case 2 was not beneficial nor justified because of the presence of a polybacterial colonization.

CONCLUSION

To conclude, PNOE is a rare disorder mostly seen in young cats. The clinical features are distinctive and the diagnosis is confirmed by histopathology. The prognosis is good; although spontaneous regression may be expected, topical and/or systemic immunosuppressive medication can be beneficial to the resolution and control of the clinical disease.

REFERENCES

Gross T.L., Ihrke P.J., Walder E.J., Affolter V.K. (2005). Necrotizing diseases of the epidermis. In: *Skin Diseases of the Dog and Cat. Clinical and Histopathologic Diagnosis*. Second edition, Blackwell Science, 79-80.

High E.J., Linder K.E., Mamo L.B., Levy B.J., Herrmann I., Bizikova P. (2020). Rapid response of hyperkeratotic

erythema multiforme to oclacitinib in two dogs. *Veterinary Dermatology 31* 330–e86.
MacAuliffe L., Sargent S., Locke E. (2020). Pathology in practice. *Journal of the American Veterinary Medical Association 257*, 287-290.
Mauldin A.E.A., Ness T.A., Goldschmidt M.H. (2007). Proliferative and necrotising otitis externa in four cats. *Veterinary Dermatology 18*, 370-377.
Momota Y., Yasuda J., Arai N., Yamamoto M., Yushimura H. (2017). Contribution of oral triamcinolone to treating proliferative and necrotising otitis externa in a 14-year-old Persian cat. *Journal of Feline Medicine and Surgery Open Reports*, 1-4.
Miller H.M., Griffin C.E., Campbell K.L. (2013). Diseases of eyelids, claws, anal sacs, and ears. In: *Muller and Kirk's Small Animal Dermatology*. Seventh edition, Saunders, p. 748.
Harvey R. (2020). Otitis. In: Noli C., Colombo S. (editors). *Feline Dermatology*. Springer International, Berlin, 175-209.
Panzuti P., Jongh O., Dony M., Vial S., Mosca M., Pin D. (2021). Extra-auricular lesions of proliferative and necrotizing otitis externa in three kittens. *Veterinary Dermatology 32*, 385.
Power H.T. (1998). Newly recognized feline skin diseases. In: *14th Proceedings AAVD/ACVD*, San Antonio, Texas, 27-32.
Stevens B.J., Linder K.E. (2012). Pathology in practice. Proliferative and necrotizing otitis externa. *Journal of the American Veterinary Medical Association 241,* 567-569.
Vidémont E., Pin D. (2010). Proliferative and necrotising otitis in a kitten: first demonstration of T-cell-mediated apoptosis. *Journal Small Animal Practice 51*, 599-603.