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Beneficial effect of oclacitinib in a case of feline pemphigus foliaceus

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Pemphigus foliaceous (PF) is a pustular, immune-mediated skin disease characterised by acantholytic cells and commonly treated with high doses of glucocorticoids. This report describes one case of feline PF successfully controlled using oral oclacitinib, suggesting a possible therapeutic alternative to glucocorticoids in some cases.

Introduction

Pemphigus foliaceous (PF) is the most frequent acantholytic skin disease in cats, and the most common autoimmune skin disease in companion animals.[1] Feline PF is most commonly treated with high doses of glucocorticoids, such as prednisolone, triamcinolone or dexamethasone. These glucocorticoids may be used for monotherapy or in combination with other immunosuppressive drugs.[2,3] However, the chronic use of glucocorticoids poses some risks to cats.[4]

Janus kinase (JAK) inhibitors interfere with the intracellular signalling pathway of JAK-STAT (Signal Transducer and Activator of Transcription) exerting a wide range of anti-inflammatory and immunosuppressive effects. This class of drugs now is being used in alternative therapies for some neoplastic and immune-mediated diseases in human beings and dogs.[5–8] This report describes the successful treatment of a cat with PF, using the JAK inhibitor oclacitinib (Apoquel, Zoetis; Madrid, Spain), which is registered for use in dogs with atopic dermatitis.

Case

A 13-year-old, spayed female domestic short hair cat was presented for evaluation of pruritic, crusting and alopecic dermatitis of six months duration. Lesions affected the haired skin of the dorsal muzzle, haired skin of the face, periocular area, both pinnae, extremities and periungual areas (Figure 1). Oral and injectable (repositol) glucocorticoids had been used already, with poor response (unknown doses and specific drugs).

An initial dermatological differential diagnosis was proposed: hypersensitivity dermatitis, dermatophytosis, pemphigus foliaceus, sebaceous adenitis, *Malassezia* dermatitis, demodicosis, paraneoplastic dermatitis, infiltrative skin tumour or viral dermatitis.

Wood's lamp examination, superficial and deep skin scrapings, trichoscopy and cytological examination of skin impression smears were performed (Table S1). Four 6 mm punch biopsy samples of lesional areas were acquired under local anaesthesia with 2% lidocaine S. C. (B-Braun Medical; Barcelona, Spain) and light general

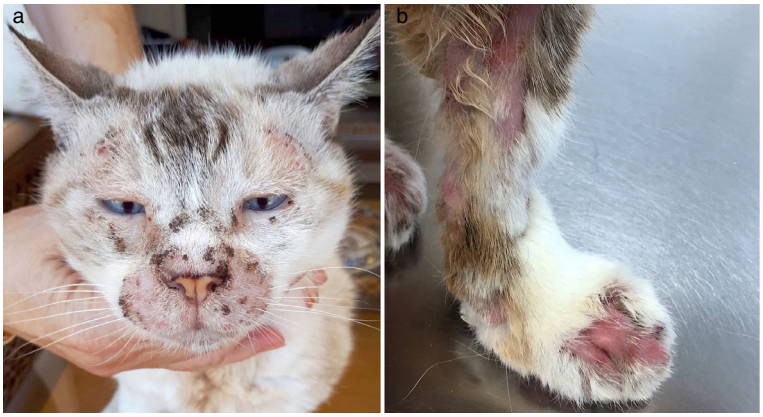

Figure 1. Macroscopic lesions on a domestic short hair cat presenting with dermatitis of six months duration.
Crusting and alopecic dermatitis affected haired skin of the muzzle, face, periocular area, both pinnae (a), extremities and periungual areas (b). Pruritus was severe.

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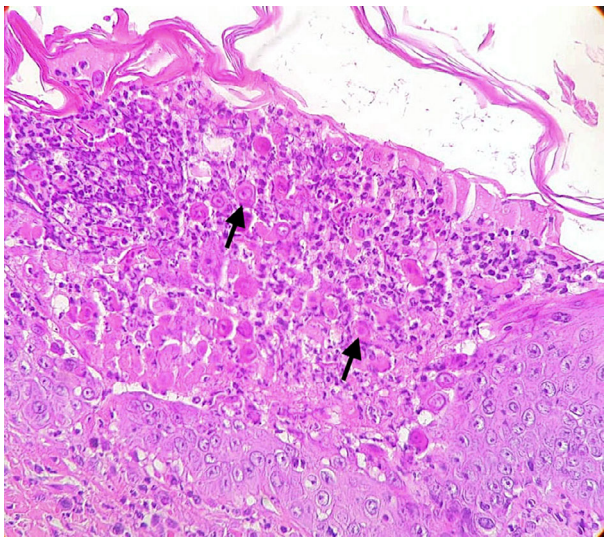

Figure 2. Histopathological evaluation of skin from a cat with crusting and alopecic dermatitis.
Note the subcorneal pustules with abundant acantholytic keratinocytes (black arrow).

sedation with butorphanol 10 mg/mL (Torbugesic, Zoetis), intramuscularly. Histopathological examination revealed subcorneal pustules and serocellular crusts with abundant neutrophils and eosinophils, mixed with acantholytic keratinocytes (Figure 2). Periodic acid Schiff staining was negative for dermatophytes. Chronic kidney disease and cardiac abnormalities were diagnosed in the course of clinical investigations (Table S2). A diagnosis of PF was made, based on history, compatible dermatological signs, exclusion of other compatible diseases and histopathological confirmation.

Owing to the presence of cardiac and renal comorbidities, use of a glucocorticoid for therapy was considered to be a risk to the cat's systemic health. Therefore, treatment with oral oclacitinib (1 mg/kg twice daily) was initiated. After seven days of treatment, >50% decrease in pruritus and severity of lesions were observed (Figure 3). This improvement was maintained during the following weeks, even after the dose was reduced to 0.5 mg/kg twice daily. After six weeks of treatment, the owners stopped the medication without seeking medical advice and the pruritus and skin lesions recurred within 24 h. Clinical signs again improved rapidly when oclacitinib therapy was resumed. No adverse effects related to the treatment were reported.

Discussion

In the present case, clinical signs of PF were quickly controlled with oral oclacitinib. High doses of glucocorticoids (2.0–6.6 mg/kg/day) are used routinely for the treatment of PF in cats, mainly during the induction phase, with a success rate of approximately 97%.[3] However, in cats with comorbidities such as heart disease or diabetes mellitus, the use of glucocorticoids pose greater risks.[4] Alternative drugs such as ciclosporin have been proposed, with longer initial remission times.[3]

Janus kinase inhibitors have been used for treatment of neoplastic and immune-mediated diseases in human medicine.[5] In dogs, the JAK inhibitor oclacitinib has been effective in controlling other immune-mediated diseases, including subepidermal blistering dermatoses, ischaemic dermatopathy and hyperkeratotic erythema multiforme.[6–8] The off-label use of oclacitinib in this case was based on these prior reports in other species, and the dose selected was based on a pharmacokinetic study in cats.[9]

Oclacitinib's mechanism of action for successful treatment of this case is unknown. Oclacitinib can modify lymphocyte proliferation and function, and cytokine production [e.g. interleukin (IL)-4 and IL-13].[10] These cytokines are important in B-cell proliferation and maturation and could modify the production of immunoglobulin (Ig)G antibodies, which are known to be involved in the pathogenesis of PF. Recently, the use of drugs interfering with B-cell development and function (tyrosine kinase inhibitors) have shown beneficial effects in some cases of canine PF.[11] Otherwise it can be speculated that some cytokines, decreased by oclacitinib, also could be directly involved in the pathogenesis of PF in cats, as observed in humans.[12]

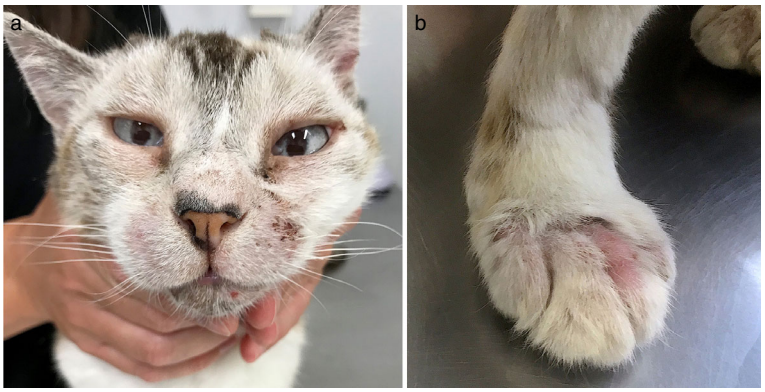

Figure 3. Lesion remission in a cat with crusting and alopecic dermatitis during the first week of treatment.
Note that erythema and crusting lesions improved markedly during this period in comparison to the respective images in Figure 1a,b.

Additional studies of cats with PF will be required to establish the expected efficacy of oclacitinib and its mechanisms of action against this autoimmune disease.

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Supporting Information

Additional Supporting Information may be found in the online version of this article.

Table S1. Results of primary diagnostic tests.

Table S2. Results of general tests performed during the first visit.

Résumé – Le pemphigus foliacé (PF) est une dermatose à médiation immune pustuleuse caractérisée par des cellules acantholytiques et traitée fréquemment par des doses élevées de corticoïdes. Cet article décrit un cas de PF félin contrôlé avec succès par de l'oclacitinib orale, suggérant une alternative thérapeutique possible aux corticoïdes dans certains cas.

RESUMEN – El pénfigo foliáceo (PF) es una enfermedad cutánea pustular, inmunomediada, caracterizada por células acantolíticas y comúnmente tratada con altas dosis de glucocorticoides. Este informe describe un caso de PF El pénfigo foliáceo (PF) es una enfermedad cutánea pustulosa, inmunomediada, caracterizada por células acantolíticas y comúnmente tratada con altas dosis de glucocorticoides. Este informe describe un caso de FP felino controlado con éxito con oclacitinib oral, lo que sugiere una posible alternativa terapéutica a los glucocorticoides en algunos casos. felino controlado con éxito con oclacitinib oral, lo que sugiere una posible alternativa terapéutica a los glucocorticoides en algunos casos.

Zusammenfassung – Pemphigus foliaceus (PF) ist eine pustulöse, immun-mediierte Hauterkrankung, die durch akantholytische Zellen charakterisiert wird und häufig mit hohen Dosen an Glukokortikoiden behandelt wird. Dieser Fallbericht beschreibt den Fall eines felinen PF, der erfolgreich mit Oclacitinib *per os* kontrolliert wurde, was einen Hinweis darauf liefert, dass es sich dabei in manchen Fällen um eine therapeutische Alternative zu Glukokortikoiden handeln könnte.

要約 – 葉状天疱瘡（PF）は、免疫介在性膿疱性皮膚疾患で、棘融解細胞が特徴であり、一般的に高用量のグルココルチコイド製剤で治療される。本報告では、猫PFの1例がオクラシチニブマレイン酸塩の経口投与でコントロールに成功したことを報告しており、症例によってはオクラシチニブマレイン酸塩はグルココルチコイドに代わる治療法である可能性を示唆している。

摘要 — 落叶型天疱疮(PF)是一种脓疱性、免疫介导的皮肤病，以棘层松解细胞为特征，常用高剂量糖皮质激素治疗。本报告描述了1个口服奥拉替尼成功控制猫PF的病例，表明某些病例的治疗可能以此替代糖皮质激素。

Resumo – O pênfigo foliáceo (PF) é uma dermatopatia pustular, imunomediada caracterizada por células acantolíticas e comumente tratado com altas doses de glicocorticoides. Este relato descreve um caso de PF felino satisfatoriamente controlado utilizando oclacitinib por via oral, sugerindo uma possível alternativa terapêutica aos glicocorticoides em alguns casos.

