Long-lasting successful treatment of a donkey with cutaneous lupus erythematosus with methotrexate

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Cutaneous lupus erythematosus (CLE) is a rare immune-mediated dermatitis. To the best of the authors’ knowledge it has not been described in donkeys. A 5-year-old male neutered donkey, living in south-east France, was diagnosed with CLE. Clinical signs included generalized symmetrical areas of alopecia, erythema, crusting and scales. Diagnosis was confirmed with immunohistochemical analysis which demonstrated an interface dermatitis with CD8+ T cells. The skin condition was successfully treated initially with glucocorticoids and methotrexate; successful long-term maintenance was associated with administration of methotrexate.

Case report

A 5-year-old neutered male donkey, living in south-east France, was presented with a generalized dermatosis of eight months duration, beginning in spring. Except for routine deworming, the donkey had received no other treatments. Previous treatments for the skin condition (ivermectin, griseofulvin, chlorhexidine shampoos, antibiotics and corticosteroids) led to partial and temporary improvement and were stopped two months before presentation. Physical examination revealed generalized cutaneous lesions consisting of multiple patches of erythema, scaling, thick and adherent crusts embedding hairs, alopecia and diffuse scaling. Scaling was mostly on the neck, trunk, dorsal, face, tail, perineal area and four distal limbs (Figure 1). Some of the crusts covered eroded, exudative and pigmented lesions. Lesions were not painful or pruritic.

Cytological examination of surface skin samples showed few cocci bacteria and neutrophils with no infectious agent under the crusts. Fungal culture was negative for pathogens. Histopathological examination from representative skin biopsy samples showed hydropic and lichenoid interface dermatitis involving the epidermis and dermal interface follicular dermatitis. The inflammatory infiltrate consisted of histiocytes, plasma cells, mastocytes and many lymphocytes (Figure 2); the presence of CD3+ lymphocyte was confirmed with immunohistochemical analysis and more lymphocytes expressed CD8+ than CD4+ (about 3:2) (Figure 3). Direct immunofluorescence did not reveal the presence of IgG at the basement membrane zone. Serum antinuclear antibody titre was within the normal range. The diagnosis was generalized exfoliative cutaneous lupus erythematosus associated with moderate secondary bacterial overgrowth.

Treatment consisted of trimethoprim sulfonamide 25 mg/kg orally twice daily for 10 days with no improvement. Topical antiseptic shampoo was not applied because of cold weather. Immunosuppressive treatment was initiated with prednisolone 0.4 mg/kg p.o. twice daily, associated with methotrexate subcutaneously, 25 mg once a week (0.1 mg/kg). Methotrexate (MTX) was chosen to avoid adverse effects of long-term glucocorticoid therapy and to evaluate efficacy in this species. The dosage was extrapolated from human dosing, beginning with a lower dose and increasing progressively. No adverse effects were observed. Within three weeks, hair regrowth appeared and the number of lesions decreased by 70%. After three months, prednisolone therapy was decreased and MTX increased up to 50 mg once weekly. The lesions were markedly reduced. Three months later, prednisolone therapy was progressively stopped and MTX increased up to 75 mg once weekly. Complete remission was observed within two weeks (Figure 4) and at the time of the writing (>one year of follow-up) the donkey’s skin lesions were in remission. Follow-up histopathological examination showed no evidence of cytotoxic lymphocytes. After one year, MTX was decreased to 50 mg once weekly and no relapse were noted during an 11 month follow-up period. No adverse effects were observed. Complete blood counts and serum biochemistry profiles, performed monthly for three months then every three months, were within normal ranges.

Cutaneous lupus erythematosus is a common autoimmune disease in humans, dogs and cats, rare in horses and never described in donkeys. Only three cases of the discoid subtype of CLE have been reported in horses, characterized by erythema, scaling, alopecia, crusts,
Figure 1. Clinical lesions in a donkey with cutaneous lupus erythematosus. (a) Lesions were widely distributed and consisted of scaling, crusts and hypotrichosis. (b) Hypotrichosis was severe in the periocular areas. (c) Scales were adherent, grey and thick on the pinnae. (d) Crust lesions were thick and oozing on the neck.

Figure 2. Histopathological findings in a donkey with cutaneous lupus erythematosus. (a) Hydropic and lichenoid interface dermatitis affecting the epidermis and the outer root sheath of hair follicles. Haematoxylin and eosin (H&E) stain. (b) Focus on epidermal lesions: lymphocyte exocytosis, hydropic degeneration and apoptosis of basal keratinocytes. H&E.
erosions, scars and variable degrees of leucoderma and leucotrichia. The prognosis is usually good although treatments are required and need to be administered lifelong.3

In this case report we successfully treated a donkey with CLE using subcutaneous MTX. The skin lesions were similar to those described in horses apart from the lack of leucotrichia.4 Because lesions first developed in winter and the donkey had normal hair thickness at that time, sun-associated causes were considered unlikely. The histological features in this case were similar to those in horses.

Methotrexate is a folic acid analogue used in human skin conditions for its anti-inflammatory, anti-proliferative and immunosuppressive actions. In one study, 42 of 43 (98%) human patients with CLE showed a positive clinical response when treated with low-dose MTX.5 We hypothesized that this drug could be effective in our case. Three publications have described the use of MTX in horses,6–8

Figure 3. Immunohistochemical findings in skin biopsies from a donkey with cutaneous lupus erythematosus.
(a) CD3 staining showed numerous lymphocytes just beneath the epidermis and encircling hair follicles. With substantial exocytosis of lymphocytes. (b) CD8+ staining revealed many CD8+ lymphocytes invading basal layers of epidermis and the hair follicle epithelium.

Figure 4. Clinical lesions in a donkey with cutaneous lupus erythematosus after treatment.
(a) Complete remission of clinical signs was observed. (b) Regrowth of hairs around the eyes. (c) No scales were evident on the pinnae. (d) Skin biopsy site on the thorax showing minimal scaling and crusting.
some with severe adverse effects. Dosage and frequency of use of MTX were high in these cases and some horses received cyclophosphamide concurrently. We decided to treat the donkey with MTX at a lower dosage once a week without going above 0.37–1.16 mg/kg; we monitored blood parameters throughout the treatment. MTX was effective and was associated with excellent control of the disease for two years without adverse effects.

References

Résumé – Le lupus cutané érythémateux (CLE) est une dermatite à médiation immune rare. A la connaissance des auteurs, il n’a pas été décrit chez le singe. Un singe mâle castré de 5 ans, vivant dans le sud-est de la France a été diagnostiqué avec CLE. Les signes cliniques incluaient des zones symétriques généralisées d’alopecie, d’érythème, de croûtes et de pellicules. Les tests diagnostics comprenaient un examen histopathologique et immunohistochimique de biopsies cutanées qui ont révélé une dermatite d’interface avec cellules T CD8+. La dermatose a été traitée avec succès initialement avec des corticoides et du méthotrexate; un traitement efficace au long cours a été associé avec l’administration de méthotrexate.

RESUMEN – El lupus eritematoso cutáneo (CLE) es una rara dermatitis imunomediada. A entender de los autores, esta enfermedad no se ha descrito en los primates. Un gorila castrado macho de 5 años de edad, que vive en el sureste de Francia fue diagnosticado con CLE. Los signos clínicos incluyeron áreas simétricas generalizadas de alopecia, eritema, crostas y escamas. Las pruebas de diagnóstico incluyeron el examen de muestras de biopsia de piel mediante análisis histopatológico e inmunohistoquímico que demostró una dermatitis de interfase con células T CD8+. La condición de la piel se trató con éxito inicialmente con glucocorticoides y metotrexato; el control exitoso a largo plazo de la enfermedad se obtuvo con la administración de metotrexato.


要約 – 皮膚エリテマトーデス（CLE）は、まれな免疫介在性皮膚炎である。著者の知る限り、ロバにおける記載はない。フランス南部の5歳、去勢雄のロバがCLEと診断された。臨床徵候には、汱発性、左右対称性の脱毛、紅斑、痂皮および鱗屑を含んだ。診断テストには、組織病理学および免疫組織化学的分析による皮膚生検サンプルの検査を含む、CD8+T細胞との境界部皮膚炎が示された。皮膚コンディションには、グルココーティオドおよびメトレキサートによる初期治療が奏効した。長期維持の成功には、メトレキサートの投与が関連していた。

概要 — 皮肤红斑狼疮 (CLE) 是一种罕见的免疫介在性皮炎。据作者所知，尚未有关于驴的相关报道。一只5岁的雄性去势驴，生活在中国东南部，被诊为CLE。临床症状包括全身对称性脱毛、红斑、痂皮和鳞屑，诊断试验包括组织病理学和免疫组化，对皮肤活检样本进行检查，证明存在CD8+T细胞性界面性皮炎，初期使用糖皮质激素和甲氨蝶呤成功治疗了皮肤疾病；成功的长期维持与甲氨蝶呤给药有关。

Resumo – O lúpus eritematoso cutâneo (LEC) é uma dermatite imunomediada rara. De acordo com os conhecimentos do autor, a doença ainda não foi descrita em jumentos. Um jumento macho castrado de cinco anos de idade, habitante do sul da França, foi diagnosticado com LEC. Os sinais clínicos incluíram
alopecia, eritema, crostas e descamação generalizadas e simétricas. Os testes diagnósticos utilizados foram avaliação de amostras de biópsia por análise histopatológica e imunohistoquímica, que demonstraram dermatite de interface com células T CD8+. A dermatopatia foi tratada satisfatoriamente inicialmente com glicocorticoide e metotrexato; a manutenção satisfatória a longo prazo foi associada à administração de metotrexato.