

ERYTHEMA MULTIFORME IN TWO HORSES

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ABSTRACT

Erythema multiforme is reported for the first time in 2 South African horses. Both horses displayed a sudden, fulminant outbreak of raised, non-alopecic and non-pruritic plaques over the dorsolateral aspects of the neck and trunk. In both cases the distribution of the lesions was bilaterally symmetrical. Histopathological findings included hydropic degeneration of basal epidermal cells, eosinophilic necrosis of individual or groups of keratinocytes, intra-epidermal and sub-epidermal cleft formation and mixed, dermal, perivascular infiltrates. An initiating cause could not be identified in either case. Both horses underwent gradual spontaneous remission within 3 months.

Key words: Erythema multiforme, horse, skin disease.

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INTRODUCTION

Erythema multiforme is an acute, self-limiting dermatosis which has been described in man¹⁻³, dogs⁴⁻⁷ and cats^{6, 8}. Two cases have been reported in horses^{9, 10}. The aetiology of erythema multiforme is unknown¹⁻³. However, in man it has been associated with infections (viral, bacterial, fungal and mycoplasmal), drugs, neoplasia, collagen-vascular disorders, contact reactions, sunlight, cold and endocrine factors. In approximately 50% of cases the precipitating factor is unknown². Cases in dogs have been associated with infections (staphylococcal folliculitis, anal sacculitis)^{6, 7} and drugs (aurothioglucose, cephalixin, chloramphenicol, diethylcarbamazine, gentamicin, levamisole, l-thyroxine, trimethoprim-sulphadiazine)⁴⁻⁷. Some cases have been idiopathic⁶. In cats, erythema multiforme has been associated with drug therapy (penicillin, aurothioglucose)^{6, 8}. In the 2 cases of erythema multiforme reported in horses, a precipitating factor was not identified^{9, 10}. In man, there is no sex predilection for

the disease, however, patients are most commonly in their second or third decade of life². No age, sex or breed predilection can be identified among cases described in dogs, although more males are represented than females⁴⁻⁷. The incidence of the disease is relatively common in man², uncommon in the dog and rare in the cat⁶.

The exact pathogenesis of the disease is unknown. In man, immunological studies of lesions less than 24 h old show deposits of IgM and C3 in the walls of the superficial dermal microvasculature. In addition, circulating immune complexes have been demonstrated^{2, 3}. It may thus be hypothesised that immune complex formation and subsequent deposition in the cutaneous microvasculature may play a role in the pathogenesis of the disease.

In man, acute attacks usually resolve within 3 to 6 weeks. Some patients show a tendency toward periodic recurrence and in most instances are free of lesions for long periods between episodes. Occasionally, however, attacks occur with such frequency that lesions persist from one episode to the next^{2, 3}. In animals the condition undergoes resolution within one to 12 weeks following removal of the precipitating factor or simply due to the natural self-limiting course of the disease⁵⁻¹¹. In severe cases, scarring may remain in places where ulceration has oc-

curred⁴. Permanent ocular sequelae include conjunctival scarring, corneal perforation, opacities and uveitis^{2, 4}.

The disease in man and dogs has variable clinical and histological manifestations, depending on the severity of the primary lesions^{1-3, 6}. Mild lesions include erythematous macules, patches, papules and plaques. Target lesions are characteristic, representing macules or papules which have expanded peripherally and cleared centrally (usually within 12 to 24 h). Severe lesions include vesicles and bullae with or without ulceration. Lesions may be seen on the skin and/or mucous membranes (notably the oral, nasal and conjunctival mucosae and mucocutaneous junctions). In mild cases the lesions are usually asymptomatic, the overlying hair coat is normal and the condition is referred to as erythema multiforme minor. Erythema multiforme major or Stevens-Johnson syndrome is a more severe form of the disease involving the skin and mucous membranes with variable degrees of visceral involvement and significant constitutional symptoms. Vesicles and bullae appear suddenly on the skin and mucous membranes and rupture, to leave painful erosions and ulcers. Ocular lesions (keratitis, corneal ulceration, purulent conjunctivitis, anterior uveitis and panophthalmitis), fever, anorexia and depression are commonly seen. Diarrhoea, paronychia, onychomadesis, polyarthritis, otitis media, pneumonia and renal failure are less common. Erythema multiforme major may be fatal.

Histological findings vary according to the severity of the lesions^{1, 3, 6}. Epidermal changes include hydropic degeneration of basal cells and eosinophilic necrosis of individual or groups of keratinocytes in mild lesions. Mononuclear cells and neutrophils may invade such areas of necrosis, and the necrotic cells subsequently lose their nuclei and coalesce. In severely affected areas, hydropic degeneration of the basal cells may result in subepidermal separation, and all keratinocytes appear necrotic, with only the horny layer remaining preserved. In other areas, however, there may be severe damage to the upper epidermal layers and less severe damage to the lower layers, resulting in intra-epidermal cleavage. Extensive epidermal necrosis in bullous-necrotic le-

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sions may be indistinguishable from that found in toxic epidermal necrolysis.

Dermal changes include a mild to pronounced perivascular infiltrate, involving mostly lymphocytes and histiocytes. Eosinophils may also be present. In some cases the infiltrate may assume a lichenoid pattern, which may be severe enough to obscure the dermo-epidermal junction. There is often pronounced oedema of the superficial dermis. In severe forms, the oedema may lead to the formation of a bulla within the epidermis with the basement membrane zone forming its roof. In some instances, the oedema may lead to epidermal spongiosis and multiple intra-epidermal vesicles associated with exocytosis. Pigmentary incontinence, vasodilatation and erythrocyte extravasation are often present in the upper dermis³.

Treatment of erythema multiforme may be unnecessary as the disease usually runs a mild course and spontaneously regresses within a few weeks^{2 6 7}. An underlying cause should be sought and corrected whenever possible. Severe cases require supportive care in order to prevent secondary infection of open lesions and to correct fluid and electrolyte imbalances when a significant proportion of the cutaneous surface is involved^{2 4}. The use of corticosteroids is controversial and probably not effective in changing the course of the disease, although it is often used in severe cases in an attempt to minimise sequelae^{2 4}.

The purpose of this paper is to report the occurrence of erythema multiforme in 2 horses, the first cases to be reported in South Africa.

CASE REPORTS

Case 1: An 8-year-old grey Arab mare was presented with a history of a sudden, fulminant onset of "ring-like" skin lesions one week previously. The existing lesions were becoming more prominent, but no new lesions had developed. Clinical examination revealed the presence of raised, non-alopecic, annular plaques over the lateral aspects of the neck (Fig. 1) and shoulders, and the dorsal aspects of the back and rump. The lesions showed a bilaterally symmetric distribution and varied between about 5 and 8 cm in diameter. They were nonpruritic but sensitive to the touch. The early lesion was firm and non-alopecic but later became eroded, moist and covered by a yellowish crust. Affected skin was thickened and lacked extensibility. The horse was otherwise normal.

Skin scrapings, hair-pluckings, bacterial and fungal cultures were negative. Histopathology revealed mild epidermal spongiosis with pronounced individual keratinocyte necrosis (Fig. 3). In some areas the keratinocyte necrosis was ex-

tensive enough to cause intra-epidermal cleft formation (Fig. 4). Hydropic degeneration of basal epidermal cells was mild to marked and in some areas there was sub-epidermal cleft formation (Fig. 5). The dermis showed a marked superficial dermal oedema and a moderate perivascular infiltrate involving lymphocytes, histiocytes and eosinophils.

A diagnosis of erythema multiforme was made. The owner was again consulted regarding the horse's possible exposure to an inciting agent e.g. drugs,

Case 2: A 5-year-old bay Hannoverian mare was presented with a history of a previous episode of "urticaria" of sudden onset, involving the dorsal aspects of the animal from the withers to the tail-base. The horse had exhibited hyperaesthesia over the affected areas. Treatment with antihistamines had been given and the horse had recovered over an unspecified period of time. Three weeks after remission, the lesions had suddenly reappeared and were first noticed when the horse was brought in from the paddock in



Fig. 1: Non-alopecic, annular plaques on the lateral aspect of the neck of a horse with erythema multiforme (Case 1)



Fig. 2: Multiple plaques arranged in a "crazy-paving" like pattern on the lumbosacral area of a horse with erythema multiforme (Case 2)

contact reactants, physical factors. No initiating factor could be identified.

Treatment involving the use of topical fly-repellents (Fly-Away, Centaur) and once daily bathing of eroded lesions with chlorhexidine solution (Hibitane, ICI) was instituted. The condition remained static for a few weeks and thereafter underwent gradual, spontaneous remission within 3 months. The horse has remained normal for 18 months.

the evening. No lesions had been noted during the morning grooming session before the horse was put out to graze. Treatment involving antihistamines, glucocorticoids, antifungal and insecticidal washes, had been ineffective.

Clinical examination revealed skin lesions on the dorsal aspect of the animal with a bilaterally symmetric distribution, which extended from the withers to the tail base and from 5 to 7cm on either side

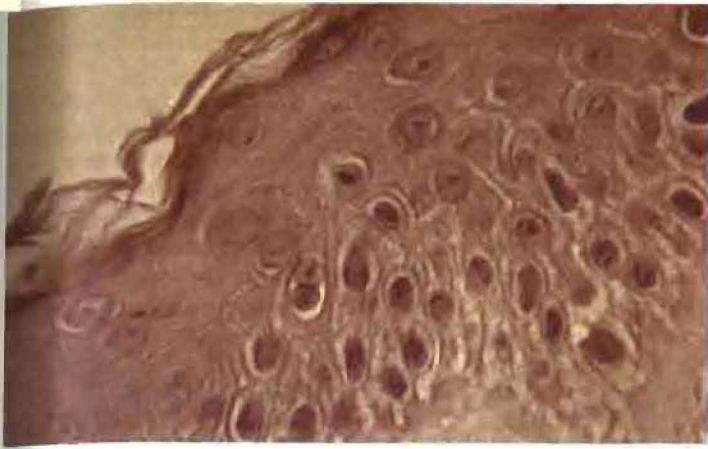


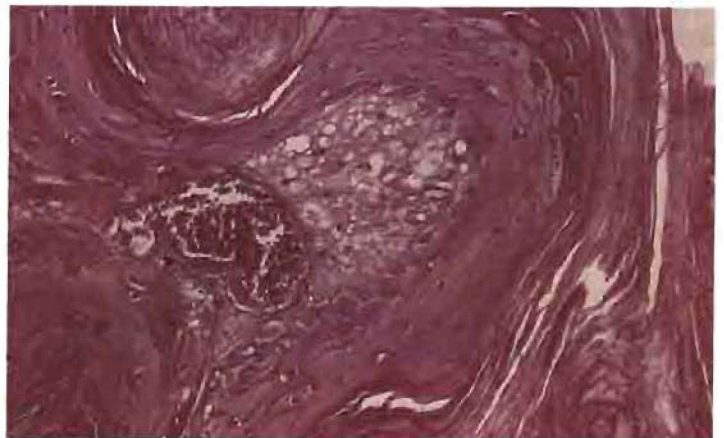
Fig. 3: Photomicrograph of skin biopsy (Case 1). Note mild acanthosis, epidermal spongiosis and eosinophilic necrosis of a single keratinocyte (H:E, X 400)

Fig. 4: Photomicrograph of skin biopsy (Case 1). Note hydropic degeneration of basal keratinocytes, eosinophilic necrosis of keratinocytes and intra-epidermal cleft formation (H:E, X 400)



Fig. 5: Photomicrograph of skin biopsy (Case 1). Note marked superficial dermal oedema with infiltration of mononuclear cells and eosinophils. Also note sub-epidermal cleft formation and necrosis of the overlying epithelium which has been retracted to the right (H:E, X 100)

Fig. 6: Photomicrograph of skin biopsy (Case 2). Note marked orthokeratotic hyperkeratosis and acanthosis. Also note the necrosis of individual keratinocytes, superficial dermal oedema and dilatation of dermal blood vessels (H:E, X 100)



of the midline. The lesions were firm, raised, non-allopecic plaques arranged in a "crazy-paving" like pattern (Fig. 2). The affected skin exhibited a decrease in elasticity and extensibility. Secondary lesions included thick crusts overlying some plaques, which could easily be removed together with the overlying hair, leaving an oozing erosion below. Pruritus was absent, but the horse was hyperaesthetic over affected areas to the extent that she could no longer be saddled. The horse was otherwise normal.

Skin scrapings, hair pluckings, bacterial and fungal cultures were negative. Direct smears made from the undersides of crusts, revealed only keratinised cells. Histopathology revealed a marked orthokeratotic hyperkeratosis and acanthosis with individual keratinocyte necrosis and focal areas of hydropic degeneration of basal keratinocytes (Fig. 6). Superficial dermal oedema was present, with dilatation of the superficial dermal blood vessels and extravasation of red blood cells in places. A moderate perivascular infiltrate involving mostly lymphocytes, histiocytes and a few eosinophils was present in the dermis, along with a moderate, diffuse pigmentary incontinence.

Erythema multiforme was diagnosed but investigation for the inciting cause was again unsuccessful. The crusts were removed during grooming and the lesions disappeared within 6 weeks. No treatment was given. The horse has remained normal for 9 months.

DISCUSSION

Very few cases of erythema multiforme have been reported in horses^{9 10}. However, an increasing awareness of the clinical and pathological features of the disease will probably result in the recognition of a greater incidence of the disease in our domestic animals.

In previous reports of erythema multiforme in the horse, no inciting cause could be identified^{9 10}. In the 2 cases reported here, we were unable to find precipitating factors in that there was no history of previous drug administration, illness or change in feed or environment.

Clinical lesions encountered in horses have been mild and self-limiting, in that spontaneous remission has occurred

within 3 months. The onset has been acute and the distribution of lesions symmetric. In all cases the primary lesions include papules and plaques which assume an annular, arciform or serpiginous configuration. The lesions are nonpruritic, although they may be sensitive to the touch, and nonalopecic. Secondary lesions involving erosions and crusting may be encountered. The lesions of erythema multiforme can be differentiated from the wheals seen in urticaria in that they are firm, do not pit on pressure and are more persistent (lasting weeks to months as opposed to hours or days). Similar lesions to those seen in erythema multiforme, are seen in cases of allergic contact dermatitis and arthropod reactions.

Severe cases of erythema multiforme have not been reported in the horse, however, in other species these must be differentiated from toxic epidermal necrolysis (considered by some workers to be a maximal expression of severe erythema multiforme, and often histologically indistinguishable), other bullous skin diseases, staphylococcal scalded skin syndrome, fixed drug eruptions, systemic lupus erythematosus, acute graft-versus-host disease and epidermotropic lymphoma.

Histological findings in horses^{9,11} are much in accordance with the findings in man¹⁻³, dogs and cats⁴⁻⁸. Epidermal changes include orthokeratosis, focal parakeratosis, mild to moderate spongiosis, focal hydropic degeneration of basal keratinocytes and necrosis of individual keratinocytes. Sub-epidermal and intra-epidermal cleavage has been encountered. Dermal changes include pigmentary incontinence, superficial dermal oedema, dilatation of dermal vessels, extravasation of erythrocytes and perivascular accumulation of mononuclear cells (and sometimes eosinophils).

The histological picture seen in mild forms of erythema multiforme, must be distinguished from that seen in allergic urticarial eruption. The latter involves papillary oedema with a mixed inflammatory-cell infiltrate and is not associated with histologic alterations of the dermo-epidermal interface. Other histologic differential diagnoses include acute fixed drug eruption, toxic epider-

mal necrolysis and graft-versus-host reactions, from which erythema multiforme cannot always be distinguished.

Specific treatment of erythema multiforme is unavailable and probably not necessary in mild cases as they have been seen in horses. However, one should attempt to establish a precipitating factor which should be removed if possible. Treatment of secondary lesions aimed at minimising fly-worry and preventing secondary infection is advisable.

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