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ERYTHEMA MULTIFORME

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Abstract

Erythema multiforme (EM) and Stevens-Johnson syndrome (SJS) are rare skin disorders affecting dogs and cats with or without mucous membrane involvement. EM is further classified into two categories, EM minor and EM major, depending on the existence of mucocutaneous lesions.

Classification of EM/SJS in veterinary medicine

Canine EM/SJS classification is based on the human international consensus clinical classification. In this article, EM/SJS patients are subclassified into EM minor, EM major, and SJS based on the following clinical findings (Hinn 1998): 1) flat or raised, focal or multi-focal, target or polycyclic lesions; 2) number of mucosal surfaces involved; 3) erythematous or pruritic, macular or patch eruption (% of body surface); and 4) epidermal detachment (% of body surface). According to the human international consensus clinical classification, canine EM cases are usually not associated with the history of drug exposure, whereas SJS, the overlap syndrome, and toxic epidermal necrolysis (TEN) are thought to be related to the administration of drugs.

In human medicine, EM minor, which exhibits indurated erythema in the extremities, is the most common form in EM/SJS patients. In dogs, EM diagnosed by dermatology specialists is mainly EM major or SJS. Canine EM minor usually manifests slight cutaneous changes, including peripherally raised focal erythema without symptoms. These lesions are often hidden by hair coats and thus may have been overlooked by owners and veterinarians (Scott 1999). That may be one of the reasons why the occurrence of EM minor in dogs is much less frequent than that in humans.

Clinical signs of EM/SJS

There have been no reports of breed, gender or age predilection in canine EM/SJS. The cutaneous presentation of EM shows annular, erythematous macula, papules, and plaques that enlarge centrifugally and often form a bizarre polycyclic pattern (Scott 1999). Target lesions become vesicular or bullous, often necrotic, and then exhibit ulcers. The lesions are distributed on the oral mucous membrane, tongue, axilla, ventral abdomen and groin, and central dorsal regions.
Histopathology of EM/SJS

The histopathology of EM/SJS/TEN in dogs includes interface dermatitis with marked apoptosis of keratinocytes at all levels of the epithelium and hair follicles (Scott 1999). Mononuclear cell infiltration into the epidermis and/or mucous membrane epithelium and dermis was more intense in SJS patients than in EM patients (Hinns 1998).

A large-scale study has implicated that histopathological examination should be restricted to the confirmation of the diagnosis of EM, and is not applicable to the subcategorization into the different entities.

Pathogenesis of EM/SJS

The pathogenesis of EM/SJS is still unclear in human and veterinary medicine. In human medicine, SJS and TEN were long believed to be part of a spectrum of disorders that included erythema multiforme majus (EMM), and SJS is an entity distinct from EMM, differing not only in the severity but also in the clinical, histological, etiological, and demographic characteristics (Bochers 2008).

In one article that dealt with the immunohistochemistry of canine EM, the expression of surface antigens in infiltrating cells and keratinocytes was investigated. The intra-epithelial infiltrates were CD3+, CD8+, TCR+ T cells (Affolter 1998). In dogs, it is believed that keratinocyte apoptosis is probably produced by signals from intraepithelial CD8+ T lymphocytes (Scott 1999).

A recent article on human SJS has expressed that keratinocyte apoptosis is triggered by drug-specific cytotoxic T lymphocytes using perforin/granzyme B. Fas-mediated apoptosis may contribute to the triggering of keratinocyte death, but it remains controversial whether the membrane-bound or the soluble form of Fas is responsible. Cytokines produced by T lymphocytes, macrophages, and possibly keratinocytes themselves are thought to contribute to the pathogenesis of SJS.

Therapy of EM/SJS

The most important factor for the therapy of EM/SJS is the investigation and elimination of triggering factors. When this is accomplished, the symptoms usually improve within one to two weeks. In idiopathic cases of EM/SJS, a large dose of glucocorticoid with azathiopurine and/or cyclosporine A may improve clinical signs. However, in human medicine, there is controversy regarding the use of glucocorticoids for the treatment of EM/SJS as glucocorticoids may elicit systemic infection.

The intravenous injection (IVIG) of human immunoglobulin into canine SJS patients is thought to be beneficial for the treatment of the condition. (Nuttal 2004)
References
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Scott DW, Miller W. Erythema multiforme in dogs and cats: literature review and case material from the Cornell University College of Veterinary Medicine (1988-1996), Veterinary Dermatology 1999; 10: 297-309

Heading: Erythema multiforme in dogs