Erythema multiforme and toxic epidermal necrolysis
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Erythema multiforme (EM) and Stevens-Johnson syndrome (SJS) are rare human and animal skin disorders with or without mucous membrane involvement. Toxic epidermal necrolysis (TEN) has been considered as a severe form of EM or SJS, but at the present time there are no generally accepted clinical and diagnostic criteria for the distinction between SJS and TEN. EM is further classified into two categories, EM minor or major, depending on the existence of mucocutaneous lesions.

Classification of EM/SJS/TEN in veterinary medicine
In an article in 1998, EM/SJS/TEN in dogs was classified through the adoption of a human international consensus clinical classification system. In this article, cases of EM/SJS/TEN were sub-classified into EM minor, EM major, SJS, SJS/TEN overlap syndrome and TEN based on the following signs: (1) flat or raised, focal or multi-focal, target or polycyclic lesions; (2) number of mucosal surfaces involved; (3) erythematous, pruritic, macular or patch eruption (% of body surface); and (4) epidermal detachment (% of body surface). According to the adoption of the human international classification system, canine EM cases are usually not associated with a history of drug exposure, while SJS, overlap syndrome and TEN are usually related to the administration of drugs.

In human medicine, EM minor, which exhibits as indurated erythema in the extremities, is the most common form of EM/SJS/TEN, whereas EM in dogs is recognised by dermatologists to be mainly EM major or SJS. Canine EM minor usually manifests as slight cutaneous changes, like peripherally raised focal erythema, without symptoms, that are often hidden by hair. Therefore many of these cases may have been overlooked by owners and veterinarians. That might be one of the reasons why the occurrence of EM minor in dogs is much less frequently diagnosed than that in humans.

Clinical signs of EM/SJS/TEN
There have been no reports of predilection based on gender, breed or age. Cutaneous presentation of EM presents as annular, erythematous macula, papules and plaques which become enlarged from the centre and often form a bizarre polycystic pattern. Target lesions become vesicular or bullous and then become necrotic, before finally forming ulcers. The lesions are often distributed around the oral mucous membrane, tongue, axilla, ventral abdomen, groin and central dorsal regions.

Histopathology of EM/SJS/TEN
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. Mononuclear cell infiltration into the epidermis and/or mucous membrane epithelium and dermis were more intense in the SJS/TEN group than the EM minor and major groups. A large scale study implicated that histopathological examination should be restricted to confirmation of the diagnosis of diseases in the EM/TEN group, but not to subcategorise the different entities.

Pathogenesis of EM/SJS/TEN
In the only article that examined canine EM by immunohistochemistry, the expression of the infiltrates and keratinocytes was investigated. The intra-epithelial infiltrates were CD3+, CD8αβ+, and TCRαβ+ T cells, CD1+ and CD11c+ Langerhans cells were more numerous, whereas infiltrating cells in the dermis consisted of CD3+, CD8αβ+ and TCRαβ+ T cells. In dogs, it is believed that keratinocyte apoptosis is probably induced by signals from intraepithelial CD8+ T lymphocytes. Noli et al. implies that the cause of the massive epidermal cell necrosis in TEN is not immune mediated, but toxic, and was observed by the staining of apoptotic cells in EM and TEN cases.

A recent article regarding human SJS/TEN expressed that keratinocyte apoptosis was triggered by drug-specific cytotoxic T lymphocytes using perforin/granzyme B. Fas-mediated apoptosis may contribute to the extent of keratinocyte death, but it remains controversial whether the membrane-bound or the soluble form of Fas is responsible, and the cellular source from which it originates. Cytokines produced by T lymphocytes, macrophages, and possibly by keratinocytes themselves are thought to contribute to the pathogenesis of the SJS/TEN spectrum.
EM/SJS/TEN therapy

The most important factor in the therapy of EM/SJS/TEN is investigation and elimination of the triggering factors.\(^5,8\) When this is accomplished, the symptoms are usually resolved within 1–2 weeks.\(^8\) In idiopathic cases of EM/SJS/TEN, a large dose of glucocorticoids with azathioprine and/or cyclosporine A may improve clinical signs. However, in human medicine, the use of glucocorticoids for treatment of EM/SJS/TEN has been controversial as their use may elicit systemic infection.\(^2,9\) The use of human immunoglobulin by intravenous injection for the treatment of canine SJS/TEN is thought to be beneficial for the treatment of the condition.\(^5\)

References

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