Hepatocutaneous syndrome

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Necrolytic migratory erythema (NME) is a rare disorder first described in 1942 that is most often associated with glucagonoma in humans. Other conditions associated with NME in humans include chronic liver disease or inflammatory bowel disease, malabsorption disorders, and malignancies. In veterinary medicine the condition has been referred to by several names including superficial necrolytic dermatitis, diabetic dermatopathy, pseudoglucagonoma syndrome, metabolic epidermal necrosis, and hepatocutaneous syndrome, in addition to NME. Although these terms all refer to the same disease syndrome, in veterinary medicine the term “hepatocutaneous syndrome (HCS)” is used when NME is associated with an underlying hepatopathy.[2]

Metabolic disturbances of the liver or abnormal glucagon balance caused by underlying disease leads to nutritional deficiencies and decreases in plasma amino acid concentrations, resulting in necrosis of skin cells. Although the definitive pathogenesis of the hypoaminoacidemia is unknown, it may be due to excessive amino acid catabolism.[3]

The most prominent plasma amino acid depletions impact the urea cycle (arginine and ornithine), glutathione synthesis (glutamine, glycine, and cysteine), and collagen synthesis (proline and hydroxyproline).[1]

Pathological mechanisms of cutaneous lesions in NME are speculated to reflect depletion of plasma amino acids required for collagen synthesis necessary to repair sites of mechanical trauma. Common skin lesions include erythema, crusting, exudation, ulceration, and alopecia on the footpads, face, perianal regions, and pressure points. Severe ulceration of the footpads may result in pain and lameness.

A diagnosis of HS is made based on a characteristic honeycomb pattern in the liver on ultrasound examination, and histopathologic evaluation of skin biopsies, including parakeratotic epidermis with striking inter- and intracellular edema, keratinocyte degeneration in the upper epidermis, and hyperplastic basal cells.[3]

The goal of treating HS is to enhance the quality of life and extend survival time by alleviating dermatopathy and resolving the underlying liver disease. Conventional medications include hepatoprotective agents, antioxidants, zinc, essential fatty acids, and topical agents that are beneficial to the skin barrier. Antibiotics should be considered if secondary skin infections exist.

The most effective treatment for HS, which is only palliative, is the IV administration of amino acids. One study reported that plasma amino acid concentrations were markedly low in dogs with HS and increased after amino acid infusions. Lesions occasionally are improved by treating the underlying disease, but this outcome is unexpected in cases of serious or irreversible liver disease.

The disease will progress, eventually leading to death. Most dogs with HS survive for <6 months but, in some cases, dogs given sufficient protein PO and periodic IV administration of amino acids can live ≥12 months after diagnosis.[3]

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