

Superficial Necrolytic Dermatitis in a Dog

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ABSTRACT

Background: Superficial necrolytic dermatitis (SND), hepatocutaneous syndrome (HCS), metabolic epidermal necrosis (MEN), and necrolytic migratory erythema (NME) are useful terms to describe a disease that likely has a multifactorial etiopathogenesis. SND is a rare and fatal disease characterized by skin lesions and liver disease. Common skin lesions include hyperkeratosis, fissures, erosion, ulceration, crusting, exudation from the paws, face, perianal regions, and pressure points. This case report aimed to report the case of a bitch that developed the rare Superficial Necrolytic Dermatitis disease, emphasizing the clinical signs of the disease, and the importance of complementary exams such as abdominal ultrasound and skin biopsy for the definitive diagnosis.

Case: A 9-year-old, mixed-breed, neutered female was referred for clinical examination with 5 months history of hyperkeratosis and ulceration of the paw pads, presenting pain, lameness and weight loss. Abdominal ultrasound revealed a liver with heterogeneous echotexture, mixed echogenicity, irregular and poorly delimited margins with hypoechoic nodules throughout like honeycombs. The gallbladder was visualized with a moderately thick layer. Histological analysis confirmed the diagnosis of SND. Skin biopsies showed an increase in thickness of the epidermis due to irregular hyperplasia and proliferation of keratinocytes in the basal layer of the epidermis, pallor of the spinous layer of the epidermis and important parakeratosis. Due to the progression of the disease, significant worsening of the patient's clinical condition and pain, associated with the impossibility of cure, the animal was submitted to euthanasia. A necropsy was performed to allow assessment of the liver and pancreas. The biopsies showed a severe proliferative chronic hepatitis, steatosis and cholestasis associated with pancreatitis and necrotic multifocal proliferative fibrinopurulent areas in the pancreas.

Discussion: Clinical signs such as lethargy, inappetence, weight loss, as well as the dermatological signs presented by this bitch are nonspecific clinical signs and require a deeper clinical, pathological and histopathological diagnostic investigation to reach the diagnosis of this disease. The definitive diagnosis is made on the basis of a characteristic honeycomb pattern in the liver or associated with a neoplastic finding in the pancreas on ultrasound examination and confirmed by histopathological evaluation of skin biopsies. Palliative treatment with corticosteroid anti-inflammatories, improvement in feed quality, with higher nutritional and protein intake and intravenous amino acid supplementation are suggested by some authors as treatment alternatives. However, not all owners can afford a costly lifetime treatment. With the progressive worsening of the condition, many owners opt for euthanasia as a way to shorten the suffering of the animal. This decision is not an easy one to make. Despite the poor prognosis of the disease, treatment options should be tried by veterinarians and owners prior to the option of euthanasia. However, new affordable nutritional and pharmacological strategies to treat or control the disease are needed in order to improve quality of life of SND patients.

Keywords: canine, bitch, SND, hepatocutaneous syndrome, metabolic epidermal necrosis, necrolytic migratory, dermatopathy.

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INTRODUCTION

Superficial necrolytic dermatitis (SND) is a rare and often fatal disease that has been associated with both endocrine neoplasia (EN) and hepatocutaneous syndrome (HCS) [3,6,7,11]. SND is an ulcerative skin disease associated with liver diseases such as vacuolar hepatopathy or cirrhosis and can be associated with long-term phenobarbital administration [2,8]. Common skin lesions include hyperkeratosis, fissures, erosion, ulceration, crusting, exudation of the footpads, face, perianal regions, and pressure points [12]. Clinical signs such as lethargy, inappetence, weight loss and lameness are also present [6].

A definitive diagnosis of SND/HCS is made based on a characteristic honeycomb like pattern in the liver or SND/EN associated with neoplastic finding in pancreas on ultrasound examination [3]. Also, it must be confirmed by histopathologic evaluation of skin biopsies, including parakeratotic epidermis with striking inter- and intracellular edema, keratinocyte degeneration in the upper epidermis, and hyperplastic basal cells [9]. The preliminary differential diagnosis includes cutaneous lupus, pemphigus, Cushing's syndrome, leishmaniasis, refractory infectious pododermatitis, canine distemper, zinc responsive dermatitis, nutritional diseases or paraneoplastic syndrome [1,2].

The typical age of onset for this disease is approximately 4 to 16 years male and female dogs represent approximately 58% and 42%, respectively [1]. The majority of reported breeds are listed as mixed-not specified [5].

CASE

Here we report a case of Superficial necrolytic dermatitis (SND) in a bitch, emphasizing the corresponding clinical and ultrasound characteristics and histopathological findings of this disease. A 9-year-old, mixed-breed, neutered bitch was referred for clinical examination with 5 months history of hyperkeratosis and ulceration of the paw pads, presenting pain, lameness and weight loss. The bitch presented, lethargy, anorexia and skin lesions. On physical examination, skin scarred lesions on the left side of the dorsum (according to the owner, the adopted animal had previously been diagnosed 4 years ago with skin burns and was treated for it), hyperkeratosis, fissures, onychogryphosis, erosions and ulceration of the paw pads with myiasis, crusting on pressure points (Figure 1).

No microscopic parasites or fungal structures were observed on skin scrapings, and no dermatophytes were isolated on fungal culture. Cytological examination of tape preparations and impression smears from skin showed numerous cocci. Also, the Leishmania test¹ [IDEXX SNAP[®]] resulted negative. Hematological examinations consisted in full blood count (FBC) and biochemicals, revealing discrete anemia and neutrophilia. Elevated results of alkaline phosphatase (ALP = 666 U/L) and alanine aminotransferase (ALT = 86.8 U/L) were detected in the serum biochemical analysis. The blood glucose, blood urea, creatinine levels were within the reference ranges.

Imaging examinations (ultrasonography and radiography) were performed, showing a liver with



Figure 1. Skin lesions at first presentation. A- Crusts, hyperkeratosis in paw pads and onychogryphosis. B- Crusting on pressure points. C- Ulceration, exudation of the foot pads associated with myiasis. D- Recovery from injuries after 2 months of treatment.

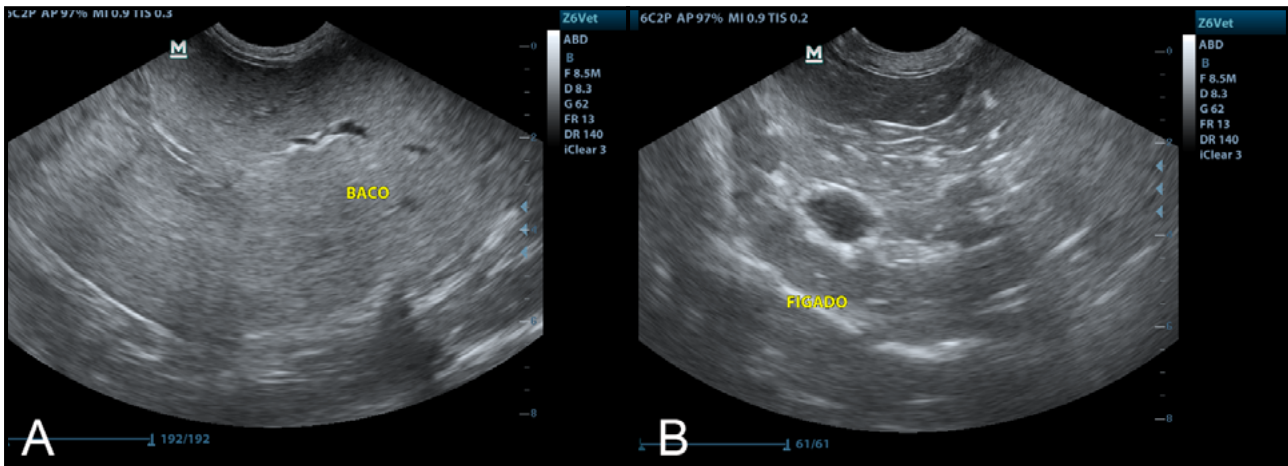


Figure 2. A- Appearance of enlarged spleen in ultrasonography. B- Liver with heterogeneous echotexture, mixed echogenicity, and irregular and poorly delimited margins presenting honeycomb.

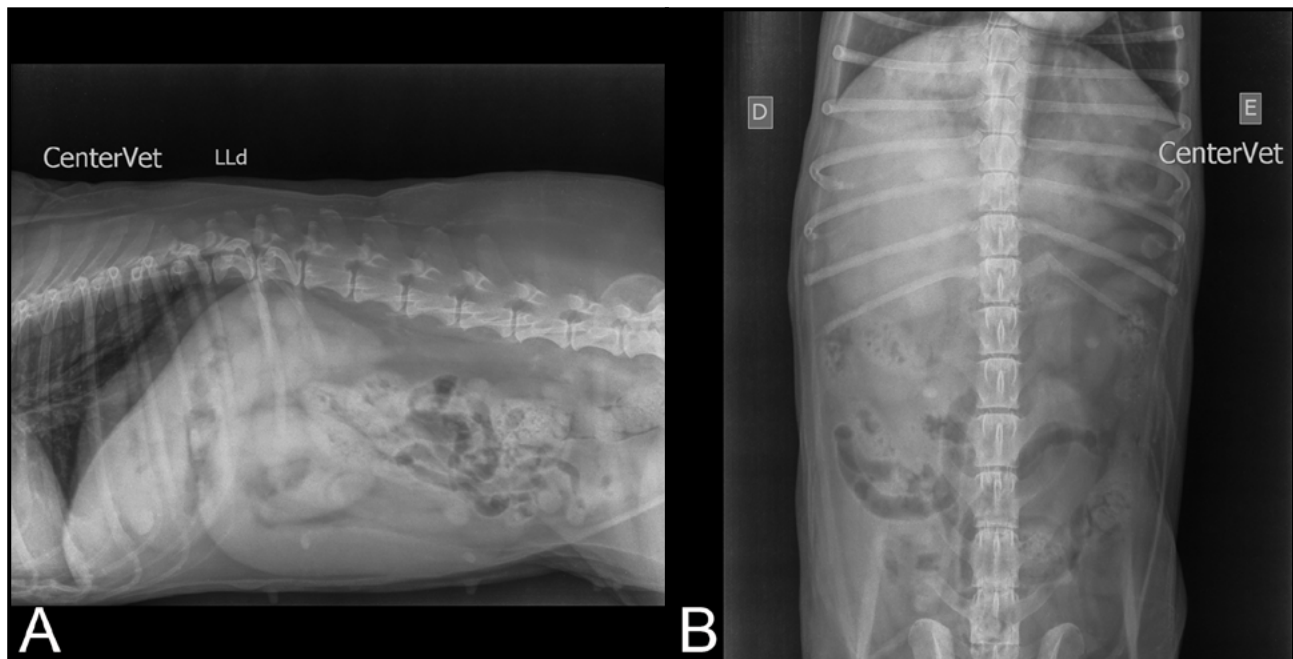


Figure 3. Radiograph showing a splenomegaly and microepathy. A- Right lateral view. B- Supine position.

heterogeneous echotexture, mixed echogenicity, irregular and poorly delimited margins with hypoechoic nodules throughout like honeycombs. Other findings consisted in the gallbladder with a moderately thick layer and splenomegaly with homogeneous tissue echotexture (Figure 2). There were no changes in other abdominal organs and thoracic radiographs were within normal limits. An abdominal radiographic examination confirmed the splenomegaly (Figure 3).

For histopathological analysis, the skin biopsies were collected and fixed in 10% neutral buffered formalin, processed routinely for histological examination, and embedded in paraffin blocks. Sections were

stained with hematoxylin and eosin and examined histologically. At the time of the biopsy procedure (under anesthesia with propofol), the hyperkeratosis of the foot pads was removed, and the nails were cut. As a result, it was observed an improvement in relieving the pain and lameness, contributing with the patient's quality of life. Histological analysis confirmed the diagnosis of SND, with skin biopsies showing an increase in thickness of the epidermis due to irregular hyperplasia and proliferation of keratinocytes in the basal layer of the epidermis, pallor of the spinous layer of the epidermis and important parakeratosis (Figure 4).

Initial treatment included amoxicillin/clavulanic acid antibiotics² [Zoetis, Synulox[®] - 13 mg/kg, PO, BID, 20 days], prednisone steroidal anti-inflammatory³ [MSD, Meticorten[®] - 1 mg/kg, PO, SID, 14 days], Silimarina liver protector⁴ [manipulated medication - 20 mg/kg, PO, SID, continuous use] and amino acid, mineral and vitamin supplement⁵ [Aminomix Pet Pills[®] - 1 pill/5 kg, PO, SID, continuous use]. Secondary infections were treated with topical washes with chlorhexidine 3%⁶ [Virbac, Hexadene Spherulites[®] - twice a week]. In addition, the diet was changed to a commercial diet with super premium feed⁷ [Farmina, Cibau Senior Medium Breeds[®]] supplemented with 2 eggs once a day.

The dog had an improvement in the skin lesions and the owner reported an improved level of activity, presumably because of reduced foot pad discomfort for 6 months. Then, the dog returned with abdominal pain and weight loss, in addition to vomit, diarrhea, jaundice skin, inappetence and anorexia. The serum biochemical

profile revealed increased alkaline phosphatase levels (1,870 U/L; reference value < 156 U/L), and alanine aminotransferase (ALT = 460 U/L; reference value < 74 U/L) and of the glucose levels (580 mg/dL; reference value from 60 to 100 mg/dL).

Due to the poor prognosis, the owner opted for euthanasia. A necropsy was immediately performed to allow assessment of the liver and pancreas. The pancreas appeared grossly normal, but the liver was reduced in size and multiple nodules of variable size were present throughout the parenchyma (Figure 5). The biopsies showed a severe proliferative chronic hepatitis (macro-nodular liver cirrhosis pattern), steatosis and cholestasis associated with pancreatitis and necrotic multifocal proliferative fibrinopurulent areas in pancreas.

DISCUSSION

The etiology of the hepatic disease in most of these cases is idiopathic [1,13]. Although, a specific etiology is described in cases uses a long-term

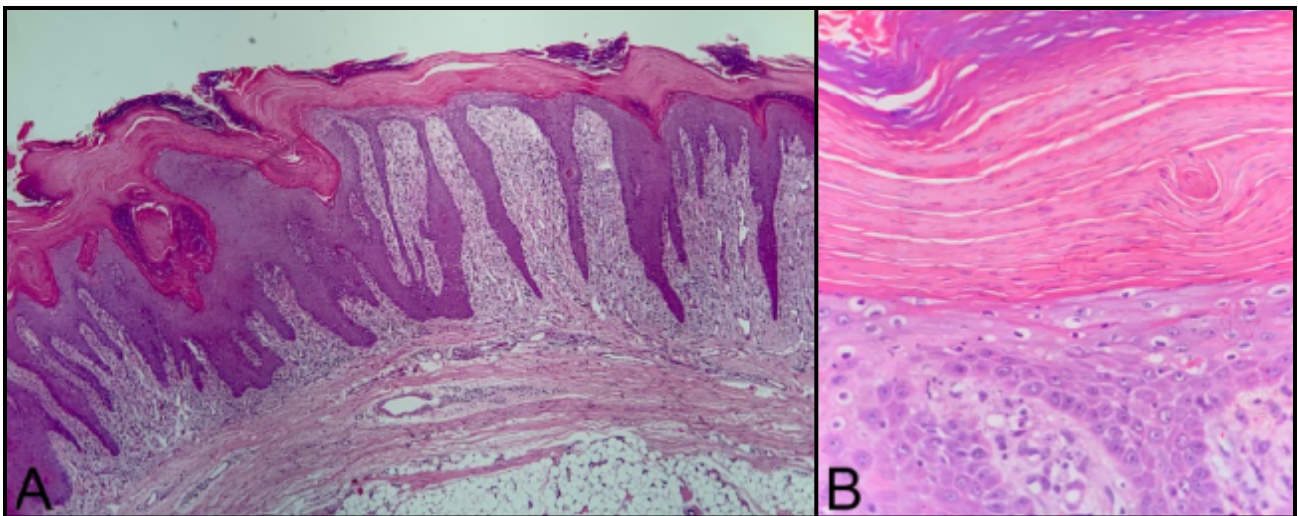


Figure 4. Histopathological appearance of the skin biopsy. Increase in the thickness of the epidermis due to irregular hyperplasia. Note the proliferation of keratinocytes in the basal layer of the epidermis, pallor of the spinous layer of the epidermis and important parakeratosis. [HE; A: 5x & B: 40x].



Figure 5. Exploratory laparotomy. A & B- Liver was reduced in size and multiple nodules of variable size were present throughout the parenchyma. C- Pancreas appeared grossly normal.

anticonvulsant therapy [2,8] however, the patient described was not using an anticonvulsant.

The results of the blood biochemical analysis were similar to articles previous episodes, where increased serum ALP and ALT are commonly reported, as in this case. Anemia and leukocytosis were reported in about 43% of cases, and these findings were present in the current case. Diabetes mellitus and hyperglycemia, present in about 40% of the cases, were also present in this case. The sonographic findings in this study matched those typically seen in previous studies of dogs with superficial necrolytic dermatitis, where a “swiss cheese” or “honeycomb” appearance of the liver was evident [8].

The pathogenesis of this disease is probably related to nutritional deficiencies or metabolic abnormalities caused by liver dysfunction. Nutritional imbalances that may be associated with this condition include zinc deficiency, hypoaminoacidemia, and decreased essential fatty acids. Profound hypoaminoacidemia has been found to be a consistent feature of this disease, with up to 80% reduction in a number of aminoacids [4].

The present patient received oral protein and essential fatty acid supplementation. Concurrent oral amino acid supplementation treatment seemed somewhat effective for the skin conditions, but the effect was not dramatic. It is possible that insufficient supplementation was given in this case, but the owner was unable to pay for the intravenous infusion. Temporary improvement in skin lesions is reported after using prednisone like this case. Importantly, although prednisone may result in improvement in skin lesions and relieve painful footpads, it may promote the occurrence of glucose intolerance and diabetes mellitus in dogs with Superficial Necrolytic Dermatitis [9]. In this case, the use of corticosteroids was the only medication that provided pain relief for the patient, but the prescription must be carefully evaluated, measuring the benefits and adverse effects it causes.

Because some of the lesions mimic other more common skin disorders in the dog, the prompt diagnosis of SND is often a challenge, especially if the lesions on the paw pads are not identified [3]. The gross appearance of the skin lesions in SND is seen in all cases, and thus, recognition of these lesions is necessary for the diagnosis of SND. The gross lesions are not, however, specific for SND, and the lesions can mimic those seen with other skin disorders such as refractory infectious pododermatitis, pemphigus

foliaceus, leishmaniasis, canine distemper, or zinc responsive dermatitis. Many dogs with SND have been treated for these presumptive disorders for weeks to months and then present with late-stage painful lesions that often prompts euthanasia [10, 13]. A skin biopsy can confirm a diagnosis of SND in these scenarios [3].

This case report shows that even though the incidence of hepatocutaneous syndrome is low [13], it should still be considered as a differential diagnosis in dogs with skin lesions. We highlighted the importance of submitting the skin biopsies for histopathology to reach a definitive diagnosis and so be able to determine the necessity for any additional therapies.

With a quick and early diagnosis of the disease, as well as the prescription of treatment when the owner has the financial means to do so, perhaps it can improve and increase the patient’s quality of life. However, with progressive worsening of the condition, frequently many owners opt for euthanasia as a way to shorten the suffering of the animal. New affordable nutritional and pharmacological strategies to treat or control the disease are needed in order to improve quality of life of SND patients.

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Ethical approval. The authors of this article declared, for all due purposes, the project that increased the present data has not been submitted for evaluation to the Ethics Committee of the Centro de Ensino Superior de Valença, Faculdade Veterinária, but we are aware of the content of the Brazilian resolutions of the National Council for Control of Animal Experimentation – CONCEA “<http://www.mct.gov.br/index.php/content/view/310553.html>” if it involves animals. This is a case report of a sick dog that was brought to Centro Clínico Veterinário by the owner. Therefore, the diagnostic procedures were necessary and are part of the diagnostic routine. Thus, the authors assume full responsibility for the presented data and are available for possible questions, should they be required by the competent authorities.

Declaration of interest. The authors report no conflicts of interest. The authors alone are responsible for the contents and writing of the paper.

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