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Successful Management of Hepatic Lipidosis Accompanied by a Feline Skin Fragility Syndrome-like Lesion in a Cat

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Abstract : A 7-year-old spayed female Somali-cross cat was admitted with a 4-week history of anorexia, vomiting, weight loss, and lethargy. The cat was diagnosed with hepatic lipidosis. With intensive care and nutritional support via a nasogastric feeding tube for 3 weeks, the clinical signs of hepatic lipidosis were improved. However, skin lesions were found in the left and right scapular regions during the treatment that were suspected to be due to feline skin fragility syndrome (FSFS). Intensive wound healing therapy with granulated sugar, laser therapy, and a surgical flap was conducted. Skin lesions improved uneventfully without other clinical signs or recurrence of any skin lesion for a year. To our knowledge, this is the first report of a good prognosis in a hepatic disorder and concurrent FSFS.

Key words **:** Cat, FSFS, granulated sugar, hepatic lipidosis.

Introduction

Feline skin fragility syndrome (FSFS) is characterized by fragile and thin skin with severe tearing that leads to the shedding of skin (4). The exact pathogenesis is not known; and has been reportedly associated with hyperadrenocorticism, diabetes mellitus, the use of progestational compounds and lymphoma (6). FSFS has also been seen in conjunction with severe liver disease, such as hepatic lipidosis, cholangiocarcinoma, and cholangiohepatitis (10). The prognosis of this syndrome is commonly poor, and most of the affected cats die spontaneously without a therapeutic response or are euthanized (5).

Case

A 7-year-old spayed female Somali-cross cat weighing 6 kg was presented with a 4-week history of anorexia, vomiting, weight loss, ptyalism, and lethargy. One seizure occurred just prior to admission to the hospital. The cat lived indoors and had changed living environments 4 weeks earlier. Vaccinations were current, and the patient was fed commercially prepared dry cat food. The vital signs were normal on physical examination. However, an estimated dehydration of 8% and jaundice were detected.

ELISA (Snap FIV/FeLV Combo Test; IDEXX Laboratories, USA) tests on a blood sample for FeLV and FIV were negative. Routine hematological assays revealed; an elevated WBC count with a left shift (40.25 $10 \times^{9}$/L; reference range: 5.5~19.5 $10 \times^{9}$/L). Abnormalities in serum biochemistry assays included increased activities of liver enzymes (Table 1). Total bilirubin levels were above the reference range, whereas glucose levels and ammonia levels were normal (Table 1). An examination of a coagulation panel indicated that the activated partial thromboplastin time (APT, 200 sec; reference interval 75-105 sec) and the prothrombin time (PT, 30 sec; reference interval 14-19 sec) were prolonged. Abdominal ultrasonography revealed severely hyperechoic liver parenchyma compared with the falciform fat, and the common bile duct was enlarged without obstruction of the gall bladder. The adrenal gland was within a normal range in shape and

Table 1. Serum biochemistry results for the cat with skin fragility syndrome with hepatic lipidosis

Blood panel	Reference range	Day 0	Day 34
ALP (U/L)	16-71	524	25
GGT (U/L)	0-6	3	Low
AST (U/L)	12-65	335	33
ALT (U/L)	22-109	588	66
Amylase (U/L)	467-1319	1349	693
BUN (mg/dL)	17.2-31.1	31.5	12.5
Glucose (mg/dL)	63-139	93	117
Phosphate (mg/dL)	2.7-8.1	3.8	5.5
Albumin (g/dL)	2.5-3.6	2.3	2.7
Cholestrol (mg/dL)	< 249	196	91
CK (U/L)	70-703	Dilute	1026
NH_3(mmol/L)	35-100	81	10
Total bilirubin (mg/dL)	0-0.2	2.4	0.2

ALP = alkaline phosphatase; GGT = gamma-glutamyltransferase; ALT = alanine aminotransferase; NH_3 = ammonia; CK = creatine kinase, np = not performed; BUN = Bloodurea nitrogen

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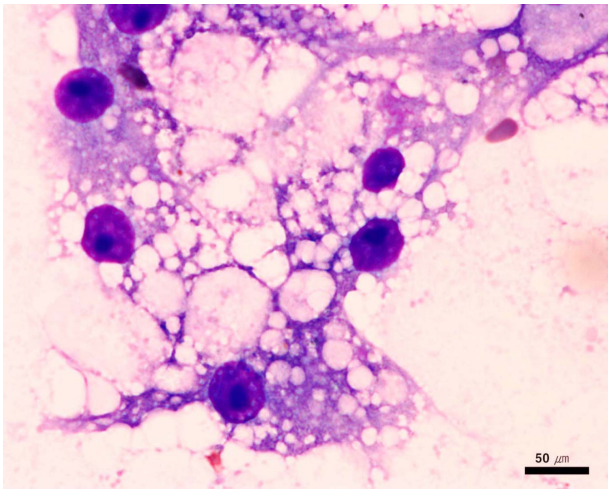

Fig 1. Fine needle aspiration of the liver. Variably sized, sharply defined, apparently empty vacuoles suspected as to be lipid vacuolation were observed within the hepatocyte cell cytoplasm.

size. On fine needle aspiration (FNA) of hepatic lesion, variably sized, lipid vacuoles within the cytoplasm of liver cells and in the background (Fig 1). Cytological impression was consistent with feline hepatic lipidosis. After hospitalization, aggressive fluid therapy for correcting the dehydration status was performed for three weeks. Concurrent supportive care was instituted with Vitamin K_1 (2 mg/kg, SC, once daily), Vitamin E (10 IU/kg, PO, once daily), maropitant citrate (1 mg/kg, SC, once daily), L-carnitine (250 mg/head, PO, once daily), s-adenosylmethionine (20 mg/kg, PO, once daily) and amoxicillin clavulanic acid (62.5 mg/head PO, twice daily). A nasoesophageal tube was placed for nutritional support. The clinical signs were improved and the nasoesophageal tube was removed on day 20 before the patient was discharged on day 21. After two weeks, the cat was re-admitted for evaluation for hepatic lipidosis. Activities of liver enzymes were all within reference range (Table 1), and a normal echogenicity of the liver parenchyma was observed. However, on physical examination, a thinning, hairless lesion with subjacent fluid, and an apparent burning sensation, a fragile skin lesion (8 × 8 cm) was noted on the right scapula (Fig 2A). The owner explained that the skin lesion initially looked

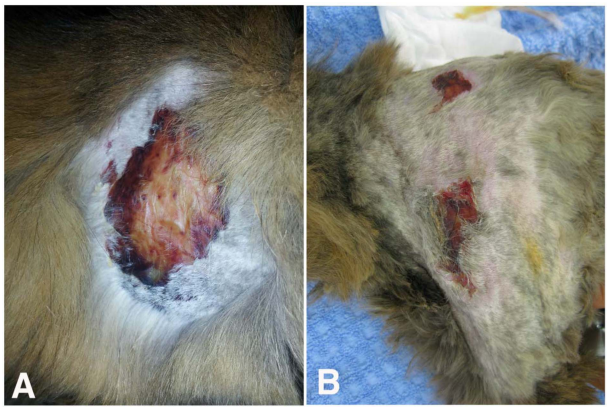

Fig 2. Skin lesions on both scapular areas. Thinning, hairless lesions with subjacent fluid and an apparent burning sensation, fragile skin lesions (8 × 8 cm) on the right scapular (A) and left scapular (B) regions were detected, and the outer skin was torn out without pain or bleeding (B).

like a paper cut but increased in width over a few days. FSFS was suspected because of the clinical manifestation, the cutaneous fragility in the absence of hyperextension and the underlying metabolic disease, hepatic lipidosis. To rule out other underlying diseases that lead to fragile skin, additional examinations were performed. Blood and urine glucose levels were within normal ranges, and the result of an adrenocorticotropic hormone stimulation test was also within the normal range. Additionally, a biopsy was performed once the lesion grew larger after a few days. A new skin lesion similar to a paper cut was found in the left scapular region, and the owner noticed that the lesion could be torn out by gently handling without bleeding or pain (Fig 2B). Microscopic examination revealed marked locally extensive ulceration. The ulcerated surface was covered with dense aggregates of neutrophils admixed with cellular debris. The area underlying the ulceration was infiltrated with a large number of neutrophils and a granuloma composed of macrophages, lymphocytes, and plasma cells (Fig 3).

Based on the patient's history of hepatic lipidosis and the apparent clinical signs, the cat was suspected to have acquired FSFS from the hepatic lipidosis, although the histopathological examination was ambiguous. The patient was

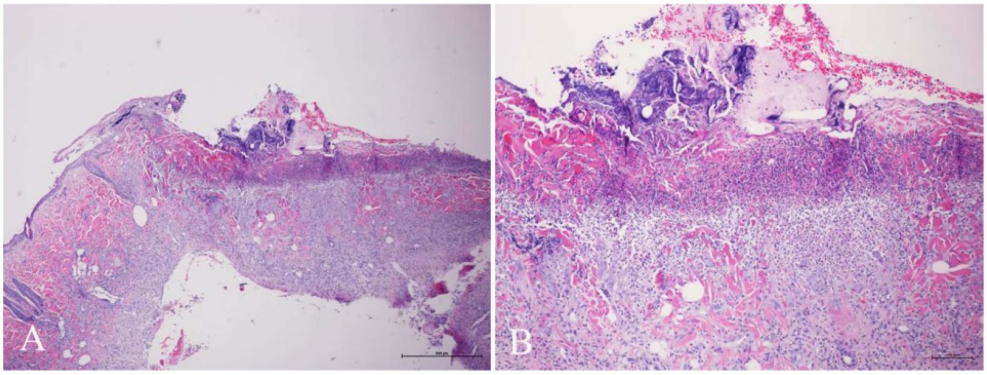

Fig 3. Histopathological examination. Skin from the right scapular region. Note the extensive ulceration covered with dense aggregates of neutrophils admixed with cellular debris (A). Higher magnification of (A). The dermis was infiltrated with a large number of neutrophils, accompanied by macrophages, lymphocytes, and plasma cells (B). H&E stain.

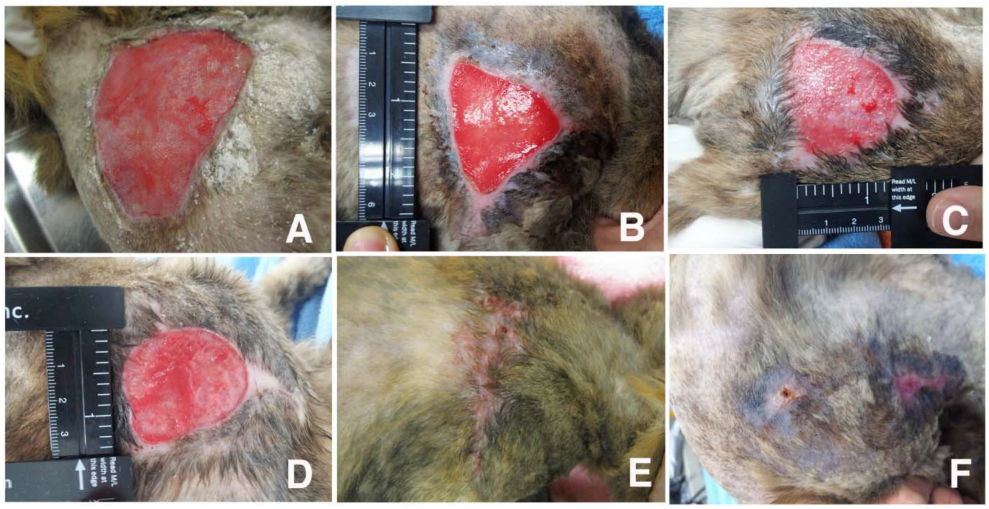

Fig 4. Skin lesion on the right scapular area. The skin lesion on right scapula was partially cured, and the affected skin area diminished 34% from the initial size (8 cm × 8 cm to 3.5 cm × 3.5 cm) (Fig 3). A surgical flap was performed to close the remaining lesion, and the outcome was successful. (A): Initial presentation after skin biopsy, (B): Day 10, (C): Day 30, (D): Day 66, (E): Day 80, (F): Day 99.

hospitalized, and granulated sugar was used as topical dressing agent. Granulated sugar was poured into the wound to a depth of at least 1 cm. A sterile absorbent wound towels were used as a primary bandage layer, and sterile lap sponges were then used as a secondary bandage. At the beginning of the sugar-dressing therapy, the dressing was changed twice daily to maintain a high osmolality. After an improvement in the accumulation of fluid, the dressing was changed daily with low-level laser therapy (Soft laser Dioss-620, Hanil ME Co., Ltd., Korea). The low-level laser therapy for wound healing was performed (7). The lesion on the left side was cured with scar tissue remaining. However, the skin lesion on the right scapula was only partially cured with the affected skin area diminishing 34% from the initial size (8 cm × 8 cm to 3.5 cm × 3.5 cm) (Fig 4). A surgical flap was performed to close the remaining lesion, and the outcome was successful. After the surgery the cat has been managed well without other clinical signs or recurrence of skin lesion.

Discussion

FSFS is very rare syndrome characterized by extremely thin and fragile skin, which is easily torn with minor trauma (1,2). Although the exact pathogenesis is unknown, an association with underlying diseases such as spontaneous Cushing's syndrome, diabetes mellitus, hepatic lipidosis, cholangiocarcinoma, renal disease or the excessive use of progestational compounds has been previously proposed (2). Middle-aged to older cats are frequently affected, and no sex predisposition has been reported. The affected skin develops irregular tears with gentle manipulation or minor trauma, and of sheets of skin are shed. Sometimes, partial alopecia may present at the most atrophic lesions. The skin is not hyperextensible; a feature that differentiates FSFS from Ehlers-Danlos syndrome. For unknown reasons, the lesions are most commonly found in the dorsal area of the trunk (2). The diagnosis of FSFS is chiefly based on clinical signs because the features of these lesions are very remarkable and unique (10). An appropriate skin biopsy for histopathological examination is difficult to achieve because of the fragile skin, the extreme atrophy of the dermis and the folding and twisting that occurs similar to that of tissue paper (2). The epidermis is thin, and the dermis is extremely atrophic. The dermal collagen fibers are severely attenuated, pale staining, and disorganized. Secondary inflammation and scarring may be present if a long-lasting lesion has been biopsied (2). Masson's trichrome stain may reveal abnormal collagen fiber cores that are stained red; in contrast, normal fibers are stained a diffuse blue (10). In the present case, the result of the histopathological examination were ambiguous; this is possibly because the skin biopsy was performed at an inappropriate time. The detection of secondary inflammation and ulceration may result from a delayed skin biopsy. In addition, although the skin biopsy was conducted on the initial lesion, the characteristics of FSFS, such as extremely fragile and atrophic skin, restrict use of the correct procedure. The biopsy samples were collected from a severe skin lesion; therefore, only extensive ulceration and necrotic features were found rather than delicate changes in the collagen fibers. Based on the histopathological examination, we suspected a traumatic event in the differential diagnosis of the skin lesion, but the gross features of such a lesion are quite different from those observed in our case, and there was no episode of trauma on taking history (1). Although the typical histopathological findings of FSFS were not noted in the biopsy sample, we suspected that this skin lesion was due to FSFS because of the following reasons: a new skin lesion occurred in the left scapular region, and some new skin lesions were scattered on the dorsal region; the healing of the lesion was delayed despite aggressive dressing; this was an apparently fragile skin lesion on gross examination; and the underlying disease of hepatic lipidosis. For the diagnosis of FSFS, the clinical symptoms from gross lesions and underlying diseases are important (4). In the histological examination, the loss of collagen layers was not found as with other FSFS cases. This may be attributed to the fact that we per-

formed the biopsy after the lesions were no longer growing larger. However, a histological examination can be used to determine a subtype and may provide evidence for a good prognosis. Not detecting the loss of collagen layers on histopathological examination may suggest or indicate a fair prognosis. Therefore, we must investigate the relationship between the results of the histopathological examination and the prognosis. To our knowledge, there are fewer than 4 cases associated with severe hepatic disorder among the reported cases of FSFS (8). In all these cases, the underlying hepatic disease became worse, and the patients died naturally or underwent euthanasia by the owner's request. In the previous cases, the cats also presented underlying diseases, such as tumors or severe conditions, for which the treatment times were too short and may have led to a poor prognosis and euthanasia. To date, the prognosis of FSFS has been reported to be poor, and the affected skin lesion was thought to be irreversible (10). However, in our case, the underlying disease was managed successfully, and we were able to focus on intensive wound management. Sugar therapy has many advantages, such as its antibacterial action, an improved granulation tissue formation and epithelialization, and an enhanced wound healing for widely open wounds (9). Granulated sugar acts as an excellent topical dressing for treating open wounds (9). Many previous studies have reported positive results with sugar dressing therapy for wound management (3). According to the guidelines for the treatment of wounds with sugar, sugar therapy can be applied to grossly contaminated wounds or for the preparation of a wound bed for skin grafting. FSFS patients have fragile skin; therefore, a skin graft is impossible. In the current case, we controlled the underlying disease first and then focused on the skin lesion. Applying sugar therapy with an alternative laser treatment, the skin lesion was kept from worsening for two months. Moreover, intensive daily dressing and being managed within a hospital environment for two months may have contributed to the successful outcome in the current case. After 2 months, the skin of the patient was no longer fragile, and a skin graft could be performed.

In conclusion, the cat was diagnosed with hepatic lipidosis and FSFS lesions were found in the left and right scapular regions during the treatment. Because of the successful management of the hepatic lipidosis and intensive wound healing therapy with granulated sugar, laser therapy, and a surgical flap, the cat had a successful outcome of the FSFS. To our knowledge, this is the first report of a good prognosis for concurrent FSFS and a hepatic disorder.

Conclusion

The prognosis of feline skin fragility syndrome is very poor and most of affected cat died or euthanized because of uncontrolled underlying disease and severe skin lesion. However at this case, feline skin fragility syndrome like lesion was successfully managed by intensive care of hepatic lipidosis and long term care with sugar therapy, low-level laser therapy and skin graft.

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고양이 피부유약증 유사병변을 동반한 지방간에 이환된 한 마리 고양이의 성공적인 치료증례

박형진 · 홍은지 · 권효정 · 박성준 · 박주민* · 송근호 · 서경원[1]

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요 약 : 7년령의 불임 암컷 소말리 교잡종 고양이가 4주 동안 지속된 식욕부진, 구토, 체중감소, 무기력을 주증으로 내원하였다. 환자는 지방간으로 진단 되었으며, 3주 동안 집중치료와 더불어 비위 영양관을 통해 유동식을 공급하였다. 치료기간 중, 지방간으로 인한 임상증상은 개선 되었지만 고양이 피부유약증으로 인한 것으로 의심되는 피부병변이 왼쪽과 오른쪽 어깨 부위에서 발견되었다. 과립당치료, 레이저치료 및 외과적 피판술을 통한 집중적인 상처 치유를 실시하였으며, 그 결과 환자는 다른 임상 증상이나 피부 병변의 재발 없이 성공적으로 치료되었다. 보고된 바에 따르면, 본 증례는 간질환과 고양이 피부유약증이 동반한 환자에서 좋은 예후를 보인 첫 번째 증례이다.

주요어 : 고양이, 고양이 피부유약증, 과립당, 지방간