Abstract

The paper presents three cases of Ehlers–Danlos syndrome, very rarely found in cats. The disease in this species is characterized by skin hyper-extensibility. Physical examination and additional diagnostics i.e. complete blood count, serum chemistry profile and histopathological examinations (including HE and van Gieson’s staining), as well as electronomicroscopic examinations. The diagnosis was based on physical examinations, and the results of additional testing. The values of extensibility index, which for the examined animals were 23.3%, 17.25%, and 21.2% respectively, were calculated. Histopathological examinations revealed a disorganized arrangement of collagen fibres. Electronomicroscopic examinations, revealed a diverse diameter of cross section of the fibres. One cat was treated with vitamin C at a dose of 50 mg/animal/d, after which a slight improvement in clinical condition was observed. Two cats were euthanized.

Key words: cats, dermal asthenia, symptoms, pathology, therapy.

Cutaneous asthenia, in human medicine known as Ehlers–Danlos syndrome, is a rare congenital skin disease in cats. It is primarily characterised by defects within the connective tissue of the dermis. Naturally occurring cases of this disease are reported in many animal species: horses (2, 13, 20, 21), cats (1, 3, 4, 6, 8, 14, 15, 17, 18), dogs (5, 12, 16, 17), rabbits (7, 10, 17), sheep, cattle, and mink. The disease was experimentally induced in transgenic mice (19). Ehlers–Danlos syndrome is also diagnosed in humans. In this case, it is divided into 10 types (11). The individual forms are connected with a dominant or recessive gene, or with chromosome X. In humans, the cause of the disease is thought to be related to some defects in collagen synthesis, e.g. in type VIIc the abnormalities are seen in the activity of procollagen peptidase. In types V, VIII, and X the functions of the mutated gene have not been described in details (11).

In cats, until recently, two types of cutaneous asthenia have been specified: the dominant and recessive mode of inheritance (5, 9, 15, 17) whereas in dogs, the disease is connected with a dominant gene. However, there are some suggestions about a recessive type occurring in this species (17).

Breed predispositions of the individual animal species to asthenia are reported. In dogs, the disease was most frequently observed in Dachshunds, Boxers, St Bernard dogs, German shepherds, Springers, Greyhounds, Irish setters, and Poodles (17). Cats in which the disease was diagnosed were Himalayans (3, 9, 17) or domestic shorthairs (5, 15, 17). Some authors claim that longhair breeds of cats are also predisposed to this skin condition (5). In neither of these two breeds sex predisposition was not found (5). In horses, cutaneous asthenia was reported in Quarter horses; and in one half-bred Arab horse (2, 20, 21). Sex predisposition of this species was not noted (20).

In cats, it was proved that defects in collagen structure that accompanies the disease are connected with a shortage of procollagen peptidase (3, 9, 17). Moreover, an increase in collagenase activity was noted (17).

In dogs and cats, clinical symptoms are mostly confined to the integument. In affected animals skin is thin and hyperextensible. It is prone to injuries, which results in typical slight bleeding wounds, which look like “fish mouth”. Sometimes haematomas are also formed (5, 17). Skin lesions are most commonly situated on the back and head. In some cases, apart from skin anomalies, disorders of other systems occur, such as joint laxity (in dogs only), or ocular disorders (e.g. lens
luxation). In affected cats, hernias are also reported (1, 5, 17).

The disease is diagnosed based on clinical signs and ancillary tests. It is very important to include a calculation of skin extensibility index in clinical examination. The average values of this parameter are over 14.5% in dogs, over 19% in cats, and 19.2% in rabbits (1, 6, 10, 14, 17).

Diagnosis is confirmed by histopathological examinations, revealing abnormal structure of collagen fibres, which lay at a distance from each other, and are fragmented into smaller parts and form an irregular pattern (17). There are, apart from the routine staining technique, several ancillary methods selectively revealing the structures of connective tissue. They are a useful tool in the diagnostic procedure. Van Gieson, Mallori and Masson staining techniques, are most commonly used (17, 18, 22). Definitive diagnosis may be established after examining a skin specimen under an electron microscope, which reveals the irregular structure of collagen fibres, having a diverse cross-section diameter (1, 2, 6, 14, 18).

The aim of the report is to present three clinical cases of cutaneous asthenia in cats.

**Material and Methods**

**Cat No. 1.** In December 2003, a one-year-old intact Burman female was presented to the Dermatological Clinic of the Faculty of Veterinary Medicine in Lublin, for the evaluation of skin hyperextensibility noticed 6 weeks before the presentation. No treatment had been previously applied. The parents of the animal, which were of Australian origin, displayed no clinical symptoms. Four months after the diagnosis numerous skin ruptures (dermatorrhexis) occurred, and the animal was euthanized.

**Cat No. 2.** In April 2004, a two-year-old male, domestic shorthair and Siamese cross, was presented to the Clinic. The owner noticed skin hyperextensibility, and 3 to 4 months before the presentation, slight bleeding wounds due to dermatorrhexis appeared. After the diagnosis was established, the cat was orally treated with vitamin C, at a dose of 50 mg/animal/d. After 6 months from initiating the treatment the wounds were not reported, though the skin was still hyperextensible.

**Cat No. 3.** In 2004, a four-month-old domestic shorthair female was presented to the Department and Clinic of Internal and Parasitological Diseases of Animals in Wroclaw. The owner noticed the first symptoms in a two-month-old animal. The owner reported skin hyperextensibility; the skin was frequently injured, which caused small slight bleeding wounds. The changes were pronounced on the head and neck. After the diagnosis the animal was euthanized.

Physical examinations were carried out in all three cases. The skin extensibility index was calculated according to the following formula:

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\text{Skin extensibility index} = \frac{\text{Length of a skin fold}}{\text{Length of an animal}} \times 100\%
\]

The length of a skin fold was measured on the back, while pulling it away from the backbone until pain was elicited. The length of an animal was measured from the tail base to the occiput (6, 14, 17).

In order to exclude parasitic and mycotic conditions, a microscopic examination of skin scrapings fixed in chlorolactophenol, and hair plucks were performed. Blood was sampled from the external jugular vein, and the parameters determined included, complete blood count, serum chemistry profile, as well as T4 level. After premedication with atropine and xylazine and local block with 1% lignocaine, two skin segments were sampled with a trepan 6 mm in diameter. The material was fixed in buffered formalin, and paraffin sections were made. For microscopic examinations, the slides were routinely stained with HE, and van Gieson’s stain. The remaining two specimens left, were fixed in 4% glutaryl aldehyde, and osmium tetroxide in phosphate buffered solution of pH 7.2, then dehydrated in alcohols and embedded in resin. The slides were stained with uranyl acetate, lead citrate, and then examined under electron microscope.

**Results and Discussion**

The overall condition of the animals was good. Hair thinning was not reported in any of the cats. In cat No. 1, skin eruptions were not present, whereas in two remaining animals wounds were surrounded by erythematous area. Skin hyperextensibility were confirmed in all cats (Fig. 1). Additionally, in cat No. 2 a slight bleeding wound was found on the back (Fig. 2), while in cat No. 3 such wounds were also present on the neck and sides of the chest. Skin extensibility index was 23.3% for the first animal, 17.5%, and 21.25% for the second and third one, respectively.

The examination of skin scrapings and hair plucks did not reveal parasites and dermatophytes. All of the haematological and biochemical parameters as well as T4 level were within the norm for this species.

The histopathological examination of HE stained specimens revealed thinning and folding of the epidermis as well as its hyperkeratosis. The collagen fibres were irregular and decreased in number (Fig. 3). Van Gieson’s staining confirmed the irregularity of collagen fibres, which were red-dyed. In some places the collagen bundles were fragmented into pieces that were separated by patchy free spaces (Fig. 4). Electron microscopy also revealed the irregular pattern of collagen fibres, and the diverse cross-section diameter (Fig. 5).
Fig. 1. Cat No. 1. Apparent skin extensibility.

Fig. 2. Cat No. 2. The area on the back – note this slight bleeding wound due to dermatorrhesis.

Fig. 3. Decrease in the number of collagen fibres and their irregular pattern. HE 100 x.

Fig. 4. Irregular pattern of the collagen fibres. In some regions the collagen bundles are fragmented and separated by patchy free spaces. Van Gieson staining, 100 x.

Fig. 5. Electronomicroscopy. Note the diverse cross-section diameter of the collagen fibres. 25 000 x.
In cats, cutaneous asthenia is a rare genetic anomaly. There are no reports in Polish-language publications. The disease is also referred to as Ehlers–Danlos syndrome, dermatosparaxis and hyperelastosis cutis (2, 3, 8, 17, 18, 21). Diagnosis is based on clinical symptoms and histopathological examinations. The increase in skin extensibility index is regarded to be the most important clinical feature. According to most authors, the value should be 19% in affected cats, whereas in dogs 14.5% is relevant for diagnosis (1, 4, 6, 14, 17). In the presented cases, values of skin extensibility index for the second cat were slightly lower (i.e. 17.25%) than suggested by the others. Some authors claim that this result depends on many factors; such as age, sex, dehydration degree, and overall condition (6). Moreover, in the case of Ehlers–Danlos syndrome in cats, values of skin extensibility index may be lower than generally accepted.

The histopathological examination of the specimens stained with HE revealed the apparent disorders in the structure of collagen fibres, the decrease in their number, as well as fragmentation and shortening of the fibres. In most of the publications, the epidermal lesions, i.e. thinning and hyperkeratosis reported in this paper, were not described (1, 5, 18).

Electron microscopy revealed the diverse cross-section diameter of the fibres and their irregular pattern. Similar findings were also reported by other authors (1, 2, 6, 14, 18, 21). In addition, some of them had noted an irregular outline of the collagen fibres (6, 18). In the cases presented, such abnormalities were not observed.

Specific treatment protocol has not been established so far, but some authors suggest that oral administration of vitamin C, necessary for collagen synthesis, to cats (50 mg/animal/d), and to dogs (500 mg/animal/d), may improve the clinical condition (14, 17). It is also necessary to provide animals with proper care and management, and to prevent skin injuries. The improvement was noted in cat No. 2, though the prognosis in case of Ehlers–Danlos syndrome is usually poor.

References