Immunological deep dermal vasculitis in a cat

Immunologische, diepe dermale vasculitis bij een kat

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ABSTRACT

In this case report, a 13.5-year-old, neutered, female domestic shorthaired cat with immunological deep dermal vasculitis is described. The patient was presented with lethargy, fever, polydipsia, anorexia and swollen distal limbs. Dermatological examination revealed partial alopecia, pitting edema and painfulness in all distal limbs. Several diagnostic examinations were conducted to confirm the suspected diagnosis and to look for possible triggers of cutaneous vasculitis. Morphological changes that were indicative for deep dermal vasculitis were seen during the histological examination of the skin. The other examinations did not reveal an underlying trigger or cause of the dermal vasculitis. The cat was diagnosed with immunological deep dermal vasculitis. The cat was treated with antibiotics, infusion, tube feeding and prednisolone. Improvement and healing of the dermal symptoms were only noticed after the start of prednisolone therapy.

SAMENVATTING

In deze casuïstiek wordt een 13,5 jaar oude, vrouwelijke, gesteriliseerde Europese korthaar beschreven met immunologische, diepe dermale vasculitis aan de distale ledematen. De patiënt werd aangeboden met lethargie, koorts, polydipsie, anorexie en opzetting van de distale ledematen. Op het dermatologisch onderzoek werd partiële alopecia, oedeem en pijn aan alle distale ledematen vastgesteld. Verschillende diagnostische onderzoeken werden uitgevoerd om het vermoeden van dermale vasculitis te bevestigen en een onderliggende oorzaak op te sporen. Op het histologisch onderzoek van de huid werden veranderingen aangetoond die duidden op diepe dermale vasculitis. De andere onderzoeksresultaten wezen geen onderliggende oorzaak voor de dermale vasculitis aan. De diagnose van immunologische, diepe dermale vasculitis werd gesteld. De kat werd behandeld met antibiotica, infuus, nasoesofagale sondevoeding en prednisolone. Verbetering en genezing van de vasculitisletsels werden slechts gezien na het opstarten van de prednisolonetherapie.

INTRODUCTION

Vasculitis is a process of inflammation and destruction of blood vessels mediated by neutrophils, lymphocytes or macrophages (Gross et al., 1992; Griffin et al., 1993). An abnormal immune response, which is not a disease itself but a symptom, leads to cutaneous vasculitis (Innerå, 2013). Common dermal symptoms of vasculitis are crateriform ulcers, necrosis, pustules or papules, hemorrhagic bullae, plaques and palpable purpurae at distal extremities, such as the paws, tail, pinnae, scrotum and oral mucous membranes (Miller et al., 2013). The location of the lesions is typically associated with the pathway of the vessels (Miller et al., 2013). To confirm the diagnosis of cutaneous vasculitis, histology of deep dermal biopsies is needed (Innerå, 2013).

In veterinary medicine, the classification of cutaneous vasculitis is based on histological inflammatory patterns (Gross et al., 2005). Vasculitides are categorized in leukocytoclastic (nuclear cell dust in and around vessel walls) or non-leukocytoclastic, and are then subdivided according to the degree of neutrophilic, eosinophilic or lymphocytic cell invasion of vessel walls (Gross et al., 2005). It must be noted that histological lesions evolve over time and that infiltrates of mixed inflammatory cells are common in older lesions (Nichols et al., 2001).

If vasculitis is diagnosed, a proper diagnostic search for an underlying cause is recommended (Innerå,

2013). In human medicine, small vessel leukocytoclastic vasculitis has been attributed to a long list of possible causes (infections: bacterial, viral, parasitic; drugs; chemical substances; chronic persistent disorders: autoimmune connective tissue diseases, inflammatory bowel diseases; neoplasia; certain foods or additives) (Carlson et al., 2005). However, in human as well as in veterinary medicine, approximately 50 % of the cases are categorized as idiopathic vasculitis (Carlson, et al., 2005; Tai et al., 2006; Jasani et al., 2008). Cutaneous vasculitis has rarely been diagnosed in cats (Miller et al., 2013), and only few cases have been described. Reported underlying causes are feline infectious peritonitis (FIP), the application of fenbendazole, cimetidine and rabies vaccine. In several cases, an underlying cause is not found (McEwan et al., 1987; Gross, 1999; Nichols et al., 2001; Cannon et al., 2005; Declerq et al., 2008; Jasani et al., 2008).

In this article, a cat with immunological deep dermal vasculitis is described.

CASE REPORT

A 13.5-year-old, neutered, female domestic short hair cat was brought to the referring veterinarian because of polydipsia, which had already been present for some months, acute lameness of the right hind limb and lethargy. The detailed history revealed that the cat had been vaccinated six months before, the owner had not changed the diet before the symptoms started and that the cat had never been treated with medication except for tolfenamic acid (Tolfedine®, Vétoquinol SA, Belgium) some years before. At physical examination (day 0), the cat was febrile (T°40.5°C) and the right hind limb was painful. Therapy with amoxicillin-clavulanic acid (Synulox®, Zoetis Belgium SA, Belgium; 8.75 mg/kg s.c., sid) and tolfenamic acid (Tolfedine®, Vétoquinol SA, Belgium; 4 mg/kg s.c., sid) was instituted. At day 2, the cat was less lethargic, but a soft swelling of the distal right hind limb (metatarsus, digits) was noticed. Temperature was 39.2°C and the cat became anorectic. Therapy was changed to amoxicillin-clavulanic acid (Synulox®, Zoetis Belgium SA, Belgium; 8.75 mg/kg s.c., sid), clindamycin hydrochloride (Antirobe®, Zoetis Belgium SA, Belgium; 25 mg bid, p.o.) and meloxicam (Meloxidyl®, Céva Santé Animale, Belgium; 0.2 mg sid, p.o.). At day 6, the cat was presented with lethargy and persistent anorexia. The referring veterinarian noticed a temperature of 37.4°C and soft painful swelling of the distal part of both hind limbs (metatarsus and digits). The owners were unable to give the clindamycin hydrochloride. The cat was hospitalized and intravenous infusion with lactated Ringer's solution (Hartmann®, B. Braun Melsungen AG, Germany) was started. The treatment with amoxicillin-clavulanic acid was continued and the treatment with meloxicam (Meloxidyl®, Céva Santé Animale, Belgium) was stopped. At day 7, the distal part of the left front limb (metacarpus, digits) was swollen too, body temperature was within the normal range and the other symptoms remained stable. The next day, force feeding was started (day 8). At day 9, serous fluid was oozing from the right hind limb and clindamycin hydrochloride (Antirobe®, Zoetis Belgium SA, Belgium; 25 mg bid, p.o.) was started. At day 10, all paws showed leakage of serous fluid. Tolfenamic acid (Tolfedine®,Vétoquinol SA, Belgium:4 mg/kg s.c., sid) was given once and buprenorphine (Vetergesic®, Alstoe Limited, United Kingdom; 10 µg/kg i.v., tid) was started. During hospitalization, there was persistent anorexia, intermittent fever and painful and swollen distal limbs. Several blood examinations were performed at day 5, 7, and 9, of which the last one at day 9 was the most comprehensive with a complete blood count (CBC) and biochemistry including protein electrophoresis (Table 1). Blood examination revealed moderate leukocytosis (mature neutrophilia, monocytosis), mild anemia (decreased hemoglobin and hematocrit), thrombocytopenia (not checked on cytology), hypoalbuminemia, increased α 1 and α 2 globulines, moderate hyperbilirubinemia, mild hyperchloremia, moderately increased lactate dehydrogenase, azotemia and hyperphosphatemia. Azotemia and hyperphosphatemia were normalized at day 9, hypoalbuminemia worsened over time.

On day 12, the cat was referred to the internal medicine service of the Department of Medicine and Clinical Biology of Small Animals, Faculty of Veterinary Medicine, Ghent University, Belgium. Physical and dermatological examinations revealed dental plaque, mild tachycardia and intense pitting edema at all distal limbs, including warm and painful skin. The hair was easy to epilate from the abdomen and tarsi. Partial alopecia was present at the proximal ventral part of the tail and at the extremities (tarsi, metatarsi, metacarpi, digits) (Figure 1). On the tarsi and digits, there were erosions and brown crusts. There was severe swelling and partial alopecia around the cuticles. On the dorsal metacarpal area of the left front limb, where the first catheter had been placed, the skin was erythematous and crusty (Figure 2). Under digital pressure, serous fluid passed through the skin of the dorsal side of the right distal front limb. The combination of fever with warm, painful edematous swelling of all distal extremities was suspicious for cutaneous vasculitis.

Several diagnostic examinations were conducted to confirm the vasculitis, and look for possible triggers (e.g. infection, neoplasia, inflammation) of cutaneous vasculitis. An impression smear of the erythematous and crusty parts of the skin of the distal limbs was made and stained with Diff Quick solution. It showed degenerated neutrophils and some cocci that were not phagocytized. Anesthesia was required for the other diagnostic tests. The cat was premedicated with methadone (Comfortan®, Eurovet Animal Health BV,

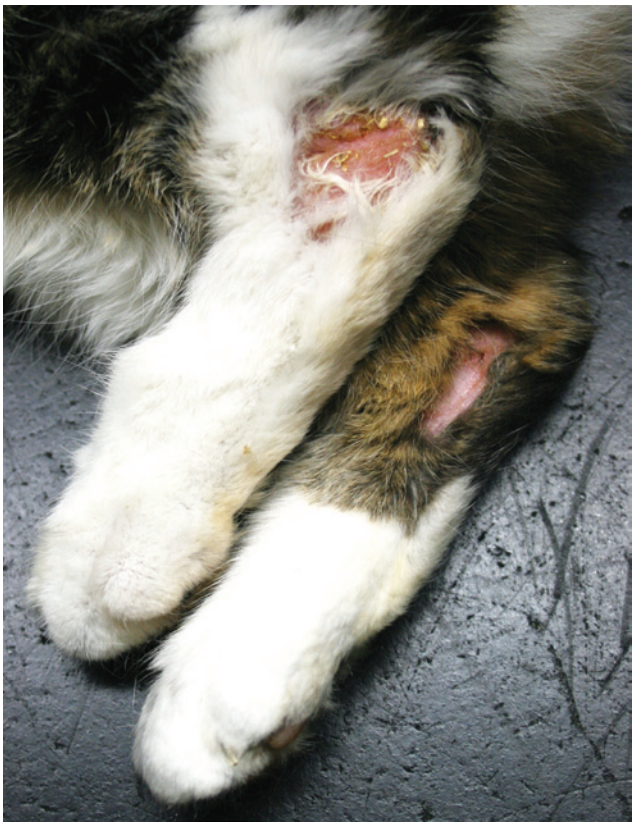

Figure 1. Brown crusts, erosions and partial alopecia of the tarsi and swollen paws.

the Netherlands; 0.02mg/kg, i.v.). For induction and maintenance, alfaxalon (Alfaxan®, Jurox Limited, United Kingdom; induction: 5 mg/kg i.v., maintenance: on effect, in total including the induction 20 mg/kg was used) were given as boli. Mouth inspection under anesthesia was done to assess if mucosal lesions or infections were present. It presented no abnormalities besides moderate dental plaque. The complete blood cell count and some biochemical blood parameters were repeated. A mild hypoalbuminemia, leukocytosis, consisting of neutrophilia and monocytosis, mild basophilia, and non-regenerative anemia were present (day 12) (Table 2). A SNAP® Combo test (IDEXX Laboratories Europe BV, the Netherlands) for feline leukemia virus antigen and feline immunodeficiency virus antibody was negative. Serum was sent to Algemeen Medisch Laboratorium Diergeneeskunde Antwerpen (MEDVET) for serology of toxoplasmosis. The titre of IgM was negative and the titre of IgG was highly positive, which indicated that the cat had immunity against *Toxoplasma*, but had no active, clinical disease. An abdominal ultrasound and thoracic radiographs were conducted to look for underlying neoplastic or inflammatory diseases. Thoracic radiographs (ventrodorsal and right lateral) revealed a mild interstitial lung pattern of the left caudal lung lobe which could have been caused by the decubitus of the cat prior to the radiographs were taken. There was also a suspicion of mild pleural effusion, but there was too little fluid to conduct a thoracocentesis. Reduced echogenicity of the liver parenchyma with prominent portal veins, mild heterogeneity of the pancreas, mildly reduced size and rounded appearance of the left kidney associated with a reduced corticomedullary definition and hyperechogenic cortex of the right kidney were noted on ultrasonography. Cystocentesis and fine-needle aspi-

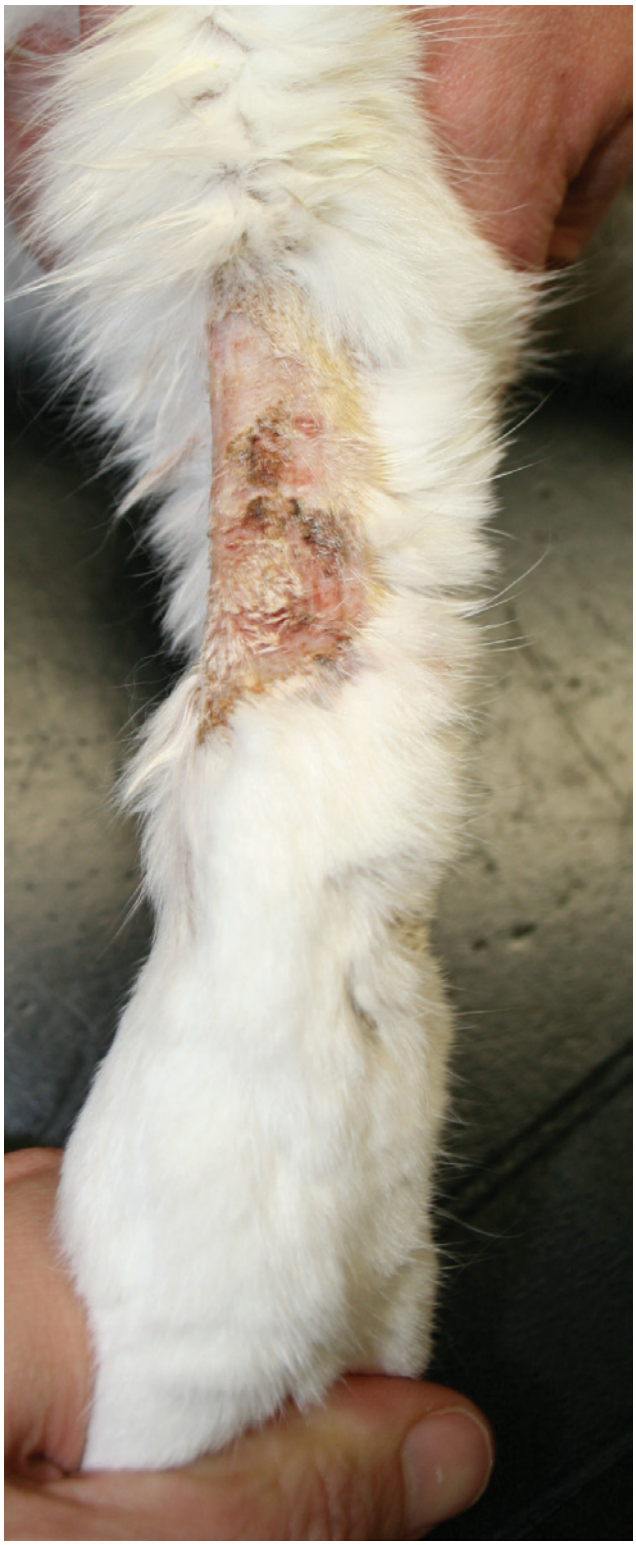

Figure 2. Erythematous and crusty skin of the left front limb.

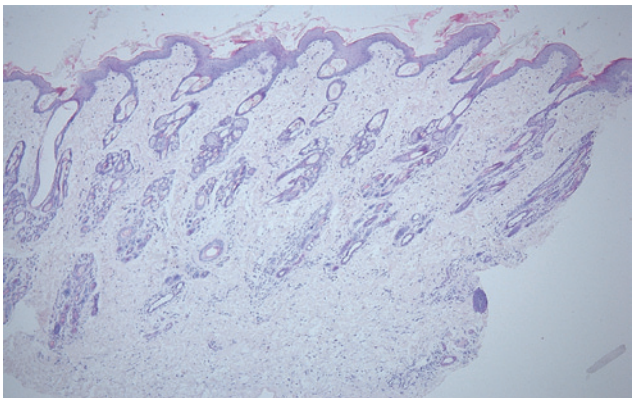

Figure 3. Skin biopsy. Serocellular crusts on the epidermis, edema of the superficial and deep dermis, perivascular to interstitial mixed infiltration of inflammatory cells (mast cells, lymphocytes, neutrophils, few eosinophils), reactive fibroblasts (magnification 5x).

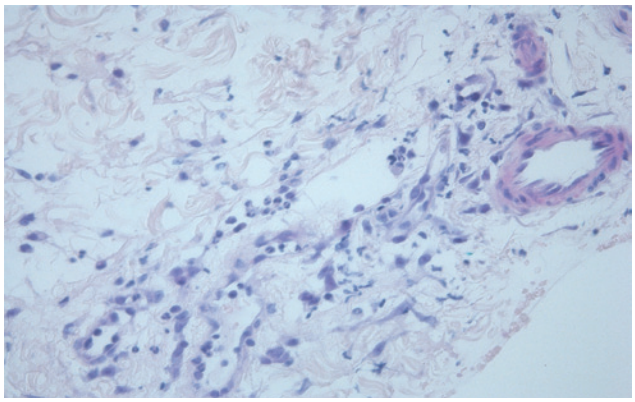

Figure 4. Skin biopsy of the deep dermis. Small arteries and venules with perivascular infiltration of inflammatory cells (mast cells, lymphocytes, neutrophils, few eosinophils), edema of the surrounding dermis, reactive fibroblasts (magnification 40x).

ration of the liver were performed to evaluate for the presence of lymphoma and hepatic lipidosis. Cytology of the liver showed mild hepatocellular degeneration, the presence of non-degenerated neutrophils in and around clusters of hepatocytes. It was difficult to distinguish if the presence of neutrophils could indicate mild lymphocytic cholangitis or if these were due to mild blood contamination. Urinalysis consisted of urine specific gravity, microscopic sediment analysis, urine dipstick (protein, glucose, ketones, hemoglobin, bilirubin, urobilinogen, acetone, nitrite, leukocytes, pH), urinary protein/creatinine ratio and bacterial culture. This was done to exclude urinary tract infection and inflammation and to assess renal function considering a possible glomerulonephritis or renal vasculitis as a representation of a more generalized vasculitis. Urinalysis only revealed isosthenuric urine (USG 1.016) and very mild proteinuria (0.4). A dorsopalmar view of the distal right hind limb was taken to evaluate bony structures, which showed no bony abnormalities. Five punch biopsies of the skin (two of the left front limb in the area of the skin lesions, two dorsally of right front limb, one of left lateral tarsus) were taken. After taking the biopsies, all biopsy sites were bandaged.

Based on the clinical and dermatological findings, an immunological dermal vasculitis was considered to be the most likely differential diagnosis. Awaiting the results of the histopathology and toxoplasmosis serology, therapy with prednisolone (Codipred®, Codifar NV, Belgium; 1mg/kg i.m., sid) was started. Amoxicillin and clavulanic acid (Synulox®, Zoetis Belgium SA, Belgium; 8.75 mg/kg s.c., sid), clindamycin hydrochloride (Antirobe®, Zoetis Belgium SA, Belgium; 12.5 mg/kg p.o., bid), buprenorphine (Vetergesic®, Alstoe Limited, United Kindom; 10 µg/kg i.v., qid) and infusion therapy with lactated Ringer's solution (Hartmann®, B. Braun Melsungen AG, Germany; 80 ml/kg/ 24 hours i.v.) were continued. A nasoesophageal feeding tube was placed and tube feeding with a protein- and calorie-rich diet (Royal Canin Convalescence Support®, Royal Canin, France) was started. On the second day in the Small Animal Clinic of the Faculty of Veterinary Medicine, (UGhent), the cat ate some food spontaneously, and the rest of its daily food requirement was tubefed. Body temperature was normal. The condition of the right front limb was unaltered. Serous fluid passed through the skin of the left front limb under digital pressure. The other limbs were still bandaged. The level of anemia and hypoalbuminemia remained stable (day 13) (Table 2). The next day, the cat ate its complete nutritional requirement spontaneously. Infusion therapy and tube feeding were stopped. The paws were markedly less swollen and less painful. There were still multiple crusts on the skin of the paws. The application

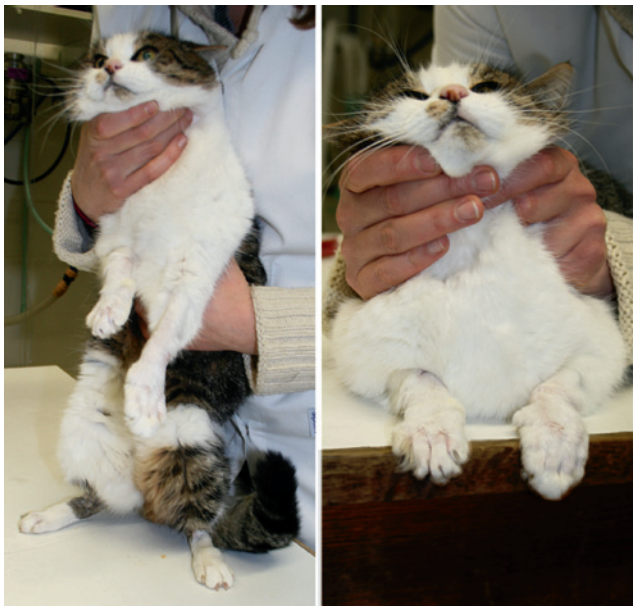

Figure 5. At recheck one month later, the paws were not swollen and hair was regrowing.

Table 1. Results of blood examinations performed by the referring veterinarian.

Parameter	Day 5	Day 7	Day 9	Month 6	Reference interval	Unit
Hematology						
Erythrocytes	7.86		5.79	7.29	5.5 - 10.0	10^{12}/L
Leukocytes	11.7		**36.5**	8.7	5.5 - 15.5	10^9/L
Band neutrophils			**1.83**		0 - 0.42	10^9/L
Segmented neutrophils	10.5		**26.2**	5.6	3.0 - 11.5	10^9/L
Eosinophils	0.21		0.4	0.9	0.05 - 1.10	10^9/L
Basophils	0		0	0	0 - 0.1	10^9/L
Lymphocytes	**0.6**		5	1.9	1.2 - 5.6	10^9/L
Monocytes	0.47		**3.11**	0.25	0 - 0.7	10^9/L
Hemoglobin	7.3		**4.7**	6.3	5.4 - 9.9	mmol/L
Hematocrit	269		**224**	272	260 - 460	ml/L
MCV	**34**		**39**	**37**	40 - 55	fL
MCH	9		8	9	8.00 - 10.6	fmol
MCHC	**27**		21	**24**	18.6 - 23.6	mmol/L
Thrombocytes	246		**126**	323	190 - 430	10^9/L
Biochemistry						
Glucose (sober)				3.9	3.5-6.0	mmol/L
Total protein		65	55	84.3	55.0 - 85.0	g/L
Albumin	**27.5**	**22.6**	**18.4**	35.6	31 - 40	g/L
Alfa 1 globulin			**2**		0,5 - 1.5	g/L
Alfa 2 globulin			**15.8**		9 - 15	g/L
Beta globulin			7.9		7 - 11	g/L
Gamma globulin			14.4		7 - 18	g/L
Urea	**34.6**	**27.3**	9.9	**17.3**	5.90 - 12.50	mmol/L
Creatinine	**403.1**	**287.3**	115.8	**225.42**	70 - 130	µmol/L
LDH			**425**		80 - 170	U/L
AST	34		43	17	< 60	U/L
ALT	**24**		**27**	47	37 - 75	U/L
Bilirubin total			**11.62**		2.50 - 3.50	µmol/L
Bilirubin direct			**11.28**		1.71 - 2.50	µmol/L
GGT			< 3		0 - 8	U/L
ALP			39	34	10 - 50	U/L
Bile acid			3	17	< 20	µmol/L
Lipase				11	< 250	U/L
Sodium		151	150	**161**	146 - 158	mmol/L
Potassium		3.8	3.7	4.6	3.40 - 5.20	mmol/L
Chloride		105	**117**	**123**	105 - 112	mmol/L
Calcium		2.2	2.1	2.63	1.80 - 3.00	mmol/L
Phosphor		**2.6**	1.5	**1.95**	1.10.- 1.60	mmol/L
Hormones						
T4	**< 6.4**			13.6	12 - 52	mmol/L

Bold written data are outside the reference interval. ALP= alkaline phosphatase, ALT= alanin aminotransferase, AST= aspartate aminotransferase, GGT= gamma-glutamyltransferase, LDH= lactate dehydrogenase, MCH= Mean corpuscular hemoglobin, MCHC= mean corpuscular hemoglobin concentration, MCV= mean corpuscular volume

of amoxicillin-clavulanic acid was changed to per os (Clavubactin®, Le Vet BV, the Netherlands; 12.5 mg/kg p.o., bid). On day 15, the clinical condition improved further. Only the toes remained painful and the distal limbs were still mildly swollen. A complete blood cell count, albumin, creatinine and total bilirubin were repeated (day 15) (Table 2). The results confirmed the anemia and a mild hypoalbuminemia, but the monocytosis and neutrophilia had improved. On the next day (day16), the cat was discharged. Therapy with prednisolone (Prednisolone®, Kela Laboratoria, Belgium; 1.1 mg/kg p.o., sid), amoxicillin-clavulanic acid (Clavubactin®, Le Vet BV, the Netherlands; 12.5 mg/kg p.o., bid), clindamycin hydrochloride (Antirobe®, Zoetis Belgium SA, Belgium; 12.5 mg/kg p.o., bid) and buprenorphine (Vetergesic®, Alstoe Limited, United Kindom; 10 µg/kg p.o.) in case of pain was continued awaiting the laboratory results. One week after discharge from the clinic, all laboratory results were available, and because there was no infection, the antibiotic therapy was discontinued. The histopathological results showed that all skin biopsies had similar morphological changes (Figures 3 and 4). On the epidermis, serocellular crusts were seen. The superficial and deep dermis were edematous. A perivascular to interstitial mixed infiltration of inflammatory cells (mast cells, lymphocytes, neutrophils, few eosinophils) and many reactive fibroblasts were seen. Small foci of extravasation of red blood cells and some thrombi in the blood vessels were present in the deep dermis and panniculus. Focally, there were several blood vessel lumina in which numerous neutrophils were seen. Although mural infiltration was not seen, the fact that the alterations were worse in the panniculus suggests that there were mural infiltrations of the vessel walls in bigger, deeper vessels, which were not included in the biopsy. The observed changes were suggestive for deep dermal vasculitis.

One month later, the cat was presented for a recheck appointment. The cat owner had not given buprenorphine as the cat did not show signs of pain at home. Because the cat had suffered from polyuria and polydipsia, the owner had decided himself to stepwise reduce prednisolone. At the time of the recheck, the cat received one quarter of a 5 mg tablet a day. Physical examination did not reveal significant abnormalities. The paws were not swollen anymore and hair was regrowing (Figure 5). The plan was to recheck blood examination (CBC, biochemistry) and urinalysis to evaluate the former abnormalities. However, the cat was too aggressive to sample blood and urine, and the owner refused sedation or anesthesia of the cat to perform these procedures. The advice was to continue therapy for three weeks with one quarter of prednisolone (Prednisolone®, Kela Laboratoria, Belgium) 5 mg every other day before stopping the medical treatment. A control appointment 6 to 8 weeks later was advised.

Table 2. Results of blood examinations performed at the Department of Small Animal Medicine, Faculty of Veterinary Medicine, UGent, Belgium.

Parameter	Day 12	Day 13	Day 15	Reference interval	Unit
Hematology					
Erythrocytes	*5.47*		*5.08*	6.54 - 12.2	1012/L
Leukocytes	*29.64*		*23.65*	2.87 - 17.02	109/L
Neutrophils	*23.47*		*20.21*	1.48 - 10.29	109/L
Eosinophils	0.36		0.39	0.17 - 1.57	109/L
Basophils	*0.4*		0.26	0.01 - 0.26	109/L
Lymphocytes	4.39		2.03	0.92 - 6.88	109/L
Monocytes	*1.02*		*0.76*	0.05 - 0.67	109/L
Hemoglobin	*6.6*		*6.2*	9.8 - 16.2	g/dL
Hematocrit	*19.2*	*26*	*21*	30.3 - 52.3	%
Reticulocytes	12		22.4	3 - 50	109/L
MCV	*35.1*		36	35.9 - 53.1	fL
MCH	12,1		12.2	11.8 - 17.3	pg
MCHC	34.4		33.9	28.1 - 35.8	g/dL
Thrombocytes	202		242	151 - 600	109/L
Biochemistry					
Total protein	61			57 - 89	g/L
Albumin	*20*	*20*	*21*	23 - 39	g/L
Creatinine	142		167	71 - 212	µmol/L
Bilirubin total	12		12	0 - 15	µmol/L

Bold written data are outside the reference interval. MCH= Mean corpuscular hemoglobin, MCHC= mean corpuscular hemoglobin concentration, MCV= mean corpuscular volume

After six months, the cat came for another control to the referring veterinarian. According to the owner, all complaints had resolved and the cat was again very active and able to hunt. Physical examination did not reveal abnormalities: the paws were not swollen anymore and hair was completely regrown. Blood could be taken, but it was not possible to take a urine sample. The blood examination (CBC, biochemistry and total thyroxine) showed that the number of leukocytes (neutrophils and monocytes) had normalized and the anemia was dissolved. Moderate azotemia and hyperphosphatemia were again present (Table 1).

DISCUSSION

Immunological deep dermal vasculitis was diagnosed in a 13.5-year-old, neutered, female domestic shorthaired cat based on clinical findings, the histological examination of skin biopsies, exclusion of possible underlying causes and response to therapy.

A detailed history was performed to detect possible triggers such as food, food additives, chemical substances, vaccinations or drugs. Based on the history, these triggers could be excluded. In the literature, a case of a dog with deep dermal vasculitis after the administration of meloxicam has been reported (Niza et al., 2007). Meloxicam was also administered in that case, but only after the onset of the symptoms. Physical examination, blood examination (CBC, biochemistry), a SNAP® Combo Test (IDEXX Laboratories Europe BV, the Netherlands) for feline leukemia virus antigen and feline immunodeficiency virus antibody, serology of toxoplasmosis, mouth inspection, an impression smear of the altered skin, thoracic radiographs, abdominal ultrasound, fine-needle aspiration of the liver, cystocentesis and urinalysis were conducted to look for infections (bacterial, viral, parasitic), inflammation or neoplasia as a possible cause of the deep dermal vasculitis.

The age of reported cases range from seven months to seven years old (McEwan et al., 1987; Gross, 1999; Nichols et al., 2001; Cannon et al., 2005; Declerq et al., 2008; Jasani et al., 2008). In comparison to these cases, the age of the cat of the present case is high. However, with the small number of cases that have been reported, it is difficult to say if there is a certain age predisposition for dermal vasculitis in cats. In the current literature, there is no information about breed or sex predisposition.

Dermal vasculitis is characterized by an immune response concerning blood vessels (Innerå, 2013). A type three hypersensitivity reaction is the most likely and generally accepted mechanism of cutaneous vasculitis in animals (Innerå, 2013). Antigen and antibodies can form antigen-antibody complexes, which may lead to immune complex deposition on the endothelium of blood vessels inducing vasculitis (Voie et al., 2012). Constitutional signs, such as anorexia, depression and pyrexia, which also occurred in the present case, can precede dermal symptoms (Miller et al., 2013). In this case, signs of dermal vasculitis involved all four distal limbs, which correspond to the distribution of dermal vasculitis in dogs (Miller et al., 2013). In humans, small vessel leukocytoclastic vasculitis also affects lower limbs and areas of the body, which are ventral of the heart (Pulido-Pérez et al., 2012). The clinically and histologically diagnosed edema, which was present in the four distal limbs of the patient of the present case, is a prevalent sign of dermal vasculitis (Miller et al., 2013; Innerå, 2013). Painful skin as was seen in this case has also been reported in the literature as a possible symptom of dermal vasculitis (Innerå, 2013).

Several abnormalities detected by blood examinations (mild anemia, moderate leukocytosis, increased α 1 and α 2 globulins, moderately increased lactate dehydrogenase activity, decreased serum thyroxine concentration) can be explained as consequences of the dermal vascular inflammation. In this case, hypoalbuminemia was probably caused by a combination of dermal vascular inflammation (negative acute phase protein), persistent anorexia and potentially protein loss by skin lesions.

Only mild abnormalities were seen on the radiographs of the thorax. Despite these, the cat never developed respiratory signs during hospitalization and follow-up. The suspicion of mild pleural effusion could be an indicator for a more generalized vasculitis. Therefore, an examination of the pleural effusion would have been ideal, but was impossible because of the little amount. However, there was no other evidence of involvement of internal organs or the presence of abdominal fluid, making generalized vasculitis unlikely. The ultrasonographic alterations of the kidneys and the initial azotemia may have indicated renal disease, such as glomerulonephritis or chronic kidney disease, but were not typical of vasculitis. Also the isosthenuria could have confirmed the suspicion of renal disease, although it might have been influenced by the infusion therapy, which had been given by the referring veterinarian until the day before urinalysis. Glomerulonephritis was ruled out by the lack of significant proteinuria. The initial azotemia could also have been caused by an acute component due to a prerenal cause (dehydration) and the therapy with non-steroidal, anti-inflammatory drugs. The rapid normalization of the azotemia after infusion therapy makes prerenal factors very likely. Although repeated measurement of the urine specific gravity would be ideal, the recurring azotemia at the last recheck by the referring veterinarian indicated chronic kidney disease. Chronic kidney disease is a frequent disease in older cats with a prevalence up to 30% in cats older than 15 years (Lulich et al., 1992). Chronic kidney disease is mainly a degenerative disease with only mild inflammation and thus less likely as a trigger of deep dermal vasculitis. Therefore, it is more likely that chronic kidney disease is an incidental concur-

rent finding in this cat instead of a possible trigger of deep dermal vasculitis.

The results of the abdominal ultrasound and fine-needle aspiration of the liver and hyperbilirubinemia could indicate a possible liver disease such as lymphocytic cholangitis. However, it is important to realize that fine-needle aspiration of the liver is not a valid diagnostic tool to diagnose inflammatory hepatic diseases or the seriousness of these diseases. In a study by Wang et al. (2004), cytology only agreed in 27.3% of feline cases of inflammatory hepatic disease with the histopathologic diagnosis. Normal blood values of alanin aminotransferase (ALT) and aspartate aminotransferase (AST), the quick decline of bilirubin and the response to therapy make non-specific reactive hepatitis more likely. Non-specific reactive hepatitis can occur secondary to extrahepatic diseases, caused by hepatic hypoxia and endotoxemia (Rothuizen, 2010). When the primary disease is treated successfully, most of these reactive hepatic changes resolve without specific hepatic therapy (Rothuizen, 2010).

Histological features of leukocytoclastic vasculitis include perivascular and mural infiltration by polymorphonuclear leukocytes, extravasation of red blood cells, fibrinoid necrosis and occasionally thrombosis (Sams et al., 1976). The histopathological results showed several of these changes, such as a perivascular mixed infiltration of inflammatory cells, some thrombi in the blood vessels and small foci of extravasation of red blood cells were present in the deep dermis and panniculus. Focally, there were several blood vessel lumina, in which numerous neutrophils were present, but mural infiltration was not seen. The histological alterations, which were seen in the dermal punch biopsies in this case suggested the presence of neutrophilic mural infiltration of the vessel walls in deeper layers, which were not included in the punch biopsy. The punch biopsies probably did not include these deep layers, because of the intense dermal edema, making deeper biopsies than usually necessary. Using excision biopsies (e.g. amputation of a digit) could have solved this problem. In both veterinary and in human medicine, the diagnostic value of a skin biopsy increases with the depth of the biopsy, when deep vasculitis is suspected (Carlson et al., 2005; Innerå, 2013).

Although multiple diagnostic tests and a detailed history were performed, an underlying cause, which could have triggered deep dermal vasculitis, was not found. This indicates an immunological cause of the deep dermal vasculitis in this case. This was also supported by the complete response to the prednisolone therapy, which would not have occurred if an underlying infectious or neoplastic cause was overlooked. The present case also shows that owner compliance is a problem in small animal medicine. The owner had reduced the dosage of prednisolone without consulting the veterinarian, despite oral and written recommendations regarding treatment. Studies have shown that about 10% to 25% of veterinary clients do not give all the medication prescribed (Maddison, 2011). As pet owner compliance is essential for an effective therapy, a lack of compliance might be a reason for treatment failure.

In this case, the cat recovered completely. In the current literature, there is almost no information about the prognosis of immunological deep dermal vasculitis in cats. Studies with dogs have shown that the majority recovers completely, when treated with immunosuppressive drugs (Parker and Foster, 1996; Nichols et al., 2001).

CONCLUSION

Although dermal vasculitis is rare in cats, it should be considered as differential diagnosis when corresponding cutaneous alterations occur at distal extremities and when there is no response to supportive therapy. Diagnostic work-up may be challenging because a detailed history and a precise diagnostic search for an underlying causes are necessary to look for possible triggers of deep dermal vasculitis. The diagnosis must be confirmed with histological examination of a deep dermal biopsy. Based on the few cases reported, the prognosis for immunological dermal vasculitis is usually good.

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