Papular cutaneous lesions in a cat associated with feline infectious peritonitis

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Abstract

A 7-month-old-intact male domestic shorthair cat was presented with fever, anterior uveitis in the right eye and respiratory distress when handled. These signs along with mild changes in serum protein levels and the exclusion of other potential causes were suggestive of feline infectious peritonitis (FIP). As the disease progressed, more clinical signs consistent with FIP, including renal involvement and later pleural effusion, became evident. Non-pruritic cutaneous lesions, characterized by slightly raised intradermal papules over the dorsal neck and over both lateral thoracic walls, were recognized at the end stage of the disease. The identification of papules in well-haired skin was difficult, and clipping of the fur facilitated their detection. Definitive diagnosis of FIP was made by histopathology and by immunohistochemical demonstration of coronavirus antigen in macrophages within kidney and skin lesions. The case was classified as a mixed form of FIP. Recognition of associated cutaneous lesions may facilitate a diagnosis of FIP in suspicious cases.

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by macrophages throughout the body. Clinical signs result from the cat's own immune reaction. FIP is an immune complex disease involving virus, antiviral antibodies and complement.¹ The development of vasculitis and granulomas was previously attributed to a type-III hypersensitivity reaction. A recent study indicated that in FIP, inflammatory processes are restricted to veins and that phlebitis is initiated by activated and feline coronavirus-infected, circulating monocytes.² FIP exists in three clinical forms: an effusive (wet) form, a noneffusive (dry) form and a mixed form.^{1,3} The effusive form is characterized by fibrinous to granulomatous serositis, with accumulation of protein-rich fluid within body cavities. The noneffusive form is characterized by granulomatous inflammatory lesions in several organs (including abdominal viscera, eyes, lungs and central nervous system). Definitively diagnosing FIP antemortem can be extremely challenging. Difficulties arise from nonspecific clinical signs; lack of pathognomonic, haematologic, and biochemical abnormalities; and low sensitivity and specificity of tests routinely used in practice. More recent diagnostic tests including immunohistochemical staining of antigen in macrophages in effusion or tissue that is 100% specific for the diagnosis of FIP.¹

Dermatological abnormalities in association with spontaneous FIP are rare. Entire male cats may show scrotal swelling.⁴ Skin lesions associated with debility have been reported. Subcutaneous oedema was observed in three cats,⁵ and skin fragility was seen in a cat with FIP and hepatic lipidosis.⁶ Only two reports have described primary cutaneous lesions: truncal papules to nodules characterized by pyogranulomatous vasculitis and mural folliculitis were described in a 1-year-old Sphinx cat;⁷ and small nodules over the neck and proximal forelimbs characterized by pyogranulomatous dermal phlebitis and periphlebitis in a 1-year-old domestic cat with concurrent feline immunodeficiency virus infection.⁸ Immunohistochemistry demonstrated coronavirus antigen within lesional macrophages in both cases. The purpose of this paper is to describe the morphologic characteristics and histopathological aspects of primary skin lesions in a cat with a mixed form of FIP.

Case report

A 7-month-old intact male domestic shorthair cat was presented for evaluation of a right eye problem and decreased appetite. At physical examination, the cat was thin with a rectal temperature of 40 °C. Anterior uveitis was present in the right eye with protrusion of the third eyelid, conjunctival hyperaemia, episcleral congestion, miosis, swelling and hyperaemia of the iris and reduction in ocular pressure assessed by tonometry. The clinical suspicion was FIP. Tachypnoea was noted when the cat

Introduction

Feline infectious peritonitis (FIP) is a common, systemic and almost always fatal disease. Cats are initially infected with an avirulent feline coronavirus that replicates in enterocytes. In some instances, a mutation occurs, resulting in the ability of the virus to replicate within macrophages, and mutated viruses are disseminated from the intestine

was handled for blood sampling, which restricted analysis to total protein, serum protein electrophoresis and infectious disease serologic tests. The level of total protein was within reference range (75 g L^{-1} reference range $55\text{--}85 \text{ g L}^{-1}$), albumin was marginally low (26.7 g L^{-1} reference range $29\text{--}41 \text{ g L}^{-1}$), globulin was mildly elevated (48.2 g L^{-1} reference range $26\text{--}44 \text{ g L}^{-1}$) and the albumin: globulin ratio was 0.55. The cat was feline immunodeficiency virus antibody and feline leukaemia virus antigen negative. Serum antibody titres for *Toxoplasma gondii* were also negative. The cat was treated with topical dexamethasone 0.1% , topical tropicamide 0.5% , oral administration of clindamycin at 22 mg kg^{-1} and ketoprofen at 1 mg kg^{-1} .

When rechecked 7 days after starting therapy, the cat had normal appetite, and a large fibrinous clot was observed in the anterior chamber of the right eye. Ofloxacin 0.3% eye drops were added to the treatment regimen, oral administration of ketoprofen was discontinued and replaced by oral meloxicam 0.05 mg kg^{-1} . Ten days later (day 17), the CAT was re-admitted for anorexia and sneezing. Rectal temperature was 39.4°C , anterior uveitis was also present in the left eye and abdominal palpation revealed enlarged kidneys. Blood urea (4.4 mmol L^{-1} reference range $5.90\text{--}12.5 \text{ mmol L}^{-1}$) was not increased. Reduced creatinine ($37.12 \text{ }\mu\text{mol L}^{-1}$ reference range $70\text{--}130 \text{ }\mu\text{mol L}^{-1}$) was attributed to young age, weight loss and muscle loss. Oral clindamycin was changed to doxycycline 10 mg kg^{-1} .

On day 25, the cat was admitted as an emergency with emaciation and severe dyspnoea. Both kidneys were large and irregular in outline upon palpation. Several papules were found over the right lateral thoracic wall. Thoracic radiographs revealed a pleural effusion. The presence of more skin lesions became evident when the thoracic wall was clipped and prepared for thoracocentesis (Fig. 1). The collected fluid was yellow and viscous, protein-rich and had a low cellularity consisting of nondegenerative neutrophils. Further clipping of the coat revealed multiple papules (more than 40) over the dorsal neck (Fig. 2), and right and left lateral thoracic walls. Lesions were nonpainful, firm, well-circumscribed intradermal, slightly raised and erythematous, measuring from 2 to 9 mm in diameter. Some smaller papules had a central depression with a yellow crust. Fine-needle biopsy was performed using a 21-gauge needle, and the cytologic preparation was stained

Figure 1. Right lateral thoracic wall, cat. Coat has been clipped for thoracocentesis. Note multiple slightly elevated papular lesions.

Figure 2. Neck, cat. Coat has been clipped to visualize smaller papular lesions.

Figure 3. Histopathology of skin lesion. Extensive oedema (1), severe perivascular (2) pyogranulomatous inflammatory reaction (3). Haematoxylin and eosin stain; bar = $100 \text{ }\mu\text{m}$.

with Diff-Quik™. Samples had a poor cellularity, but contained macrophages and nondegenerative neutrophils. Cytologic interpretation was pyogranulomatous inflammation.

The suspicion of FIP was raised, and given the poor prognosis the owners accepted euthanasia. In addition to pleural effusion, necropsy revealed the presence of a small amount of yellow abdominal fluid and multiple pyogranulomas in both kidneys. Lesional skin and kidney samples were submitted for histopathology and to Prairie Diagnostic Services (Saskatoon, Canada) for immunohistochemical detection of feline coronavirus antigen. Histopathology of the kidneys revealed severe extensive pyogranulomatous inflammatory lesions, with destruction and necrosis of normal renal tissue and fibrosis. In the skin, pathological lesions were restricted to the mid and deep dermis. There was severe oedema, prominent dermal veins, multifocal pyogranulomas often centred around veins (Fig. 3), dermal necrosis and haemorrhage. In one section, moderate atrophy of hair follicles and sebaceous glands was seen (Fig. 4). Feline coronavirus antigen was detected in the cytoplasm of macrophages in tissue samples of kidney and skin by peroxidase antiperoxidase method using a mouse monoclonal antibody (FIPV3-70, Custom Monoclonals, West Sacramento, USA) (Fig. 5), confirming the diagnosis of FIP.

Figure 4. Histopathology of skin lesion. Pyogranulomatous inflammatory reaction around follicular complex. Note atrophy of the adnexae (arrows). Haematoxylin and eosin stain; bar = 100 μ m.

Figure 5. Immunohistochemical staining of skin lesion. Macrophages within the granulomatous infiltrate express feline coronavirus antigen (arrows). Notice the veins (+) within the lesion and the hair follicle (*). Peroxidase antiperoxidase method; bar = 100 μ m.

Discussion

The young cat in this report was initially admitted with fever, unilateral anterior uveitis and respiratory distress when handled. These signs along with the mild changes in serum protein levels and the exclusion of other potential causes were suggestive of FIP. Serology testing for feline coronavirus antibody was not performed because results are often of limited value for clinical diagnosis.⁹ A positive titre does not provide support for this diagnosis as many cats without disease have positive titres. A negative titre in a sick cat does not rule out FIP because some cats with fulminant FIP may present with negative titres resulting from anergy or antigen-antibody complement formation that limits the ability to detect virus-specific antibodies.⁹ As the disease progressed, more suggestive clinical signs such as renal involvement and pleural effusion became apparent. At this clinical stage, Rivalta's test could have been performed on pleural fluid and, if positive, antigen could have been detected in macrophages by immunofluorescence or immunohistochemistry. Detection of intracellular feline coronavirus antigen is the only way to

definitively diagnose FIP.¹ In the present report a definitive diagnosis was made by histopathology and immunohistochemistry on lesional tissue of kidney and skin. Clinical findings at the time of euthanasia and postmortem included uveitis, pleural and mild abdominal effusion and granulomas in both kidneys and in the skin. The case was accordingly classified as a mixed form of FIP.

The presence of cutaneous lesions in this case was subtle and had not been noted by the owner or on previous examination. Lesions over the lateral thoracic wall were not recognized until the end stage of the disease (on day 25) when the skin was prepared for sampling. A thorough examination and palpation of the skin then revealed several other but smaller lesions over the dorsal neck and over both lateral thoracic walls. Detection in haired skin was difficult because alopecia was not associated and the intradermal lesions were only slightly elevated. Only when the fur was clipped did the extent of cutaneous involvement become evident. None of the cats in this and earlier reports, had lesions on the less-haired abdomen.

Primary cutaneous lesions associated with FIP were described in the first report as raised, red nodules of approximately 2 mm diameter associated with partial alopecia.⁸ A nodule, by its clinical definition, is a circumscribed solid elevation greater than 1 cm in diameter.¹⁰ The morphologic description of the cutaneous lesions in the first report without providing clinical pictures may confuse clinicians. The lesions would have been properly defined as papular, quite similar to the lesions in the present case with the exception of the alopecia.

The time of onset of skin lesions in the cat of the present report was unknown and their presence may have been a missed opportunity to diagnose FIP in a timely manner by histopathology and immunohistochemistry on skin biopsies. Feline coronavirus antigen-positive macrophages were observed in all skin samples although they were less abundant than in the kidneys.

In summary, antemortem diagnosis of FIP can be a challenge to practitioners, and recognition of associated cutaneous lesions may facilitate a definitive diagnosis of FIP. As skin lesions can be difficult to detect in well-haired skin, clipping of the fur and visualizing the skin may be rewarding in suspect cases.

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Résumé Un chat Européen mâle non castré âgé de 7 mois a été présenté avec de la fièvre, une uvéite antérieure de l'oeil droit et une détresse respiratoire. Ces signes associés à des modifications modérées du taux de protéines et à l'exclusion des autres diagnostics différentiels étaient suggestifs d'une péritonite infectieuse féline (FIP). La maladie a progressé et d'autres signes cliniques compatibles avec une FIP sont apparus, notamment un épanchement pleural et une atteinte rénale. Des lésions cutanées non prurigineuses, caractérisées par des papules intradermiques modérément en relief, sur le cou dorsal et sur les faces latérales du thorax ont été notées. La mise en évidence des papules était difficile en peau velue et une tonte a facilité leur visualisation. Le diagnostic définitif de FIP a été fait par l'histopathologie et la démonstration immunohistochimique des antigènes de coronavirus dans les macrophages du rein et des lésions cutanées. Le cas a été classé comme un cas mixte de FIP. La reconnaissance de l'association de lésions cutanées peut faciliter le diagnostic de FIP dans les cas suspects.

Resumen Un gato doméstico no castrado de siete años de edad se presentó con fiebre, uveitis anterior en el ojo derecho y distres respiratorio cuando era manipulado. Estos signos junto con cambios leves en las proteínas del suero y la exclusión de otras causas potenciales eran indicativos de peritonitis infecciosa felina (PIF). Según la enfermedad progresaba se observaron más signos clínicos característicos de PIF, incluyendo lesiones renales y más adelante una efusión pleural se hizo evidente. Se observaron en estadios finales de la enfermedad unas lesiones cutáneas no pruríticas que consistían en pápulas intradérmicas ligeramente elevadas sobre el dorso del cuello y en las paredes laterales del tórax. La identificación de papulas en zonas con denso pelo era difícil y el rasurado del pelo facilitó su detección. El diagnóstico definitivo de PIF se realizó mediante técnica de inmunohistoquímica demostrando el antígeno de coronavirus en macrófagos en el riñón y las lesiones de la piel. El caso fue clasificado como una forma mixta de PIF. El reconocimiento de las lesiones cutáneas podría facilitar el diagnóstico de PIF en casos sospechosos.

Zusammenfassung Eine 7 Monate alte, unkastrierte männliche kurzhaarige Hauskatze wurde mit Fieber, Uveitis anterior im rechten Auge und Atemnot bei Handling vorgestellt. Diese Anzeichen, gemeinsam mit geringen Veränderungen der Serumproteinwerte und der Ausschluss anderer potentieller Ursachen wiesen auf feline infektiöse Peritonitis (FIP) hin. Als die Krankheit weiter fortschritt, wurden weitere klinische Anzeichen, die mit FIP vereinbar waren, einschließlich einer Beteiligung der Nieren und später ein Pleuralerguss, offensichtlich. Nicht-juckende Hautveränderungen, die durch leicht erhöhte intradermale Papeln über dem dorsalen Hals und über der Thoraxwand beidseits charakterisiert waren, wurden im Endstadium der Krankheit gesehen. Die Identifizierung der Papeln in der gutbehaarten Haut war schwierig und das Rasieren des Fells erleichterte ihre Erkennung. Eine definitive Diagnose für FIP wurde histopathologisch gestellt, sowie mittels immunhistochemischer Demonstration des Coronavirus Antigens in den Makrophagen innerhalb der Nieren- und Hautveränderungen. Der Fall wurde als eine gemischte Form der FIP eingestuft. Die Erkennung von dazugehörigen Hautläsionen kann eine Diagnose von FIP in Verdachtsfällen erleichtern.