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CASE REPORT
Pansteatitis and severe hypocalcaemia in a cat

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A 13-year-old Siamese cat was presented for investigation of lethargy and progressive abdominal enlargement. Serum chemistry revealed severe reduction of total and ionised serum calcium. The omentum appeared hyperechoic with scattered hypoechoic foci on abdominal ultrasound examination. Elevated serum parathormone and low fractional excretion of calcium excluded a parathyroid disorder and renal loss of the electrolyte. During laparotomy the omentum appeared opaque, white and firm. Post-mortem examination revealed that the thoracic and subcutaneous fat was also affected. Histopathology confirmed the diagnosis of pansteatitis with diffuse calcium soaps formation. While, severe hypocalcaemia is occasionally seen in cats, the association with pansteatitis has not been reported previously. In man, a cause-and-effect relationship between calcium soaps and hypocalcaemia is recognised, though the association is rare.

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A 13-year-old, spayed female, 3.6 kg, Siamese cat was presented to the Clinic for Small Animal Internal Medicine, Vetsuisse Faculty, University of Zürich, with a 3-week history of anorexia, lethargy and progressive abdominal enlargement. Abdominocentesis 1 week prior to presentation by the referring veterinarian identified a fluid having a specific gravity of 1.022, proteins of 30 g/l, 4000 cells/μl (60% mature neutrophils, 20% mesothelial cells, 20% lymphocytes, macrophages). Bacterial culture of the fluid was sterile, and a serum antibody titre for coronavirus was negative. Treatment with enrofloxacin (5 mg/kg, once daily) did not improve the condition. The cat was regularly vaccinated and fed a commercial maintenance diet containing beef as source for animal proteins.

On physical examination, the abdomen was moderately distended, tender, with a palpable fluid wave. The remainder of the physical examination was unremarkable. Upon haematology, leukocytosis (26 700/μl; reference range, 4600–12 800/μl) with a marked left-shift (8010/μl; reference range, 0–123/μl) was observed. Biochemical abnormalities were moderate hypoalbuminaemia (21 g/l; reference range, 30–40 g/l), mild hyperbilirubinaemia (15.7 μmol/l; reference range, 1.7–7.2 μmol/l), increased lipase activity (1070 U/l; reference range, 8–26 U/l), and severe hypocalcaemia (total calcium 0.94 mmol/l; reference range, 2.4–2.8 mmol/l; ionised calcium 0.65 mmol/l; reference range, 1.20–1.35 mmol/l). The other blood values, including phosphate and magnesium, and urinalysis were normal. Commercial serological tests for feline leukaemia virus (FeLV) antigen and feline immunodeficiency virus (FIV) antibodies were negative. Radiography of the thorax was unremarkable. Upon abdominal ultrasonography the liver appeared hyperechoic and slightly enlarged, without extra-hepatic obstruction. The pancreas had normal echogenicity. The omentum appeared hyperechoic with hypoechoic foci (Fig 1). The effusion was confirmed to be a modified transudate and peritoneal cytology did not provide additional information.

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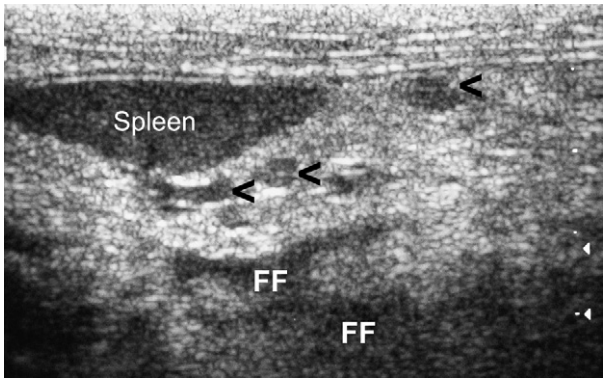

Fig 1. Ultrasonography of the abdomen. Hyperechoic omentum with hypoechoic foci (arrowheads). FF, free fluid.

At this time, important differentials considered for peritoneal disease were the presence of neoplasia (eg, mesothelioma, carcinomatosis), peritonitis, and pancreatitis with secondary omental involvement. Reduction of albumins could have been related to vasculitis and sequestration, although reduced hepatic synthesis was not definitely excluded, based on the combined hyperbilirubinaemia and diagnostic imaging features. A pancreatitis could also have explained the hyperlipasaemia and hypocalcaemia, although for the latter the contribution of a concomitant parathyroid disorder was not ruled-out.

The cat received intravenous amoxycillin and clavulanate (12.5 mg/kg, twice daily), and slow intravenous boluses of calcium gluconate 10% (1 ml/kg) were given to correct hypocalcaemia. Prior to treatment, an ECG was performed to evaluate potential abnormalities associated with hypocalcaemia. This proved to be normal. To elucidate the pathogenesis of hypocalcaemia, serum parathormone was measured and urine fractional excretion of calcium was determined. Bile acids test was undertaken to better characterise the hepatopathy.

The serum parathormone concentration was increased (271 pg/ml; reference range, 3–21 pg/ml) excluding hypoparathyroidism, and fractional excretion of calcium was very low (0.2%), indicating adequate renal response to parathormone and ruling out renal loss. As serum bile acids test results were within normal limits, liver function was not considered to be the primary pathology. Despite treatment calcium remained low (total calcium 0.94 mmol/l; ionised calcium 0.65 mmol/l), but clinical signs of hypocalcaemia did not develop.

To clarify the uncertain nature of the peritoneal abnormality, an exploratory celiotomy was performed. The omentum appeared thick, firm and chalky-white (Fig 2). Many adhesions were found, and in many instances the pathologic omentum entrapped intestinal loops. Fat necrosis was suspected and, considering the massive involvement of the omentum and the lack of therapeutic potential, a poor prognosis was given, euthanasia was elected. Histopathology identified severe and diffuse necrosis of the omentum with calcifications within adipocytes (Fig 3). As fat necrosis was also identified in the thoracic and subcutaneous fat, the final diagnosis was pansteatitis. In addition, moderate liver fatty degeneration was found. The pancreas was normal.

This report shows a rare case of pansteatitis in a cat with associated severe hypocalcaemia. In felines, pansteatitis is an uncommon diagnosis and in many cases diets rich in unsaturated fatty acids relative to vitamin E are considered the cause (Watson et al 1973, Flecknell and Gruffydd-Jones 1978, Tidholm et al 1996, Niza et al 2003). Indeed, commercial diets containing abundant amounts of unsaturated fatty acids capable of inducing oxidative stress such as red tuna, cod and other fishes are common (Tidholm et al 1996). The role of unsaturated fatty acids in the development of pansteatitis was confirmed by Cordy in 1954. In this study the administration of a commercial food containing 90% fish caused the disease in kittens. Supplementation with alpha-tocopherol prevented development of the

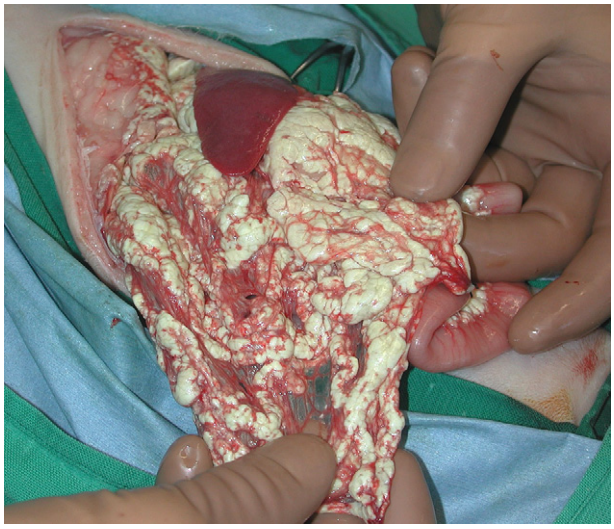

Fig 2. The omentum appears diffusely nodular, firm, yellowish and opaque.

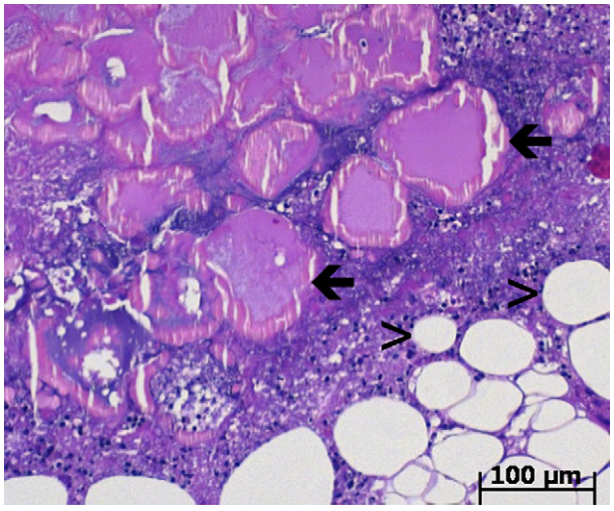

Fig 3. Fat necrosis in the omentum: necrotic adipocytes (arrows) with lipid saponification and normal adipocytes (arrowheads). Haematoxylin and eosin stain.

pansteatitis (Cordy 1954). In the present cat a dietetic factor, though not completely excluded, seems a less probable cause as a balanced commercial maintenance diet without fish and with standard contents of vitamin E was administered. Aside from nutritional factors, pansteatitis in cats is rarely described with other conditions, such as abdominal injury (Suter and Olsson 1969, Aydin et al 2002), pancreatitis (Suter and Olsson 1969, Ryan and Howard 1981) and pancreatic adenocarcinoma (Fabbrini et al 2005), all of which can be excluded in our cat. As in the present case, many cats with pansteatitis are brought to the veterinarian because of non-specific signs, like progressive anorexia and lethargy (Tidholm et al 1996). Less frequently, skin nodules due to concomitant involvement of the subcutaneous fat are first observed (Fabbrini et al 2005). On physical examination cats are often febrile and manifest abdominal pain during palpation. Haematology reveals variable leukocytosis and blood chemistry is unremarkable (Niza et al 2003, Fabbrini et al 2005), although results of complete profiles also including electrolytes have not been reported. The gross anatomy of adipose tissue in pansteatitis appears firm, granular, white-yellow and opaque (Watson et al 1973, Tidholm et al 1996), similar to our case. In some cats, the diseased fat may be also interspersed with liquefied adipose tissue having an orange-brown colour (Fabbrini et al 2005). On microscopic examination, fat drops within adipocytes become finely granular, cell membranes loose their definition and a mixture of acute and chronic inflammatory infiltrates, with macrophages being predominant, is evident (Watson et al 1973, Tidholm et al 1996, Niza et al 2003). Tissue mineralisations may be found, though uncommonly (Watson et al 1973). Independent from the triggering factor, the pathogenesis of pansteatitis follows a common pathway. Thus, any cause damaging adipocytes to a certain degree can provoke the release of stored lipases and initiate hydrolysis of glycerol from fatty acids (Ribelin and Deeds 1960). Then, free saturated fatty acids, especially those with long chains, more easily crystallise and induce chemical trauma and the activation of a mild and chronic inflammatory response that is responsible for the amplification and perpetuation of the fat disorder. Free fatty acids may also bind to calcium ions to form insoluble soaps (Ribelin and Deeds 1960).

To the best of the authors' knowledge, this is the first report of hypocalcaemia with fat necrosis. Concomitant total and ionised hypocalcaemia in cats is most frequently identified with pancreatitis (Kimmel et al 2001) and diabetic ketoacidosis (Bruskiewicz et al 1997). Uncommon causes are preparturient hypocalcaemia (Fascetti and Hickman 1999), hypoparathyroidism (Peterson et al 1991), vitamin D-dependent rickets (Schreiner and Nagode 2003), and nutritional secondary hyperparathyroidism (Tomsa et al 1999). Although an association between pansteatitis and low calcium levels in cats has not been reported so far, in the present case there was most likely a cause-and-effect relationship between the massive fat disorder and the severe hypocalcaemia. Given that upon histopathological examination crystals were found through the fat tissue, we hypothesise that calcium soap formation within necrotic adipocytes represented one leading factor by which calcium could be trapped. Indeed, in a human with fat necrosis owing to pancreatic fistula, severe hypocalcaemia was reported and shown to be caused by the formation of calcium soaps in the omentum. Coupled measurement of serum and abdominal fluid calcium was used to demonstrate the contribution of saponification to the pathogenesis of hypocalcaemia. The given explanation was that calcium soaps are not easily reabsorbed into the circulation therefore increasing the relative concentration of the electrolyte in the abdomen (Stewart et al 1986). Alternatively, diffuse fat necrosis and the accompanying inflammation might have increased cellular permeability, leading to a calcium shift into the intracellular compartment. A similar mechanism is demonstrated in the pathogenesis of hypocalcaemia in dogs with

inflammatory conditions such as pancreatitis and sepsis (Bhattacharya et al 1985, Steinhorn et al 1990). Finally, inflammation and increased vascular permeability could have also contributed by causing sequestration of albumin into the third-space with subsequent reduction of the bound calcium fraction. However, this possibility does not explain why the ionised calcium was also severely reduced.

In brief, severe hypocalcaemia is described in a cat with pansteatitis. Neither the cause of pansteatitis nor the exact mechanism of hypocalcaemia was clarified, though formation of calcium soaps is thought to be responsible for the hypocalcaemia.

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