Anaemia and Lipaemia in two four-week-old Kittens

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\textbf{ABSTRACT}

Anaemia and lipaemia were recognised in two unrelated four-week-old kittens. Both kittens were presented for inappetence and one of the kittens also had signs consistent with a peripheral neuropathy affecting the thoracic limbs. Two littermates of the latter kitten were also anaemic and lipaemic but clinically normal. Weaning both clinically affected kittens resulted in complete recovery. The signs noted in these kittens are similar to those previously reported in cats with an inherited defect of lipoprotein lipase activity although a definitive diagnosis was not made in either case. This condition has not been previously reported in Australia. [Baral, RM \textit{et al} (2002) \textit{Aust Vet Pract} \textit{32},60]

\textbf{CASE REPORTS}

Case 1
A four-week-old female Oriental Shorthair kitten (Fig 1) was presented for ill thrift, inappetence for the previous 24 hours and a stumbling forelimb gait. The kitten was not weaned and its dam’s diet consisted of a commercial dry food\textsuperscript{1} formulated for kittens (22\% fat content by weight).

The kitten was small (0.45kg) but in relatively good body condition. Its mucous membranes were very pale and it was hypothermic (37.2\degree C). Proprioceptive deficits were evident in the left forelimb. Withdrawal reflexes of this limb were absent though pain perception was present. Hind limb withdrawal reflexes were evident but possibly decreased. These neurological deficits were most consistent with lower motor neuron (LMN) disease.

Over the next 24 hours the condition progressed to

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{image1.png}
\caption{Four-week-old Oriental Shorthair (Case 1). Note the abnormal forelimb carriage.}
\end{figure}

\textsuperscript{1}Kitten dry food, The Jams Company
involve the right fore limb and resulted in inactivity of the thoracic limbs to support weight. The kitten was lightly anaesthetised by mask induction with halothane in 100% oxygen in order to perform cervical radiography, which was unremarkable. During venipuncture severe lipoaemia was immediately evident with the appearance of strawberry milk-like blood. The packed cell volume (PCV) was 0.13L/L (reference range: 0.21-0.33L/L) (Meyers-Wallen et al 1984). In-house blood biochemistry testing failed likely due to extreme plasma turbidity and due to the severity of the anaemia more blood was not collected for further testing at a commercial laboratory. Blood was subsequently collected from the two littermates, both samples were lipoaemic and the PCV were 0.17L/L and 0.20L/L.

The clinically affected kitten was wormed with pyrantel and niclosamide and weaned onto a commercial canned cat food formulated for adult cats (fat content: 3.9% by weight). Iron supplementation1 was instituted at 0.1mg twice daily and the forelegs were splinted to enable the cat to support weight and ambulate. The kitten recovered uneventfully over the next 10 days and remained normal for the next six months with no residual neurological deficits, anaemia or ill thrift. The cat went missing at this time precluding further detailed investigations of the underlying biochemical disorder. The other two kittens from this litter showed no clinical signs at any time and no specific treatment was instituted apart from immediate weaning onto a commercial dry food2 (22% fat content by weight).

Case 2
A four-week-old female British Shorthair kitten presented for inappetence. The kitten had lost 0.04kg bodyweight in 48 hours and had stopped suckling. The owner had attributed the weight decrease to inadequate milk production by the queen so had supplemented the kitten's diet for these two days with a commercial milk replacer. This had been formulated according to the manufacturer's directions (30% fat content by weight) but with added egg yolk. The dam's diet comprised a commercial canned food (fat content 3.9% by weight), commercial dry food (fat content 20% by weight), low-fat cow milk and purified water.

Abnormal physical findings included poor body condition, extremely pale mucous membranes, dyspnoea and a soft systolic heart murmur. There were no fleas or flea dirt observed and faecal flotation testing was negative for intestinal parasites.

Blood collected by jugular venipuncture had the appearance of strawberry milk suggesting severe lipoaemia. Haematology demonstrated a severe, poorly regenerative, microcytic, hypochromic anaemia. The PCV was 0.07L/L.

The owner declined a blood transfusion and the kitten was weaned immediately onto a lean, fresh meat diet (although it continued to suckle occasionally) with vitamin supplementation. The cat has shown no further clinical signs over the subsequent two years and the owner has declined all requests for follow-up examinations.

DISCUSSION
The function of chylomicrons (CM) and very low density lipoproteins (VLDL) is to transport triglycerides in the circulation. Cholesterol transport predominantly depends on low-density lipoproteins (LDL) and high-density lipoproteins (HDL) (Whitney 1992). Lipoaemia refers to serum or plasma with a milky appearance and is invariably a result of hypertriglyceridaemia, since it is the triglyceride-carrying lipoproteins (CM and VLDL) that impart a milky appearance to serum or plasma when present in large quantities. In contrast, increased concentrations of LDL and HDL cause hypercholesterolaemia but have no effect on the gross appearance of serum or plasma (Whitney 1992). Therefore, in the cases reported here, it can be determined from the gross appearance of the sera that marked hypertriglyceridaemia was present. No comment, however, can be made about cholesterol concentrations.

The standing plasma test can be performed on lipoaemic serum to differentiate increased CM from increased VLDL. This test requires the lipoaemic plasma sample to stand undisturbed in a refrigerator overnight. Formation of a cream layer over clear plasma indicates chylomicronaemia as the cause of the lipoaemia because CM are less dense than other components of serum. If no cream layer forms, lipoaemia is due to excessive VLDL levels, as the majority of VLDL particles remain suspended. Formation of a cream layer over cloudy serum indicates that the lipoaemia is due to a combination of excessive CM and VLDL (Whitney 1992, Barrie & Watson 1995). The standing plasma test would have been simple to perform and a useful test for both cases reported here. Plasma triglyceride and cholesterol concentrations were unable to be quantified using dry chemistry analysis, presumably because of the plasma turbidity. Recent advances in the development of combined ultracentrifugation and precipitation techniques have provided methods for the quantification of lipoproteins in cats and dogs (Barrie & Watson 1995).

Kittens prior to weaning have recently been shown to have higher plasma triglyceride concentrations than previously thought and it has been suggested that the upper reference limit for plasma triglyceride concentrations in these kittens should be increased from 1.00 to 1.70mmol/L (Butterwick et al 2001). Despite this, lipoaemia in kittens is always abnormal since it only becomes grossly detectable at 3.39-4.52mmol/L (Whitney 1992).

Hyperlipidaemia occurs as a result of excessive dietary intake of lipids, excessive endogenous production or mobilisation of lipids, ineffective clearance of lipids from the blood or a combination of these factors (Whitney 1992). Hyperlipidaemia can occur as a primary defect in lipid metabolism or secondary to diabetes.
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mellitus, hyperadrenocorticism, nephrotic syndrome, hypothyroidism, cholestasis or drugs (e.g. megestrol acetate) (Bauer 2000).

The condition described in these kittens bears remarkable similarity to the primary familial hyperchylomicronaemia first described by Jones et al (1985). This disease entity has been recognised subsequently in young kittens on several occasions (Bauer & Verlander 1984, Smerdon 1990, Watson et al 1992, Gunn-Moore et al 1997). Electrophoretic assessments in these kittens have shown increases in CM predominantly, with VLDL increased to a lesser degree (Jones et al 1986, Johnstone et al 1990, Gunn-Moore et al 1997) and triglyceride concentrations in these kittens have ranged from 2.5 to 143.8mmol/L. This condition has not been described previously in Australia. Although hyperlipidaemia secondary to other diseases was not excluded definitively, these would seem very unlikely explanations in such young kittens. Furthermore, spontaneous resolution after weaning suggests that the lipaemia in these kittens was due to a primary lipid metabolism disorder. There was no history of drug administration to the queens or kittens.

CM and VLDL require the enzyme lipoprotein lipase (LPL), with apolipoprotein C-II (apoC-II) as a co-factor, to hydrolyse triglycerides, thereby releasing free fatty acids and monoglycerides (Jones 1995). Ineffective clearance of CM and VLDL must therefore be due to decreased activity of LPL, apoC-II, or both. Several reports have demonstrated normal levels of apoC-II but abnormal LPL activity (Watson et al 1992, Gunn-Moore et al 1997) although Gunn-Moore et al (1997) noted that LPL activity was not profoundly reduced in the kittens they studied. Several investigators have demonstrated hypertriglyceridaemic cats with high circulating LPL levels but little or no LPL activity (Jones et al 1986, Peritz et al 1990) and it has been determined that a point mutation renders the LPL functionally inactive (Ginzinger et al 1996). The observation that cats with reduced LPL activity can recover from all clinical signs (Watson et al 1992, Gunn-Moore et al 1997) further indicates that other factors, such as a high fat diet, are important for overt clinical signs to develop. Jones et al (1983) demonstrated that the condition can be inherited as an autosomal recessive trait.

The suspicion of peripheral neuropathy in one of these kittens was likely due to xanthomatous infiltration of nerve trunks, most likely at the level of the nerve roots, as described by Jones et al (1986) and Johnstone et al (1990). Peripheral neuropathy was the most consistent sign (aside from hyperlipaemia) in a study of 20 cats with this condition (Jones et al 1986). Interestingly, the neuropathies occurred in different anatomical locations in different cats and resulted in diverse signs including Horner’s syndrome, recurrent laryngeal nerve paralysis and tibial and radial nerve paralysis.

There are relatively few papers investigating the PCV of normal kittens up to three months of age (Anderson et al 1971, Weiser & Kociba, 1983, Meyers-Wallen et al 1984). These papers consistently demonstrate that the mean PCV for normal kittens is approximately 0.25/L. Weiser & Kociba (1983) documented that this anaemia is due to transient iron deficiency (as previous papers had postulated), likely in association with rapid growth rate and an all-milk diet. In 70% of the kittens studied, the anaemia was microcytic. Increasingly severe microcytosis occurred with increasingly severe anaemia and each was positively correlated to serum iron levels; four of the 44 kittens studied had a PCV of 0.12-0.19/L. Microcytosis was evident in Case 2; thorough haematological studies were not performed for Case 1.

The anaemias noted in this report were far more severe than those generally recognised in kittens but iron deficiency may have contributed. These life-threatening anaemias are consistent with those reported by others describing lipaemic kittens (Bauer & Verlander 1984, Watson et al 1992, Gunn-Moore et al 1997). In most cases (including the kittens of this report), the cause of anaemia was not determined. Feline infectious anaemia, flea infestation and relative iron deficiency have been suggested as contributing causes of anaemia in these kittens (Gunn-Moore et al 1997, Bauer & Verlander 1984) but it seems most likely that hyperlipidaemia causes increased erythrocyte cell membrane fragility which results in haemolysis (Gunn-Moore et al 1997). Watson et al (1992) and Gunn-Moore et al (1997) both noted that the severity of the anaemia was positively correlated with the magnitude of the hypertriglyceridaemia. Furthermore, it is known that lipaemia predisposes to haemolysis in vitro (Barrie & Watson 1995). Hypertriglyceridaemia has been documented subsequent to haemolysis of various causes in people (Drumul et al 1991) and, interestingly, kittens with anaemia and lipaemia in Britain have had rapid resolution of their hyperlipidaemia following blood transfusion (Sparkes, A 2000 pers comm). It is therefore possible that hyperlipidaemia initiates a haemolytic anaemia but that each condition subsequently contributes to the worsening of the other. It is also possible that clinical signs only occur in kittens with decreased LPL activity when there is concurrent severe microcytic, iron deficient anaemia. This may explain why, despite having lipaemia, the littermates of Case 1 had less severe anaemias than the affected kitten and showed no other signs of ill health.

All reports of hyperchylomicronaemia in cats have noted improvement in clinical signs, including reversal of peripheral neuropathies, after weaning and/or implementation of a low fat diet. In many cases, additional supportive therapy such as iron supplementation or blood transfusion was provided. That the condition should occur in an unweaned kitten is not surprising as dietary fat intake is very high at this time (Watson et al 1992), especially if the queen is eating a high fat diet since increased fat in the queen’s diet results in increased fat content of milk (Gunn-Moore et al 1997). The diet fed to the queen in Case 1 contained 22% fat by weight, presumably contributing to the severe signs seen in that kitten. This kitten was not weaned to a specifically formulated low fat diet, as the significance of the lipaemia in relation to the anaemia was not initially appreciated. Weaning to an adult formulation of timmed cat food (with a fat content of 3.3%) was evidently sufficient to correct the problem. Interestingly, its littermate, which had no clinical signs despite
Lipaeic serum and moderate anaemia, were weaned onto a relatively high-fat kitten diet (22% fat by weight) without obvious problems. It is conceivable that some kittens may have unrecognised asymptomatic hyperlipidaemia.

Whilst these cases were not definitively diagnosed with inherited LPL dysfunction, it is the first time that kittens with consistent clinical signs have been reported in Australia. The finding of concurrent anaemia and lipaeic with or without peripheral neuropathy should raise the suspicion of this diagnosis in a kitten. Awareness of anaemia and/or neuropathy concurrent with hyperlipidaemia in kittens is important as full recovery of this syndrome occurs with diet change.

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