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Feline Geriatric Medicine Mini Series

Session Three: Fading away.... Investigation of weight loss in elderly cats

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Fading away; An approach to the elderly cat with weight loss

Key points:

Low serum albumin does not occur secondary to the anorexia that we see clinically and is instead an indication of underlying disease

Low B12 and/or folate indicates some intestinal disease. Normal B12 and folate does not exclude intestinal disease

Screening imaging, particularly abdominal (preferably ultrasound) can be invaluable in the investigation of weight loss, even when blood sample results are normal

Central disease quite commonly leads to anorexia in cats

Nutritional intervention is indicated whenever a feline patient has eaten nothing for 2-3 days, where <50% of the caloric requirement has been consumed daily for 5 days or more, or where there is associated rapid weight loss of 5% body weight or chronic weight loss of 10% body weight

A high proportion of elderly feline patients present for investigation of weight loss. As such the list of differentials and potential diagnostic tests is extensive and good attention to history and clinical examination findings starts the process of narrowing down the list of suspicions. When constructing a relevant list of differentials in a patient with weight loss, it is helpful to think in terms of three broad causative categories;

1. Inadequate intake
    - Pain
    - Pyrexia
    - Nausea
    - Central loss of appetite
    - Inability to eat
2. Malabsorption or malassimilation of nutrients
    - Intestinal disease
    - Exocrine pancreatic insufficiency
    - Protein losses
3. Hypermetabolic state
    - Hyperthyroidism
    - Diabetes mellitus
    - Neoplasia causing consumption of nutrients
    - Cancer cachexia

In some cases there may be a combination of factors, for example cancer will often lead to a reduced appetite, and cachexia. Almost any disease can lead to anorexia, and differentials will be extensive. It is generally accepted that while dental disease (sometimes severe) is seen with some frequency in

cats, it is nevertheless an uncommon cause of appetite reduction or anorexia. Owners may report that their cat is grinding the teeth, or dropping food from the mouth while eating. Sometimes a cat may ask for food repeatedly but eat very little. These are all most likely to be signs of abdominal pain or nausea, rather than indicative of clinically significant oral disease.

Intestinal disease is common, it frequently shows few signs on physical examination, biochemistry, and even imaging. It can lead to increased or decreased appetite, and there is not always accompanying vomiting or diarrhoea. If vitamin B12 or folate levels are low, intestinal disease should be suspected regardless of imaging findings (Jugan 2017). Conversely, the absence of alterations to these parameters does not exclude the possibility of intestinal disease. Various studies have evaluated the efficacy of ultrasound in discriminating between low grade intestinal lymphoma and inflammatory bowel disease (eg Briscoe KA et al 2011, Daniaux et al 2014, Diana et al 2003, Tucker et al 2014, Zwingenberger et al 2010). The information is conflicting; in some papers there is apparent diagnostic significance to increased intestinal thickness (particularly the muscularis layer) and/or changes such as abdominal lymph node enlargement, indicating that lymphoma is more likely where these changes are present. Other studies contradict, demonstrating that increase lymph node size and intestinal thickening can equally occur where inflammatory enteropathy is the diagnosis. Ultrasound's primary role may be more to exclude the presence of small focal lesions that cannot be palpated, in the intestine or elsewhere. Ultimately, only biopsy is going to offer a definitive diagnosis in the majority of cases, and given the difficulties in differentiating between small cell lymphoma and intestinal inflammation even histologically, and bearing in mind that lymphoma has a predilection for the jejunum and ileum, some authorities would always recommend biopsies to be collected at laparotomy rather than endoscopically (Evans 2006, Lingard et al 2009). In a clinical setting, a more pragmatic approach may be adequate in some cases, particularly in elderly cats. Much can be achieved without proceeding to invasive tests if there is reluctant on the part of an owner to proceed in a fragile, geriatric patient. A response to a hypoallergenic diet is not uncommon (30-50% of cases, Guildford et al 2001), and certain antibiotics may be beneficial in inflammatory enteropathy, either by virtue of their ability to alter the intestinal microbiome to the positive, or because of an immunomodulatory effect. Even when these measures are ineffective, biopsy may not be compulsory if the owner has a full understanding of the implications of trial treatment. Given that a combination of prednisolone and chlorambucil shows efficacy for both small cell intestinal lymphoma (Lingard et al 2009, Kiselow et al 2009) and inflammatory enteropathy, the results of biopsy may not alter the treatment plan for many patients.

A logical, step by step approach is required to investigate weight loss, as with any other medical problem. However, given the sign is vague and numerous, wide ranging underlying causes are possible, the clinician must be prepared to widen the search beyond the usual, expected cause of weight loss. This may include imaging of the thorax and central imaging, rather than concentrating on the abdomen alone. Another point to bear in mind, is that some diseases may be genuinely too subtle to detect in their early stages, and where initial investigations are negative, a careful discussion with

the owner is required to explain that in some cases, only time and progression of the disease is going to make apparent the causative illness.

The three most common “geriatric” diseases of cats, hyperthyroidism, diabetes mellitus, and chronic kidney disease (CKD), all have the potential to lead to weight loss. Diabetes mellitus rarely presents a diagnostic challenge. Recent research has lead to the development of symmetric dimethylarginine (SDMA) as a diagnostic test for CKD in cats. SDMA is produced at a continuous rate in all cells and excreted essentially exclusively by the kidneys. It has detects kidney disease earlier than does creatinine, and as it is unaffected by muscle mass, it can be a useful test alongside creatinine in an underweight cat (Hall et al 2014). Note that hydration status affects SDMA levels as it does creatinine, so although it is said to rise before a reduction in concentrating ability, it should be assessed alongside specific gravity. The SDMA test is commercially available at a few laboratories (exact test methodology seems to vary), and IRIS guidelines include information on how results of the test should be interpreted in the light of other findings. As yet, the test would not be relied upon as the sole test for CKD and it has not replaced creatinine measurement for the diagnosis of CKD, mainly because very little is known about its specificity, particularly where there is concurrent disease such as hyperthyroidism, diabetes mellitus, sepsis etc. However as it does seem to show better sensitivity, over time it may become the preferred test for the early diagnosis of CKD.

For the most part, the diagnosis of hyperthyroidism does not present a great challenge. However with an increased prevalence and/or awareness of feline hyperthyroidism, much more subtle or atypical signs relating to the condition may be detected much earlier by either owner or clinician, and these early cases or those compounded by non-thyroidal illness, may present more of a diagnostic challenge.

In early cases or particularly those where concurrent non-thyroidal illness is present, a total T4 may be suppressed into the high-normal or even upper half of the normal range. In such cases a free T4, which should be measured by equilibrium dialysis, may be helpful. This parameter tends to be more consistently raised in hyperthyroid cats even with non-thyroidal illness. However it is not a suitable first-line test for hyperthyroidism mainly because it is paradoxically less specific for the disease, with occasional sick euthyroid cats showing marked elevation of free T4 (reasons unknown) (Peterson et al 2001). Therefore FT4 results should always be interpreted in conjunction with a total T4 rather than relied upon in isolation. A high FT4 will be supported by a high-normal TT4 in a hyperthyroid animal, but in a patient with a very high FT4 and low-normal or sub-normal TT4, a euthyroid sick status should be suspected. T3 levels tend to add little to diagnosis, as they are rather less sensitive than TT4 levels.

Canine THS (cTSH) measurement, in conjunction with other tests, may be of diagnostic value in detecting early or mild cases of feline hyperthyroidism, or those compounded by non-thyroidal illness. Studies have demonstrated that a measurable cTSH is very unlikely to occur in a hyperthyroid cat (2% of cases in the largest, recently published study, Peterson et al 2015), that this could be used as a rule out for hyperthyroidism in equivocal cases. In screening cats for hyperthyroidism, the cTSH

sample is insensitive, but the addition of a total T4 (or free T4) increased the sensitivity to near 100% while sacrificing very little specificity.

Dynamic tests are rarely performed or required in hyperthyroid patients. Frustratingly, they often do not add much in exactly the patients where supplementary tests would be required, i.e. those with concurrent hyperthyroidism and non thyroidal illness suppressing the total thyroxine levels. Usually a better approach is to control any non-thyroidal illness and then re-test for hyperthyroidism.

Cats that are not eating are susceptible to hepatic lipidosis, particularly if they start out as overweight. However, aside from this condition, there are many ways in which anorexia is undesirable, via immediate effects such as electrolyte imbalance and enterocyte damage, and the catabolic state that is induced. Anorexic patients suffer prolonged recovery times, direct detriment to the enterocytes, poor wound healing, and re-feeding syndrome when nutritional intake is finally achieved. During starvation, adaptive mechanisms take place to preserve vital organs and functions in the face of reduced nutrition. Gluconeogenisis within the liver reduces, and protein mobilisation from distant sites decreases; fat stores are mobilised first. The metabolic rate decreases and insulin secretion decreases. Glucose utilisation is decreased, and fatty acids are used as an energy source where possible. Potassium, magnesium and phosphate levels inevitably become depleted despite adaptive mechanisms to preserve these. Serum concentrations of these substances are unlikely to reflect true whole-body levels. Re-feeding syndrome refers to a number of metabolic and electrolyte disturbances that occur in a chronically malnourished patient when feeding is recommenced. The effect can be particularly marked if parenteral nutrition is used. Serum phosphate concentrations initially drop further as utilisation increases and hypophosphataemia may become severe enough to cause haemolysis. Vitamin deficiencies probably play a role as demand is increased as the metabolic rate is increased further. Hypokalaemia frequently occurs and can be profound and remarkably resistant to supplementation. The patient tends to be glucose intolerant, potentially insulin resistant, and fluid overload and sodium retention are common problems. Respiratory complications and /or congestive failure can result in part due to cardiac changes that have occurred during the starvation period.

There is no established consensus over the point at which nutritional intervention should be initiated in an anorexic patient. The following are suggestions;

- When a patient has eaten nothing for 3 days
- Where <50% of the caloric requirement has been consumed each day for 3-5 days or more
- Where there is associated rapid weight loss of 5% body weight
- Or chronic weight loss of 10% body weight

Caloric requirement (resting energy requirement, RER) = 30x BW +70
As an easy rule of thumb, and often quoted for hepatic lipidosis, feed the patient 60-65 kcal/kg.

Nutrition must be introduced gradually where a patient has been chronically under-nourished, 1/3 of the total energy requirements is given on day 1, 2/3 on day 2, and the full amount from day 3 onwards.

Problems associated with syringe feeding;

- Food aversion
- Aspiration
- Inadequate caloric intake

Appetite stimulants

- Mirtazepine (safe and effective in CKD; Quimby et al 2013)
- Cyproheptadine (Periactin)
- (Diazepam) unlikely to be useful > once-twice

Options for assisted feeding

- Feeding tube
  - naso-esophageal (no sedation needed)
  - esophagostomy (ease of placement, suits many patients)
  - Gastric (surgically placed or PEG)
  - J tube (post-placement care more complicated, but can be placed through a gastric tube)
- Partial parenteral nutrition
- (Total parenteral nutrition)

Parenteral nutrition

Even “total” parenteral nutrition (TPN) does not provide all of the nutrients the patient requires, the term refers to the aim that 100% of the energy requirements are met. It is rare that this method is used in veterinary medicine. Partial parenteral nutrition (PPN, also called peripheral parenteral nutrition) provides 40-70% of the calories. A mixture of dextrose, lipid emulsion, and amino acids are generally provided. Lipid emulsions are calorie dense, but amino acids are an essential component of PPN to preserve nitrogen balance and lean body tissues. Electrolytes and multivitamins are also usually added. The mixtures must be made up immediately prior to use, and done so aseptically, which is not always practical (a laminar flow hood is ideal). Ready-made solutions are available, but these generally contain fewer calories per ml than compounded PPN. PPN must be administered through a dedicated, aseptically placed intravenous catheter. PPN can be given via a peripheral catheter if needed, as its osmolality is much less than TPN, which must be administered via a jugular catheter. The mixture must be given via a closed system, and preferable through an in-line filter.

Complications are not infrequent (more so with TPN than PPN). Hyperglycaemia, hyperbilirubinaemia, and hypertriglyceridaemia, may be seen, but are usually either transient or relatively easily managed by temporarily reducing the rate of administration of the mixture. Thrombophlebitis and/or sepsis, are more serious complications but less common.

PPN may be a suitable method of nutritional support in some cases, but it should never be used where enteral nutrition would be effective, and the impression must not be held that PPM provides anywhere near a full or well balanced nutritional intake.

Treatment of hepatic lipidosis

Investigation – the condition may not be primary

60-65 kcal/kg/24 hours

IVFT, correcting electrolyte imbalances

Amino acids; taurine, methionine, arginine, L-carnitine

Potassium, phosphate

B, E, K vitamins (K prior to any invasive procedures)

SAMe

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