INTRODUCTION

Feline gingivostomatitis (FGS) is a condition of unknown, but probably multifactorial, aetiology that is frequently refractory to treatment. Feline calicivirus (FCV) has been implicated in the pathogenesis of the disease and is present in up to 100 per cent of cases (Knowles and others 1991, Reubel and others 1992). However, FCV may simply be an opportunistic infection, rather than the cause. Although acute FGS can be induced experimentally by infecting cats with a FCV strain from a case of FGS, chronic FGS cannot (Knowles and others 1991, Reubel and others 1992). Nevertheless, the prevalence of FCV in cats with chronic FGS is very much higher than in the general cat population (Knowles and others 1991).

The mouths of normal cats generally contain between seven and 16 species of cultivable bacteria (Love and others 1990), and others which have not yet been cultivated may also occur. Gingivitis in the cat has been associated with an increased anaerobic population compared to the normal feline mouth (Mallonnee and others 1988, Love and others 1990). However, it is widely accepted that antibiotics alone will not usually cure FGS (Williams and Aller 1992).

There is an immune-mediated component to FGS. Examination of the cytokine messenger RNA (mRNA) content of biopsies of FGS lesions by Harley and others (1999) showed a tendency towards a mixed T helper 1 (Th1) and Th2-type cytokine profile rather than the predominantly Th1-type cytokine profile found in normal oral mucosa. These findings prompted the present authors to consider thalidomide as a treatment, as it is widely used in human conditions where a Th1 response is preferable to a Th2 response, such as human immunodeficiency virus (HIV) infection, Mycobacterium tuberculosis infection and tumours (Verbon and others 2000, Dredge and others 2002). In contrast, corticosteroids, which are often used to treat FGS, suppress both Th1- and Th2-type responses (Moreira and others 1997, Rowland and others 1998). Additionally, thalidomide has been reported to reduce some proinflammatory cytokine responses (tumour necrosis factor-α, interleukin [IL] 6 and IL-10) (Moreira and others 1997, Rowland and others 1998) and has been successfully used in the treatment of oral aphthous stomatitis in humans (Weinstein and others 1999).

Lactoferrin was also considered as a therapeutic component as it has been reported to be beneficial in cases of FGS (Sato and others 1996). Lactoferrin aids the phagocytic activity of polymorphonuclear leucocytes and binds iron, rendering it unavailable to bacteria that require iron to replicate (Hasegawa and others 1994). Lactoferrin has also been reported to have antiviral activity (Hasegawa and others 1994, Harmsen and others 1995, Marchetti and others 1996, Superti and others 1997, Swart and others 1998), although not specifically against FCV.

CASE HISTORY

Presentation

An entire male domestic shorthaired cat was presented to the referring veterinary sur-
geon in January 1998 as an ex-stray of unknown age, with gingivitis. The cat was castrated, and vaccinated with attenuated FCV, feline herpesvirus, feline panleuco-penia virus and inactivated feline leukaemia virus (FeLV) (Katavac Eclipse; Fort Dodge Animal Health). The cat's gingivitis was treated with antibiotics and non-steroidal anti-inflammatory drugs (NSAIDs). The cat continued to be treated for chronic gingivitis and stomatitis with clindamycin (Antirobe; Pharmacia & Upjohn), amoxicillin (Clamoxyl; Pfizer), spiramycin and metronidazole (Stomorgyl; Merial), marbofloxacin (Marbocyl; Vetoquinol), prednisolone, carprofen (Rimadyl; Pfizer) and ketoprofen (Ketofen; Merial) until referral to the University of Glasgow Veterinary School in July 1999.

The cat was examined by one of the authors (D. D. A.) on seven occasions. Results of the physical examination were recorded on a form based on that of Sato and others (1996) (Fig 1), so that a clinical score could be devised. The results are shown in Table 1. On presentation, the cat had a clinical score of 16, which was high; a normal score would have been 7 (see Fig 1). The worst possible score would be 25 without weight loss (see Table 1) and 27 with weight loss; however, the cat was not weighed at first presentation. In addition, the mouth lesions were recorded on a mouth map.

A questionnaire was completed at each examination, recording what the cat ate and drank, and establishing that it was occasionally exposed to cigarette smoke, was not known to hunt, and that the owner was not applying any dental care products. The animal was from a single cat household and was free-ranging.

At the beginning and end of the study, the cat was FeLV negative (Jarrett and Ganière 1996) and negative by immunofluorescence for feline immunodeficiency virus (Pedersen and others 1987) and

Please circle which descriptions most appropriately describe the cat's mouth at present:

- Pain on vet opening cat's mouth
  (1) no evasive reaction
  (2) slight evasive reaction
  (3) obvious evasive reaction
  (4) threatening and bite action

- Salivation
  (1) none
  (2) slight
  (3) moderate
  (4) marked

- Appetite
  (1) normal
  (2) ⅓ to ⅔ of usual food intake
  (3) ⅓ or <⅓ of usual food intake
  (4) no appetite

- Oral inflammation
  (1) normal
  (2) reddened
  (3) severe congestion
  (4) ulcerative inflammation and proliferation of granulation tissue in fauces

- Haemorrhage from lesions
  (1) none
  (2) some bleeding when swabbed
  (3) spontaneous haemorrhage

- Halitosis
  (1) normal cat breath
  (2) present
  (3) dreadful

- Submandibular lymph nodes
  (1) normal
  (2) one or other enlarged – please specify which
  (3) both raised

- Cat's weight today:

Table 1. Clinical score based on the questionnaire shown in Fig 1. A lower clinical score indicates improvement

<table>
<thead>
<tr>
<th>Date</th>
<th>Lymph node enlargement</th>
<th>Halitosis</th>
<th>Pain score</th>
<th>Salivation</th>
<th>Appetite</th>
<th>Inflammation</th>
<th>Haemorrhage</th>
<th>Weight score*</th>
<th>Weight (kg)</th>
<th>Total score</th>
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<tr>
<td>14/7/99</td>
<td>2</td>
<td>2</td>
<td>2.5</td>
<td>1</td>
<td>2.5</td>
<td>4</td>
<td>2</td>
<td>ND</td>
<td>ND</td>
<td>16</td>
</tr>
<tr>
<td>3/8/99</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>-1</td>
<td>4.1</td>
<td>9</td>
</tr>
<tr>
<td>20/10/99</td>
<td>2 (left only)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>16/2/00</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>-1</td>
<td>4.3</td>
<td>11</td>
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<tr>
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<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>-1</td>
<td>5.18</td>
<td>9</td>
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<td>1-5</td>
<td>1</td>
<td>+2</td>
<td>4.3</td>
<td>9.5</td>
</tr>
<tr>
<td>2/5/01</td>
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<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>+2</td>
<td>3.9</td>
<td>10</td>
</tr>
</tbody>
</table>

*Weight loss = +2, Weight gain = –1, Same weight = 0
ND = Not done
Corona virus antibodies (Addie and Jarrett 1992). The lesions are shown at three time points in Fig 2. At each clinical examination an oropharyngeal swab was collected into viral transport medium for calicivirus isolation. Bacterial culture was also performed at each examination. Two swabs were rubbed into the lesions and used for bacteriology. A smear was made of one swab and Gram stained for examination for the presence of spirochaetes. The second swab was put into bacterial transport medium (Transwab; Medical Wire & Equipment Company, Corsham, Wiltshire) for both aerobic and anaerobic culture. Swabs were transported by hand to the bacteriology laboratory and examined immediately. Swabs were inoculated onto 7 per cent sheep blood agar and MacConkey agar for aerobic incubation, onto 'chocolate' agar for incubation in 10 per cent carbon dioxide, and onto 7 per cent horse blood agar for incubation in an anaerobic workstation (Don Whitley Mark III). Organisms considered to be of clinical significance were identified using the appropriate analytical profile index (Biomerieux). The results of these examinations are presented in Table 2.

Treatment
From July 1999, one 50 mg capsule of thalidomide (Sauramide; Penn Pharmaceuticals, Tredegar) was given daily by mouth in the evening. In accordance with advice from the Veterinary Medicines Directorate, the owner was informed that thalidomide is not licensed for use in cats. Lactoferrin powder (200 mg) was sprinkled directly onto the lesions each day and the cat's mouth was held closed for a few minutes to stop it expelling it. Treatment was not given during December 1999 and January 2000, when the owner was unable to attend the clinic, and the cat's condition deteriorated. Significant improvement was noted 11 months after the start of treatment and a gradual withdrawal of treatment was effected, with thalidomide being given every other day and lactoferrin for four days in seven; all treatment had ceased.
On subsequent occasions, profuse cultures of the bacterial flora present was very sparse. The inability to isolate FCV from these samples at any time.

**DISCUSSION**

To the authors’ knowledge, this is the first time that FCV has been monitored for the duration of a case of natural FGS, and that FCV shedding has been recorded to cease when clinical signs resolved. This finding contrasts with other studies performed in experimental infections (Dawson and others 1991), and this cat was clearly prone to prolong long-term shedding of FCV (Weinstein and others 1999) and cats treated with lactoferrin were reported to have shown an improvement in two weeks (Sato and others 1996). However, the cat’s appetite did improve soon after the beginning of treatment and the lesions ceased to bleed when swabbed. Veterinary surgeons in practice treating a further two cases of FGS in collaboration with the authors have noted a similar clinical improvement using thalidomide, although neither cat recovered completely, even after months of treatment, and FCV was isolated from both cats every time they were sampled, on 21 occasions. Some cases of FGS spontaneously regress, and that may have happened in this case.

The immunomodulatory properties of thalidomide are not fully understood, and have never been examined in the cat. The literature contains conflicting reports of the drug’s immunomodulatory effects: Mchugh and others (1995) reported that it induced Th2 and inhibited Th1 cytokine production in peripheral blood mononuclear cells in vitro; however, a single dose of thalidomide given to human volunteers enhanced their Th1-type immune response (Verbon and others 2000). Thalidomide is used widely in humans where a shift towards the Th1 response is protective, while a Th2 response is deleterious, for example, in...
References


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