The eosinophilic granuloma complex (EGC) has a history of being confusing to veterinary dermatologists and practitioners alike. Since 1975, based on clinical and histopathologic criteria it has been divided into three separate entities: the indolent (or eosinophilic) ulcer, the eosinophilic plaque and the eosinophilic granuloma. While a large number of etiologies have been attributed to these lesions, the majority appear to be allergic in nature. Response to treatment has, in some cases, been frustrating with non-responsive or relapsing lesion, while in others, lesions have resolved spontaneously.

CLINICAL FEATURES

Characteristically, lesions are firm, well-circumscribed papules (intradermal) or nodules (extending beyond the dermis into the subcutis). Initially, the overlying skin and hair coat appear normal, however, over time alopecia develops and the lesions become discoloured (erythematous, yellow, orange). These often ulcerate and have a serous crust. Three presentations are recognized:

1. When located at the mucocutaneous junction of the upper lip, either uni- or bilaterally, initially a shallow ulcer, these lesions are known as “indolent-”/”rodent-”/”eosinophilic-ulcers”. They are raised, well demarcated, occasionally eroding the upper lip dramatically. They do not appear to be pruritic.
   a. Differentials include focal trauma or neoplasia (squamous cell carcinoma [SCC], mast cell tumour)².

2. “Eosinophilic plaques” may be found in any haired location, most commonly on the ventral abdomen, face, neck, inguinal region, thighs (medial and caudal) or on the pads of the paws. They are well demarcated, erythematous, raised, often alopecic, flat-topped plaques. They may be covered with a serous crust and are intensely pruritic. In some cases they look like coalescing military dermatitis lesions³.
   a. Differentials include dermatophytosis, neoplasia (lymphoma, mast cell tumour, SCC, mammary adenocarcinoma), cutaneous viral disease (FHV-1), mycobacterial or fungal infection².

3. The granulomatous variant may present as a well demarcated, raised, hard, non-inflammed, erythematous linear lesion (“linear granuloma”) on the caudal thigh. They may also appear as firm nodules in the interdigital spaces or on foot pads. Alopecia may be present. If affecting the chin, a range of presentations is seen from a soft swelling (“fat”/”pouty” lower lip/chin) to a hard, even ulcerated lesion exuding yellow-white gritty material. Small popular lesions occur uncommonly on the pinnae. Unless ulcerated, the cat doesn’t appear to be perturbed by this form. Oral lesions may be raised or ulcerated on the tongue or palate; in the latter case, significant, (but inapparent, as swallowed) blood loss may occur if ulceration involves blood vessels of the hard palate.
   a. Differentials include all of those listed for eosinophilic plaques as well as bacterial folliculitis/furunculosis or abscess, foreign body reaction or sterile granuloma².

Distribution: In one study of 55 cases of idiopathic eosinophilic granuloma, 42% of the cats had lesions were found on lips (+/- commissure or chin with one having lesions on caudal thighs and one with fore paw pad lesion). Twenty-two percent of cats had caudal thigh lesions, 18% had chin lesions. Eight-two % of cats had lesions in more than one location¹. The incidence of EGC among 1407 feline patients seen by this dermatology service, for which follow-up was available, was 4%⁴.
ETIOLOGY
In the majority of cases, EGC is a hypersensitivity (hs) reaction to environmental allergens, (atopic dermatitis), food, insects (fleas or possibly mosquitoes, although mosquito-bite hs is probably a separate disease entity). Feline self-allergens have also been suggested as a cause (antibodies to epithelial components$^5$ or Fel d 1 (a salivary allergen)$^6$: if Fel d 1 is involved, it is likely that exposure is through grooming already abnormal skin.

Other, less common causes include mites, bacteria (e.g., Staphylococcus), dermatophytes, feline herpesvirus-1 (FHV-1), and foreign bodies (plant or insect parts, hair shafts). It is difficult to know whether intracellular bacteria seen on cytology are causing the reaction or whether the tissue has become infected secondary to the tissue damage. Two studies suggest a genetic predisposition (eosinophil dysregulation) in some cats when exposed to allergic triggers$^7$-$^9$.

DIAGNOSTICS
Despite the majority of lesions of the EGC having an allergic component, it is important to confirm the diagnosis in order to rule out the differentials that might not respond to or be made worse by immunomodulatory therapy$^2$. Cytologic samples may be harvested by making touch impressions of ulcerated lesions with glass microscope slides. When large numbers of eosinophils are found, EGC is strongly suggested. When intracellular bacteria are seen in neutrophils, culture and sensitivity is recommended. Other tests include Wood’s lamp examination (performing fungal culture on appropriate hairs) and microscopic examination of skin scrapings. Surgical biopsies are warranted in non-ulcerated lesions as well as some ulcers, especially those in the oral cavity.

The presence of concurrent systemic disease may affect therapeutic choices. A minimum database of a complete blood count (CBC), serum biochemistries, FeLV and FIV serology and urinalysis should be included in the work-up. A peripheral eosinophilia occurs in some, but not all cats. If high doses of cyclosporin are being considered, a toxoplasmosis titre is indicated: cats with pre-existing titres are unlikely to manifest recurrence of latent disease whereas those who do not have antibodies may be a risk for developing disease if exposed during treatment with this agent$^2$.

Unless evidence of fleas is noted, an ectoparasite elimination trial should be performed over 6-8 weeks. All in-contact animals should be treated as well for the same time period. Environmental contamination must be considered as a source of reinfection.

A strict dietary trial using a novel protein or hydrolyzed protein diet should be instituted restricting the patient to this diet for a full 6-8 weeks.

Unless controversial, serum allergy testing or (if appropriate), intradermal skin testing may be considered$^2$. This can be helpful in order to determine which allergens should be avoided in the atopic individual.

THERAPY
Unless primary disease is identified for which specific treatment exists (e.g., itraconazole for dermatophytosis, avoidance of trigger dietary allergens or fleas), immunomodulatory therapies for feline allergic disease are indicated. These include glucocorticoids, cyclosporin, chlorambucil and essential fatty acids.
Oral prednisolone is preferable to injectable daily dexamethasone or methylprednisolone acetate as the dose can be titrated to effect and the risk of complications, including that of developing diabetes mellitus\textsuperscript{10}, is lower. Initial dose is 1-2 mg/kg PO q24h; some patients may need higher doses. Once lesions have resolved, the dose should be tapered to the lowest effective alternate day dose. Cyclosporin at 5 mg/kg PO q24h is as effective as prednisolone at 1 mg/kg\textsuperscript{11}; higher doses may be needed. After a four-week course of therapy, treatment is tapered to alternate day with eventual twice-weekly treatment. Numerous drug interactions are known, therefore when other agents are indicated that might compete for cytochrome P 3A enzymes, the dose should be reduced\textsuperscript{12}.

Chlorambucil can be given concurrently with prednisolone at 2 mg/cat PO two-three times a week. It may also be considered as a sole agent when lesions are refractory to corticosteroid therapy or in a patient in which corticosteroids are contraindicated. Because of the possibility of reversible marrow toxicity, CBC should be monitored every two weeks for the first three months of use.

Omega 3:6 fatty acids may prove beneficial as adjunctive therapy by dampening inflammatory cascade as well as improving skin barrier function.

One author has suggested, based on follow-up of 55 cases of idiopathic EGC, as only 22% received treatment yet all cats went into remission over a period of one to nine months, that spontaneous resolution of lesions may occur\textsuperscript{1}. When underlying etiology is allergic and the offending allergen cannot be eliminated, immunomodulation is, however warranted.

REFERENCES

12. Effect of Drugs and Other Agents on Cyclosporine Pharmacokinetics and/or Safety