UPDATE ON CANINE DEMODICOSIS

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JONATHAN HARDY looks at a range of studies into this parasitic skin condition in dogs, considering transmission, presentation and the treatment choices

Summary

Demodicosis or demodectic mange is an inflammatory parasitic disorder. It is characterised by excessive numbers of demodectic mites. *Demodex* mites are normal residents of canine skin and *Demodex canis* is recognised as the most common species in dogs. *D canis* is found in the hair follicles and sebaceous glands and survives on epidermal debris, cells and sebum. *Demodex* mites are transferred by direct contact from the bitch to the neonates in the first two to three days of life.

Localised demodicosis usually presents with one or more small areas of variably pruritic alopecia most commonly on the face and limbs and is typically a benign disease. Generalised demodicosis presents with alopecia, marked follicular hyperkeratosis, comedo formation and follicular casting.

An hereditary *Demodex*-specific T-cell defect of varying proportions might help to explain the pathogenesis. The licenced treatments for demodicosis in the UK include amitraz and moxidectin. Demodicosis should be suspected in any young dog with focal alopecia, especially affecting the face and feet, and where follicular casting and comedones are seen. Older dogs with similar lesions, or unexplained pyoderma should also be sampled for *Demodex* mites and an underlying cause should be investigated.

Key words

Demodex, amitraz, alopecia

DEMODICOSIS or demodectic mange is an inflammatory parasitic disorder characterised by the presence of larger than normal numbers of demodectic mites in the skin (Miller, Griffin and Campbell, 2013).

Demodex mites are considered normal residents of canine skin and *Demodex canis* has long been recognised as the most common species in dogs. *D canis* resides in the hair follicles and sebaceous glands and survives on epidermal debris, cells and sebum.

In the 1980s, a short-bodied mite was identified and named *D cornei*. Apart from its size, it seems to share many characteristics of *D canis* although it has been suggested it occupies a more superficial location on the skin. Since its identification, it has been increasingly found in clinical cases. It is reportedly not uncommon to find *D canis* and *D cornei* from the same patient and this is relatively common in the author's experience.

Sequencing the parasite's mitochondrial 16s rDNA has indicated *D cornei* might be the same species as *D canis* with up to 99.6 per cent sequence homology (Sastre et al, 2012). In the same study, a third canine demodectic mite named *D injai* was analysed and judged to be a separate species with only 76.6 per cent identity with *D canis*.

*D injai*is a long-bodied *Demodex* mite and was first identified in the 1990s. *D injai* also resides within hair follicles, sebaceous glands and sebaceous ducts, but usually produces disease with a different presentation to the other two *Demodex* mites.

Published studies indicate treatment success is similar regardless of the specific mite involved (Mueller et al, 2011).

Transmission

Demodex mites are transferred by direct contact from the bitch to the neonate in the first two to three days of life. Puppies delivered by caesarean section and reared away from the dam do not have *Demodex* mites, and stillborn pups do not harbour mites either, suggesting they pass by direct contact. Contact with the dam during nursing in these early days is thought to explain why the face and feet are predilection sites for disease.

Unlike sarcoptic mange, demodicosis is not considered a contagious parasitic disease for other dogs or incontact humans.

Studies attempting to transfer disease with mite-laden solutions to the skin of healthy dogs only produced mild transient lesions that resolved spontaneously, so it seems that mites are only "infectious" during this narrow two to three day window after birth.

Clinical signs

Demodicosis typically presents as localised or generalised disease, although there is no universally accepted way to distinguish the two. Both classic presentations are usually caused by infestations with *D canis* or *D cornei*.

Demodicosis can present as juvenile-onset disease with clinical signs generally starting between three and 18 months of age and adult-onset disease, which typically presents in dogs greater than four years old. However, some cases present with an age of onset in between.

Localised demodicosis usually presents with one or more (usually one to five) small areas of variably pruritic alopecia, most commonly on the face and limbs, and is typically a benign disease. These areas can show fine scaling and erythema and can also become hyperpigmented.

Most localised cases pre-sent as juvenile-onset disease between the ages of three and six months. Localised juvenile-onset cases only rarely become generalised and, at present, no evidence suggests treatment of localised cases prevents them becoming generalised if they were destined to do so.

Generalised demodicosis, however, represents one of the most severe canine skin diseases. Lesions usually cover a large number of areas (more than six), an entire body region such as the face **(**Figure 1**)** or involve more than two feet. Clinical signs present as alopecia, follicular hyperkeratosis, comedones **(**Figure 2**)** and follicular casting. Secondary bacterial infections are common, presenting with papules, pustules and sometimes nodules and furuncles. Severe cases also often show marked lymphadenopathy. Over time, the lesions can become lichenified, crusted and frequently nodular from the resulting folliculitis and furunculosis.

In contrast, demodicosis due to *D injai* proliferation has been reported with a different presentation. Cases can show facial lesions, but are normally associated with dorsal greasy seborrhoea with low numbers of mites found at affected sites. It seems terrier breeds may be over-represented in this type of demodectic mange (Ordeix et al, 2009).

Pathogenesis

Low numbers of *Demodex* mites are part of the normal cutaneous fauna and, in the majority of dogs, a healthy immune system maintains levels of these mites in low numbers.

In young dogs, endoparasiticism, malnutrition and debilitation, along with genetic factors, may lead to an immunocom-promised state (Mueller et al, 2011). In juvenile-onset cases, it is clear affected dogs do not succumb to other systemic infections, so a mite-specific immunocompetence of varying severity helps to explain this.

Studies have looked at neutrophil and complement function in affected dogs and found no abnormalities. Likewise, studies investigating defects in humoral immunity have failed to find a specific anti-body defect or deficiency linked to demodicosis.

However, studies assessing T-cell function as measured by the lymphocyte blastogenesis test (IVLB) have shown depressed T-cell activity. Because affected dogs are not lymphopaenic, it may be a defect of T-cell function rather than T-cell number. As a result, the current hypothesis proposes a hereditary *Demodex*-specific T-cell defect of varying proportions in addition to factors such as endoparasiticism and malnutrition (Miller, Griffin and Campbell, 2013).

In older dogs, immuno-suppressive diseases or drug treatments may allow mite proliferation. True adult-onset generalised cases are quite rare, but can be even more severe and difficult to treat than generalised juvenile-onset cases, depending on the underlying cause. In these dogs, *Demodex* mites previously controlled by the immune system in low numbers for many years suddenly start multiplying out of control. If the host becomes immunocompromised, mites are able to proliferate and cause disease.

Underlying immunosup-pressive disorders linked with this condition include hypo-thyroidism, hypercortisolism (including naturally occurring and iatrogenic), leishmaniosis and neoplasia. Immunosup-pressive and anti-inflammatory treatments for other neoplastic, autoimmune and allergic diseases have also caused adult-onset demodicosis.

However, in up to 50 per cent of cases, despite an exhaustive search, an underlying cause cannot be found. These idiopathic cases seem to be associated with a poorer prognosis than those where an underlying cause can be identified and corrected (Miller, Griffin and Campbell, 2013). Conversely, a relatively rapid therapeutic response can be expected in cases where the underlying cause can be removed, such as following curative surgery for visceral neoplasia.

Diagnosis

Demodex mites reside within the hair follicles, so deep skin scrapings or hair plucks from multiple sites are required for diagnosis. Affected skin can be squeezed to extrude mites from the follicles before performing skin scrapes.

In sites such as the face and feet, hair plucks are an excellent way of finding mites and many dogs tolerate this better than skin scrapings. Hairs are plucked carefully from affected sites and as with skin scrapes, are examined under a microscope with a cover slip, mineral oil and a low power lens.

As the sensitivity of hair plucking may be lower than skin scraping in some cases (Saridomichelakis et al, 2007), it may be advisable to perform both tests where possible.

Direct examination of exudate from nodules or draining tracts, or ear wax from cases of

ceruminous otitis externa, can also reveal mites through low power microscopic examination. Finally, in some nodular or fibrosed lesions, and in breeds such as the Shar Pei, skin biopsies may be required for diagnosis.

Whichever method is used, high numbers of mites are usually demonstrated in clinically affected skin, often with multiple life stages (eggs, larvae, nymphs and adults) present. As *Demodex* mites are considered normal fauna, the finding of an occasional mite warrants further sampling. However, it is not normal to find mites easily in the skin of healthy dogs (Fondati et al, 2009)

Treatment

Although the standard textbook of canine dermatology suggests spontaneous resolution of juvenile-onset generalised demodicosis may occur in more than 30 per cent to 50 per cent of cases (Miller, Griffin and Campbell, 2013), Mueller et al (2011) observed that, in the absence of placebo-controlled therapeutic trials, the rate of spontaneous remission in canine demodicosis is not known.

Treatment is normally recommended, especially in generalised cases with significant discomfort, or in dogs with secondary pyoderma. Owners should be counselled on the protracted course of the disease, with some cases requiring up to a year to reach remission (Miller, Griffin and Campbell, 2013). In fact, some cases of adult-onset demodicosis where an underlying immunosuppressive disease cannot be identified need life-long treatment to keep mite numbers under control.

The licensed treatments for demodicosis in the UK include amitraz and moxidectin. Amitraz rinse has been used for many years and has been recommended as an effective treatment for demodicosis in systematic reviews (Mueller et al, 2004; Mueller et al, 2011). In the UK rinses are performed weekly with a 0.05 per cent solution that is left on the skin to dry without being washed off. Clipping the coat is strongly recommended in medium to long-haired dogs.

The spot-on application of amitraz, containing 15 per cent amitraz and 15 per cent metaflumizone, showed success in pilot studies when used monthly (Fourie et al, 2007) and every two weeks (Rosenkrantz, 2009) and is licensed for monthly application. However, a study in *Veterinary Dermatology* linked this product to pemphigus foliaceus-like drug reactions (Oberkirchner et al, 2011).

Spot-on moxidectin, containing 2.5 per cent moxidectin and 10 per cent imidocloprid, showed promising results in initial studies (Heine et al, 2005; Fourie et al, 2009) and obtained a licence for monthly application. At veterinary discretion, it can be applied once a week in severe cases (European Public Assessment Report). Studies suggested more frequent application achieved better results (Fourie et al, 2009; Paterson et al, 2009). In the blinded randomised comparison study by Paterson and others in 2009, there was an 89 per cent reduction in total live mite counts over four months following weekly treatment with the moxidection/imidoclo-prid product.

In comparison, daily oral treatment with ivermectin at 0.5mg/kg achieved a 98 per cent reduction in total live mite counts, but this difference was not statistically significant. It has been suggested the efficacy of moxidection/imidocloprid is better in milder forms of the disease and for juvenile-onset cases (Mueller et al, 2009).

Treatment failures, unavailability and adverse effects with licensed products might lead veterinary surgeons to consider the use of unlicensed treatments for this disease. Milbemycin is a macrocyclic lactone licensed for the treatment of demodicosis in some European countries, although it is not licensed for this purpose in the UK. It is used at a daily oral dose of 0.5mg/kg to 2mg/ kg and has been recommended as an effective treatment in evidence-based reviews (Mueller, 2004; Mueller et al, 2011). It is reportedly more effective in juvenile-onset cases and can be given to collie dogs with care.

Dogs homozygous for the ABCB1-delta1 (formerly MDR-1) mutation develop neurological side effects with the higher doses, but can tolerate doses up to 0.6mg/kg/day.

Oral ivermectin, although unlicensed in the UK, is also an effective treatment for canine demodicosis (Mueller et al, 1999; Mueller et al, 2011). It is usually prescribed at a dose of 0.3mg/kg to 0.6mg/kg and, due to the risks of neurotoxicity, the dose is usually increased gradually from a starting dose of 0.1mg/kg.

Testing for the ABCB1-delta1 mutation is possible and advisable in collie dogs and their crosses if a macrocyclic lactone is being considered. However, other mechanisms of neurotoxicity exist so care is needed with this drug even if dogs do not carry this mutation.

When using ivermectin, it is important to consider other concurrent drug therapy, as other p-glycoprotein inhibitors can increase the likelihood of adverse reactions.

Two open, uncontrolled studies have also evaluated doramectin (Johnstone, 2002; Murayama et al, 2010), another macrocyclic lactone, for the treatment of demodicosis. Based on these studies, it seems to be an effective treatment when given orally or injected subcutaneously at 0.6mg/kg at weekly intervals. However, it remains an unlicensed treatment in the UK and further evaluation in randomised controlled trials is needed.

Whichever treatment option is used, medication should continue until parasitological cure is reached. Clinical resolution usually precedes this, but treatment should be continued until two sets of negative tests (skin scrapes or hair plucks without any live or dead mites) a month apart are obtained.

Premature cessation of treatment is a common cause for treatment failure and relapse. As a general rule, dogs are not considered cured until there has been one year without medication and without relapse.

Conclusion

Demodicosis is a relatively common disease in dogs and, although treatment can be costly and protracted, the outcome is usually good. It is essential to address any secondary infections present and to treat them concurrently.

Demodicosis should be suspected in any young dog with focal alopecia or erythema, especially affecting the face and feet, and especially where follicular casts or comedones are seen. Older dogs with similar lesions, or unexplained pyoderma should also be sampled for *Demodex* mites. In these cases, a search for underlying cause is also paramount. Due to the genetic links in juvenile-onset generalised disease, neutering is advisable in such cases.

• Some treatments mentioned are not licensed for use in the UK.

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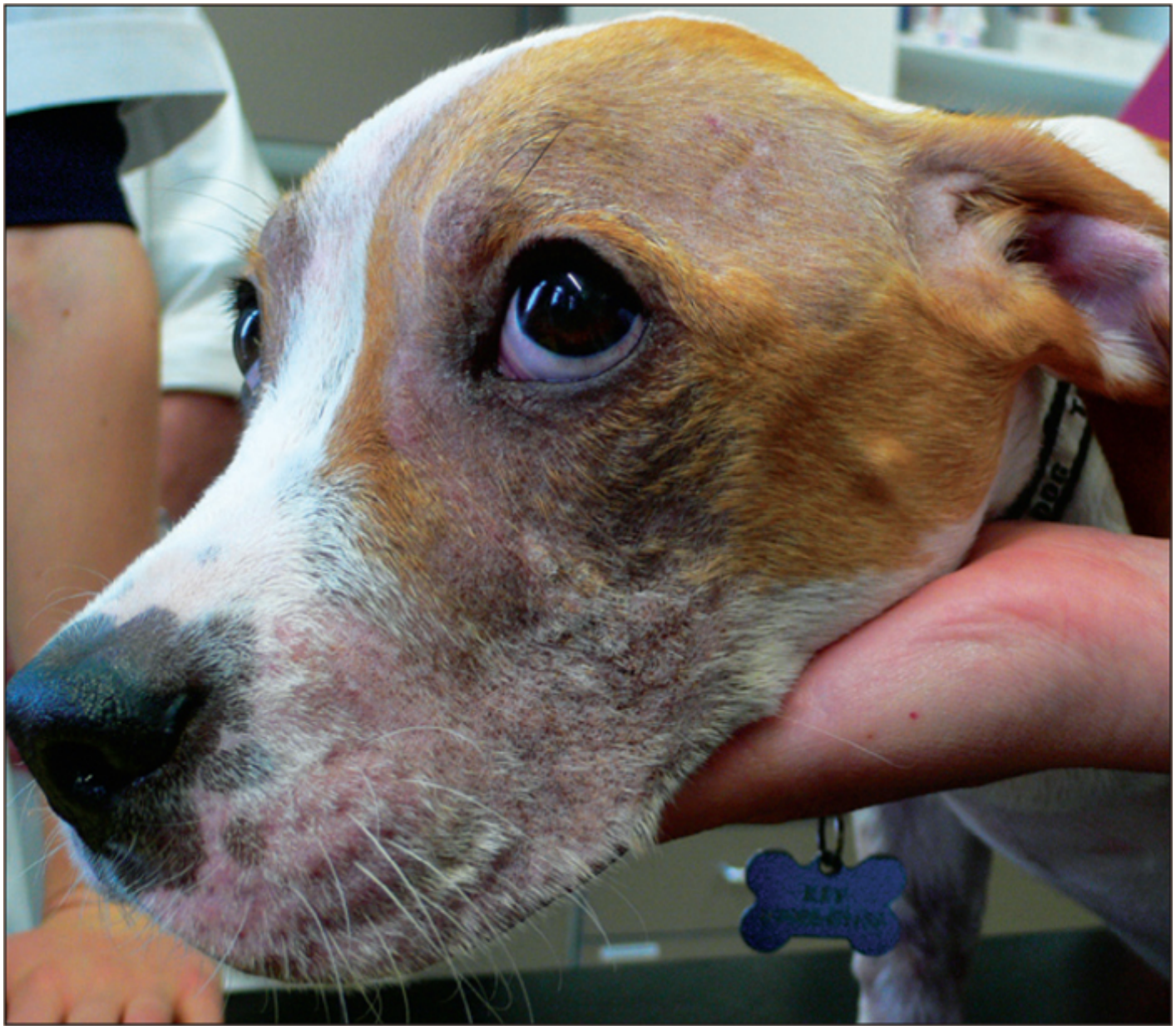

Figure 1. Facial erythema, alopecia and comedones in a case of juvenile onset generalised demodicosis.

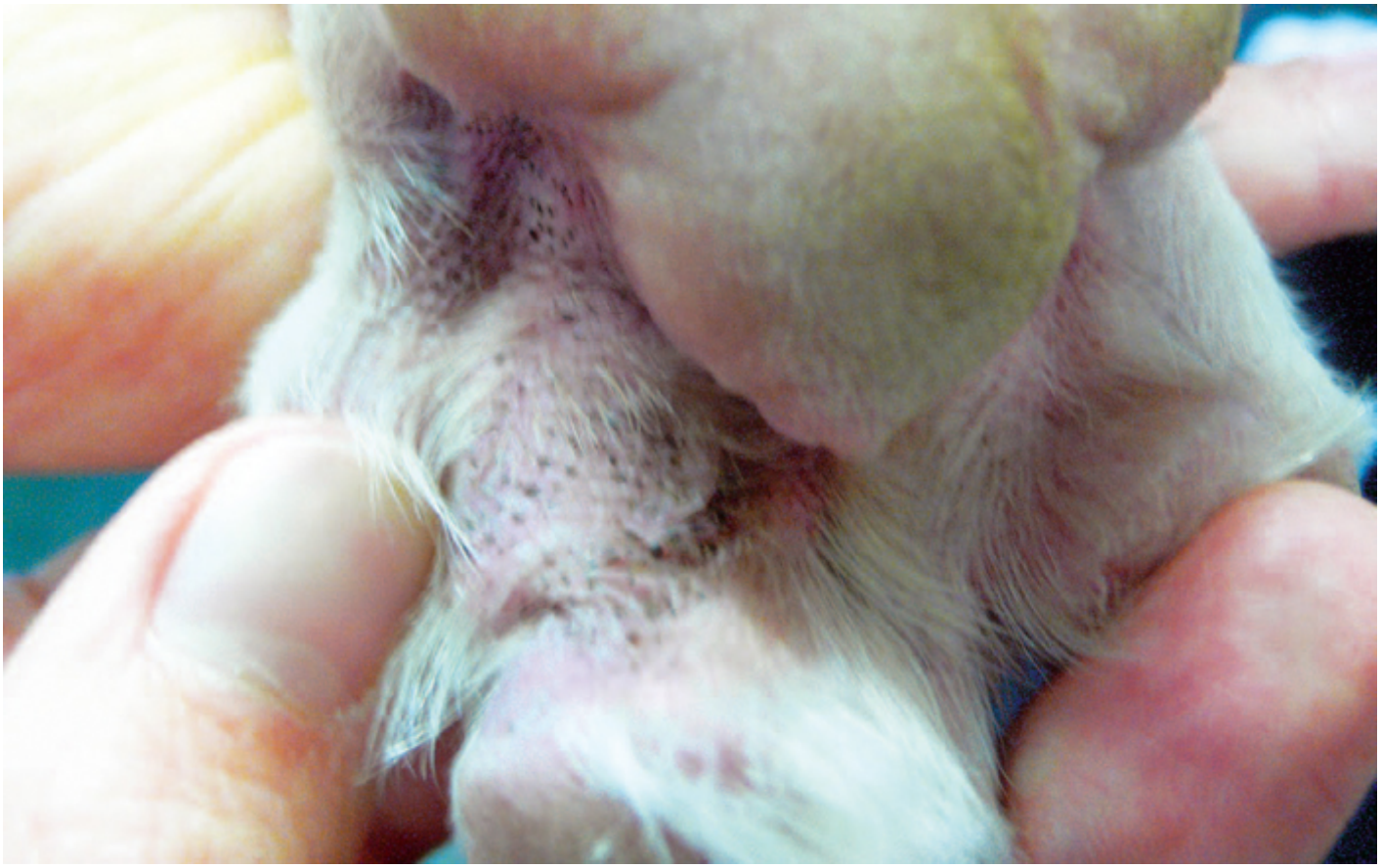

Figure 2. Interdigital comedones from the dog in Figure 1.