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Review on Canine Demodicosis

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Introduction

Demodicosis/Canine demodex infestation is a common mange of dogs, usually non contagious and seen in immuno-suppressed animals. It is clinically characterized by non-pruritic erythema, greasy seborrhoea, thickening and peculiar bad odour from skin, lichenification (Chronic cases) and due to its not contagious property the whole life of the demodex mite mostly limited to a single host. Predilection site is hair follicles hence called as follicular mange and infestation is also called red mange due to characteristic generalized erythema in adult dogs lead to the complete redness of skin.

Key words: Immunosuppression, Erythema, Deep pyoderma, Isoxazolines.

Aetiology: Causes by Demodex mites (non-zoonotic).

For *Demodex canis, Demodex injai, and Demodex cornei*, dog is considered as the final host or definitive host. (Amita Tiwari *et al*., 2023). Mites resides as normal commensals in the hair follicles and sebaceous glands of skin and feed on debris, when host's immune system is failing in defence, these commensals over proliferate and causes dermatitis.

Mite's Characteristics: Cigar shaped elongated mites with distinct head, thorax and abdomen. Thorax on ventral portion has 4 pairs of legs in nymphs (protonymphs and deutonymphs) and 3 pairs of legs in adults. Abdomen is long, transversely striated and becomes bluntly pointed at the end. Females are slightly larger than males and lays spindle shaped eggs.

Description (S.C Mandal, 2012);

1. There are two nymphal stages - protonymph and deutonymph.
2. The female mates deposits their eggs in hair follicle and sebaceous gland.
3. After hatching the larva comes out. Larva transforms to the nymph.
4. Along with the sebaceous material the larva and nymph come to the outlet of hair follicle and gets mature there.

Epidemiology: According to the study by Sharma P *et al*, 2018.

The prevalence of demodicosis was found higher in the dogs of 0-1 years of age (36.36%) than in the dogs of 1-3 years of age (31.81%). Infestation of Demodex was significantly ($p<0.05$) higher in male (81.82%) than female (18.18%) dogs.

Heredity: the tendency to develop generalised demodicosis is inherited. Although the precise mode has yet to be elucidated, it is clear that the condition can be transmitted both by the dam and the sire. (Pierre Jasmin, 2011).

Predisposing factors: Demodicosis is commonly seen in animals with low or suppressed immunity. It can be due to hormonal imbalance (Ex// Hypothyroidism, hyperadrenocorticism), parasitic infections, poor nutrition, corticosteroid therapy, tumours, age etc. In such conditions rapid proliferation of mites can be correlated with decreased defence response of skin.

Breed Predisposition: Purebreds are likely to develop the disease.

Predisposed breeds are Boxers, Chinese Shar peis, American cocker spaniels, Great danes, Pitbull terries, Doberman pinschers, German shepherd, Staffordshire terriers and Old English sheepdog. (Chintan G Satasiya *et al.*, 2022).

Transmission: Demodex mites are not usually contagious so transmission between adult dogs is not noticed much, but there are many evidences of transmission between infected bitches to suckling puppies via skin contact (probably due to the immune response in young ones) in such cases entire litter of infected bitches may show juvenile demodicosis.

Types

They are classified under different basis;

1. Age: Juvenile onset and adult onset demodicosis.
2. Duration: Acute and Chronic (Characterised by deep pyoderma & lichenification)
3. Distribution on the body: Localised and Generalised demodicosis.
4. Forms: Adult on set is further divided into squamous form and pustular form
5. Location: Pododemodicosis, Otodemodecosis etc.
6. Complications: Simple and Complicated (Ex// Pyodemodicosis - 2° Pyoderma)

Juvenile onset demodicosis: usually seen in 3 months and above age. Lesions usually localised and limited to some areas like around the mouth, periocular area and paws etc. Usually self-limiting, this localised form sometimes may flare up and proceed to generalised form called as juvenile generalised demodicosis.

Adult onset demodicosis: seen in adult dogs already suffering with malnutrition / parasitic infection / poor management / endocrine disorders. Initially squamous form noticed where mites proliferate and lead to hyperkeratinisation of skin, followed by pustular form where due to secondary bacterial infection (Ex// Staphylococcus sp, Pseudomonas Sp. etc.) pustules formation, deep pyoderma with furunculosis and cellulitis occurs.

Pododemodicosis, lesions confined to paws and inter digital spaces

Otodemodicosis, mites reside and lesions confined to ears causing severe otitis externa.

Pathogenesis (B.B Bhatia *et al.*, 2016);

Invading *demodex* mites affect the dermal cells of the host by putting pressure on cell membrane and

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by abrasive action of leg claws and palpal spines. Follicular plugging with keratinization is common feature. The mites penetrate the cell membrane using their needle-like chelicerae and feed on the cytoplasm. Secondary superficial infection on ruptured follicles produces typical inflammatory response. There is extensive epithelial hyperplasia followed by small papules and nodules by granulomatous reactions. This is followed by secondary bacterial infection of the dermis. A heavy infiltration of polymorphonuclear leucocytes, lymphocytes and plasma cells in the dermis results in septic pustule formation which may become large abscess.

Immune response – according to research study by Pamela A *et al*., 2023, there is an

- Increase in the T cell population, specifically Th1 and Treg cells in dogs with demodicosis. In addition, whilst immunosuppressive cytokines such as IL-10 and IL-13 were up-regulated, there was also an upregulation of immune check point molecules including PD-1/PD-L1 and CTLA-4 suggest that Demodex spp. Mites do modulate the host immune system to their advantage through upregulation of various immune tolerance promoting pathways.
- Activation of PD-1 and CTLA-4 results in reduced TCR signalling, reduced T cell proliferation and survival as well as increased T cell exhaustion and increased Treg cell activity, all of which would aid the evasion of the immune system by demodectic mites.

Euthyroid Sick Syndrome and demodicosis: Some of the "hypothyroid" dogs that have demodicosis may have euthyroid sick syndrome due to occult tumors rather than having the hypothyroidism as the reason that demodicosis developed (Charach MG., 2018).

Clinical signs

Usually, signs vary based on the type and age.

In localized demodicosis, lesions usually are confined. Animals will be presented with periorbital or perioral hair loss / alopecia, multiple localized erythematous lesions. It may progress to generalized form in some cases, where severe thickening of skin due to hyperkeratinisation, comodones and crusts formation, foul odour from skin and scaling will occur, pruritus will not be noticed till condition complicated by 2° bacterial infections.

***Pododemodicosis*:** usually affects forelegs but can affect all the limbs. Animals are presented with severe erythema, alopecia from manus (fore limb) and pes (hind limb) regions, localised oedema, severe pain, scaling and discoloration of skin.

Otodemodicosis: causes otitis externa. Ear flaps and ear canal will become inflamed, animal will vigorously shake the head and the ears, dark brown aural discharge noticed.

Adult onset demodicosis: [signs noticed similar to Juvenile onset (generalised) as discussed above]. This condition has 2 forms, Squamous and pustular form.

Initially in *squamous form*, hyperkeratinisation and thickening of skin occurs and becomes reddish (Hence called Red Mange). Skin becomes greasy, foul smelling, depigmented, wrinkled and formation of comodones occurs.

Later followed by *pustular form* where opportunistic bacteria will complicate and leads to pustule formation on skin. Furunculosis (deep pyoderma) is evident here. Due to proliferation of bacteria animal odour become more offensive. In severe chronic cases cellulitis, local lymphadenopathy occurs, animal losses it's

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condition and dies due to toxaemia.

Diagnosis

Based on clinical signs (Tentative diagnosis)

Confirmatory diagnosis is done by Microscopic examination of mites,

To rule out the differentials (Fungal dermatitis) hair pluck can be used but to confirm the presence of follicular mange, deep skin scraping (considered as gold standard) is necessary. Scraping of skin should be done till capillary bleeding occurs.

Scrapings should be further used for

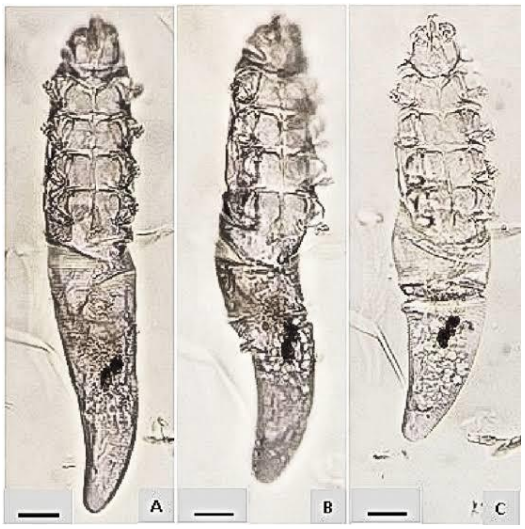
1. Direct microscopic examination
2. 10% KOH method: Add scrapings to the boiling test tube containing 10% KOH (10ml) and boiling should be done till hair in tube completely gets digested. Then subject the sample to centrifugation at 2000 RPM for two minutes. Discard the supernatant and the sediment can be used for identification of mites under microscope 40x and 100x magnification.

Other methods: Biopsy, Acetate tape method, Trichograms also can be used. According to study by Lubna Fathima *et* al., 2017; Indirect ELISA to detect the presence of IgG antibodies against *Demodex canis* (Sensitivity – 70.58%, Specificity – 76.92%).

In deep pyoderma, impression smears and swabs should be taken and should be subjected to microscopic examination by gram staining followed by culturing and antibiotic sensitivity testing (ABST).

Differential Diagnosis: Initially differentiate from generalized fungal dermatitis, Other mange (Ex// scabies). In generalized cases rule out the other causes of deep pyoderma and allergies.

Figure 1. Specimens of *Demodex canis*, female, in the in vitro test: (A) live mite; (B) initial opisthosomal



wrinkling, immediately after contact with pure tea tree oil (100%); and (C) dead mite, with complete wrinkling of the opisthosoma and clarification of the opisthosomal cuticle, 6 min after contact with the oil (bar in A-C = 20.92 µm). (Neves RCSM *et al*., 2020). *Reference figure*.

Treatment

Treatment can be followed using single or multiple drugs (multimodal approach) in combination along with supportive therapy. (Ex// Injectable or oral miticidal drugs along with topical medication like shampoos and oral vitamin supplementation)

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In *Juvenile onset demodicosis*, as it is self limiting condition, immunity boosting is mostly enough. if the puppies are not shows any signs of recovery, topical applications can be used. Commercially available herbal liquids can be used in 1:2 dilutions. (Ex// Zerokeet ™).

In *Adult onset demodetic mange*, many miticidal drugs are commercially available.

Formamidine Insecticides – Amitraz (Drug of choice) used in dip / wash. Frequency - once weekly to 15 days less interval (topically). Using in increasing concentration with less intervals yield better result. For dog - 0.025 to 0.05 % solution higher concentration for demodetic mange (Harpal Singh Sandhu, 2013).

Isoxazolines - Given in single dose as chewable tablets.

- Fluralaner @ 30mg/kg P.O (P. Sree Krishna Sai *et al.*, 2022)
- Sarolaner @ 2-4 mg/kg P.O (Becskei C *et al*., 2018)
- Afoxolaner @ 2.7 mg/kg alone or afoxolaner (2.5 mg/kg) with milbemycin oxime (0.5mg/kg) [Lebon *et al*., 2018] P.O.
- Lotilaner - Dogs were treated with 20 mg/kg P.O on days 0, 28 and 56. (Mueller RS *et al*.,2020).

Macrocyclic lactones –

- Ivermectin - The currently recommended protocols generally employ 300–600 mg/kg P.O. once daily until four to eight weeks beyond parasitological cure. Despite its frequent successful use in the treatment of demodicosis, it is unlikely that ivermectin will ever become labelled for this purpose due to its potential toxicity. (Muller RS *et al*.,2020). Administration of Ivermectin was the most efficacious protocol whilst weekly subcutaneous (S.C.) administration at 0.4 mg/kg. (Scott DW *et al*., 1985). Sometimes may yield poor results.
- Milbemycin oxime - 1-2 mg/kg P.O (Garfield RA *et al*., 1992).
- Moxidectin – When oral administration (500 µg/kg) was compared to the subcutaneous route (500–1,000 µg/kg), each administered every 72 h, rates of cure were 75% and 86%, respectively (Muller RS *et al*.,2020).
- Doramectin – 0.6 mg/kg weekly, injection subcutaneously (John H C Hutt *et al*., 2015).

Neonecotinoid insecticides – Imidacloprid, available as 10% Spot on (Harpal Singh Sandhu, 2013).

Pyrethrins: available as shampoos (Ex// Permethrin based shampoos).

Use of other miticidal and insecticidal drugs is infrequent due to less efficacy and drug toxicity (Demodex treatment and recovery is difficult and depends upon the efficacy of drug). Lufenuron and Levimasole should not be used in demodicosis.

Antibiotic Therapy: in cases of deep pyoderma, to counter bacterial proliferation broad spectrum antibiotics should be used.

- *Lincosamides*, Ex// Clindamycin (11 mg/kg q 12hrs),
- *Cephalosporins*, Ex// Cephalexin (22 mg/kg q 12hrs),
- *Penicillins*, Ex// Amoxicillin + Pottasium clavulanate (12.5 mg/kg q 12hrs).

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Adjuvants in therapy and other protocols;

1. Shampoos containing Benzoyl peroxide and salicylic acid can be used, they have follicular flushing and keratolytic properties respectively, aids in removing of mites from the follicles and cleaning of skin debris.
2. Chlorphenaramine maleate (0.2 to 0.5 mg/kg q 12hrs) injectable or Cetirizine (1mg/kg q 24hrs), levocetirizine or Hydroxyzine (2 mg/kg q 8-12 hrs) as oral medication. To counter pruritis due to pyoderma.
3. Multivitamin, multimineral and essential fatty acids supplementation, to enhance the immunity and aids in skin healing and repair.
4. Hypoallergenic diet while undergoing treatment.
5. Homeopathy – according to Muller RS *et al*.,2020;

Homeopathic preparations containing Sulphur 200, Heparsulphuris 200 or Psorinum 200 were given orally at five drops daily for five weeks to three groups of six puppies experimentally infected with *Demodex canis*. The post-treatment mean demodicosis indices were lower in the groups treated with Sulphur 200 and Psorinum 200 compared with the group treated with Heparsulphuris 200 and a control group, but neither complete clinical nor microscopic resolution could be achieved. A herbal preparation containing extracts of Cedrus deodara, Azadirecta indica and Embelia ribes was sprayed on lesions of 14 juvenile dogs with apparent generalized demodicosis. Dogs were re-evaluated after 24 h and if skin scrapings were still positive for *D. canis*, dogs were retreated once. Subsequent weekly skin scrapings for six weeks were negative in all dogs.

1. Metaflumizone plus amitraz spot on, Treatment at monthly or two-weekly intervals for 3 months resulted in a rapid reduction in mite numbers (>94 and >99% for the monthly and two-weekly treatments, respectively) and an improvement in clinical signs. Success rates, based on zero mite counts in skin scrapings at Day 84 were 42.9 and 62.5% of dogs for the monthly and two-weekly regimens, respectively (Fourie LJ *et al*., 2007).
2. Inactivated parapoxvirus ovis (iPPVO) could help to accelerate treatment with acaricidial therapy by altering the immune response (Pekmezci D *et al*., 2014).

Commercial Drug Preparations;

- Amitraz: Dip concentrate liquid, 12.5% w/v concentration.
- Fluralaner: Bravecto ™, available in 112.5 mg, 250 mg, 500 mg, 1000 mg, 1400 mg chewable tablets.
- Sarolaner: Simparica ™, 40 mg and 80 mg chewable tablets. Also available in combination – Sarolaner, Moxidectin and Pyrantel (Simparica trio ™).
- Afoxolaner: Nexgard™, Available in 68 mg and 136 mg chewable tablets.
- Lotilaner: Credelio™, 56.25 mg, 112.5 mg, 225 mg, 450 mg, 900 mg chewable tablets.
- Milbemycin oxime available as chewable tablets.
- Moxidectin: available as injection 1% w/v, spot-on (combination of Moxidectin 2.5 w/v and imidacloprid 10% w/v Ex// Advocate ™) and also tablets.

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- Ivermectin: available as Injectable (10 mg/ml), tablets and pour on (usually cattle preparation).
- Imidacloprid: available as chewable tablets and also as spot on alone or combination with other drugs (Ex// Moxidectin).

Key notes:

1. Animal is considered as successfully recovered from demodicosis, when consecutive 2 deep skin scrapings are negative for mites.
2. Dosage of above miticidal drugs should be proper and over dosing can lead to toxicity and death.
3. Most of the drugs show neurological signs in over dosing and early treatment intervention in such cases is necessary to save the animal life.
4. If the owner is applying external insecticide, should have protective covering over the hands and eyes & should not have any cuts/ abrasions. Entrance to chemicals into systemic circulation is very dangerous. If the compound spilled into eyes, rinse them thoroughly and should consult a physician immediately.
5. Animals should not lick the topical application and if accidentally done, should consult the Veterinarian immediately.
6. They should be out of reach to children and pets to prevent accidental ingestion.
7. At the time of prescribing medicine (in positive cases), physicians should keep in mind regarding the cost bearing capacity of the owner, the treatment should vary based on that.

Prevention and Control

As demodicosis is seen in immuno-suppressed dogs, having proper immunity is utmost important. It can be done by proper management with balanced nutrition, free from parasitism, early diagnosis of underlying conditions or endocrine disorders can decrease the suffering of dogs.

Conclusion

Treatment of demodicosis show promising results but early intervention and proper drug therapy with supplementation is needed to reverse skin damage and to prevent the progress of deep pyoderma and worsen the health condition.

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