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Canine juvenile cellulitis: An overview

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Abstract

Canine Juvenile cellulitis is an uncommon granulomatous and pustular disorder of the face, pinnae, and submandibular lymph nodes mostly affecting young puppies, between one and six months of age. This condition is currently regarded as idiopathic, meaning that its cause is currently unknown. It is an immune-mediated disease. Therefore, treatment of juvenile cellulitis relies upon suppressing the immune system, to stop the auto-immune reaction. The treatment of choice in canine juvenile cellulitis is judicious use of the proven anti-inflammatory agent, glucocorticoid: Prednisolone, singly or in combination with broad-spectrum antibiotic in a well-planned oral therapeutic regimen.

Keywords: Canine, cellulitis, immune-mediated disorder, juvenile

1. Introduction

Canine juvenile cellulitis, skin disorder affecting puppies of 3 to 24 weeks of age, is characterised by sterile granulomas with pustules, pyogranulomatous dermatitis and lymphadenitis (Scott *et al.*, 2001; Park *et al.*, 2010) [28, 24]. First chronicled as 'lymphadenitis apothematosa' by Kral in 1957, this skin disorder of ill-defined aetiology is rare (Scott *et al.*, 2001; Gross *et al.*, 2005) [28, 10]. The synonyms are 'puppy strangles' and 'juvenile sterile granulomatous dermatitis'. The pathogenesis is not clearly delineated yet. However, since the cutaneous lesions respond well to the glucocorticoids involvement of an immune-mediated component seems logical.

On presentation, the affected puppies may exhibit general clinical signs: subdued fever, depression and anorexia. The classical symptoms: acute swelling of the muzzle, lips, and eyelids are the landmark. Sterile cutaneous pustules often develop in these specified areas. Otitis externa is a common observation, and the ear pinnae are often indurated and oedematous. Small ulcers, draining tracts, seropurulent exudates, or crusts may develop from some of the ruptured pustules. Sub-mandibular lymphadenopathy is a common clinical observation (Gupta *et al.*, 2020) [11]. Occasionally, the lymph nodes get ruptured and drain. Nodules over the trunk, preputial/ perineal areas are also reported. Patchy alopecia and scarring may ensue from the lesions, if extensive. Microscopic examination reveals epithelioid macrophage as the dominant inflammatory cell type (Inga *et al.*, 2019) [13].

2. Epidemiology

- **Age:** Canine juvenile cellulitis in puppies occurs typically from 5-20 weeks in the range of 3-36 weeks post-partum (Mason *et al.*, 1989; White *et al.*, 1989) [16].
- **Gender:** Though there is no established gender predilection, the incidence is higher in the males (Mason *et al.*, 1989; Scott *et al.*, 2007) [16, 27].
- **Breed:** Genetic predisposition is supported by the increased susceptibility of certain genotypes: Golden Retriever, Miniature Dachshund, Labrador Retriever, Siberian Husky and Lhasa Apso (Bassett *et al.*, 2005) [2]. Some other breeds, namely Beagle, Pointer and Rottweiler, Cairn Terrier, Weimaraner, Rhodesian Ridgeback, Miniature Poodle, English Springer Spaniel, Chesapeake Bay Retriever (Bassett *et al.*, 2005; Miura *et al.*, 2005, Scott *et al.*, 2007) [2, 21, 27] are also stated to be predisposed.
- **Individual idiosyncrasy:** In a single litter, the incidence may vary from one puppy to two-thirds of the young puppies (Scott *et al.*, 2001) [28].
- **Season:** Canine juvenile cellulitis cases occurred most commonly in winter and early spring (Kral, 1957).

- **Microenvironment:** The cutaneous disorder may be precipitated by the distemper virus infection, allergic reactions, poor hygiene and sanitation, malnutrition, endoparasites and stress (Scott *et al.*, 2007) [27].

3. Aetio-pathogenesis

Canine juvenile cellulitis in the young puppies remains enigmatic (Scott *et al.*, 2001; Gross *et al.*, 2005) [28, 10]. Special stains and electron microscopic examination of tissues do not reveal the causative microorganisms, if any and cultures are negative. Attempts to transmit the disease through the topical application of lesional tissues have been unsuccessful (Reimann *et al.*, 1989) [25]. Rapid development of sterile granulomatous pustules that respond dramatically to glucocorticoids (Scott *et al.*, 2001; Hutchings, 2003; Park *et al.*, 2004) [28, 24, 12] suggests the strong possibility of some unidentified pathobiomechanism whereby the immune system targets the puppy's own skin. The early age of onset with frequent occurrence after post-vaccinations schedule has raised serious concerns regarding vaccine reactions. However, the redeeming feature is that- irrespective of what triggers the disease, it is self limiting; the affected puppies spontaneously recover over a period of 4 to 12 weeks (Reimann *et al.*, 1989) [25].

4. Clinical Symptoms

- The initial lesion is manifested classically as acutely swollen face, especially on the eyelids, lips and muzzle. Within 24- 48 hours, papules and pustules develop. The affected skin areas are oedematous, and lesions typically progress to fistulates, that may drain and form crusts (Fig.1). Prominent submandibular lymphadenopathy is observed. In some individual puppies, the lesions may be limited to the swollen lymph nodes, while the remaining affected litter mates may exhibit the classic skin lesions (Reimann *et al.*, 1989) [25].
- Some of the affected puppies exhibit sterile pyogranulomatous-granulomatous panniculitis with subcutaneous nodules: firm-fluctuant in consistency, or fistulated (Scott *et al.*, 2001; Gross *et al.*, 2005) [28, 10].
- Some dogs may present other clinical signs, such as lethargy and lameness (Scott and Miller, 2007; Miller *et al.*, 2013) [28], but the absence of marked anorexia and pyrexia is a noteworthy differentiating feature from severe pyoderma, generalized demodicosis, fungal infection and sterile nodular panniculitis (Mason *et al.*, 1989) [16].
- Older dogs may reveal more conspicuous symptoms with pyrexia (Bassett *et al.*, 2005) [2].



Fig 1: Typical juvenile cellulitis in a Golden Retriever. (L) Symmetric swellings of the muzzle and pustules, papules and draining tracts. (R) Purulent-haemorrhagic discharge from the draining tracts.

5. Diagnosis

- **Anamnesis:** The complete case history is systematically recorded. This includes the age, sex, breed, onset of the disease, season, sudden change in the diet, duration of disease, concurrent disorders, clinical signs: acute onset of facial swelling with crusts and pustules on the muzzle, eyelids, ear pinnae and inguinal areas, the duration of disease with previous treatment and its outcome.
- **Clinical examination:** On presentation, clinical parameters of the puppy, namely rectal temperature, body weight, colour of the visible mucous membranes of the oral cavity and conjunctiva, lesions in the facial region, and any swelling on the muzzle and sub-mandibular lymph node are recorded.
- **Skin lesions:** The initial dermatological signs include swelling of the face, especially the eyelids, lips and muzzle that may progress to draining pustules and crusts. Papule, pustule, otic discharge, sub-mandibular lymphadenopathy, erythema, alopecia, ulceration and necrobiotic degradation may also be observed occasionally.

5.1 Laboratory tests

- **Complete blood count:** Published reports (Scott and Miller, 2007) [27] revealed mild normocytic, normochromic anaemia with low grade leucocytosis, neutrophilia, and monocytosis in nearly 40% of the affected puppies.
- **Skin scrapings/ hair plucks:** Samples mounted in liquid paraffin and examined under the light microscope showed no evidence of ectoparasites and/or arthrospores.
- **Cytology:** Representative samples from the exudative lesions, stained with modified Wrights stain (Diff-Quick) reveal a large number of intact neutrophils along with small number of fragmented neutrophils and macrophages, suggestive of purulent-pyogranulomatous inflammation (Neuber *et al.*, 2004) [22].

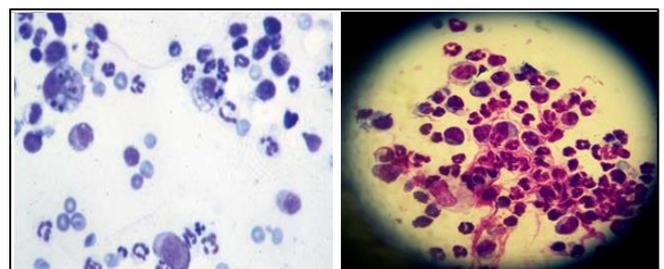


Fig 2: Impression smear from exudative lesion: numerous neutrophils and macrophages consistent with pyogranulomatous inflammation. L 400x; R 1000x.

- **Fine needle aspirate cytology:** Representative samples from the lymph node stained with modified Wrights stain (Diff-Quick): A large numbers of degenerated neutrophils and macrophages are observed.
- **Microbiological examination:** Samples collected from the lesion for culture with a sterile swab for microbial examination, tests negative for bacterial growth (Reimann *et al.*, 1989) [25], provided there is no secondary infection.
- **Histopathology:** Skin and lymph nodes biopsies are fixed in 10% neutral buffered formalin solution, embedded in paraffin wax, sectioned, stained with H&E and examined under the microscope. Multiple confluent

granulomas and pyogranulomas comprising epithelioid macrophages and neutrophils are clearly discernible.

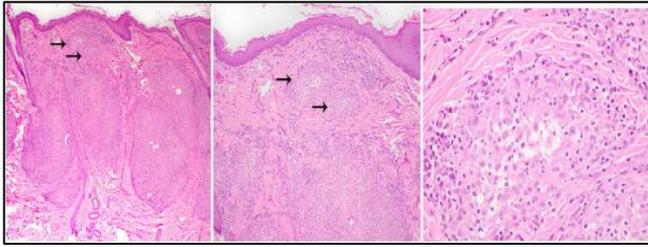


Fig 3: Photomicrograph H&E stain (L) 40x showing effacement of the adnexal units by nodular pyogranulomas with follicular degeneration.(M) 100x Pyogranulomas in the epidermis with no follicular association (→).(R) 400x Pyogranuloma with epithelioid macrophages and neutrophils.

5.2 Differential diagnosis

A) Canine juvenile cellulitis, *cf.* pyoderma

- The hallmarks of pyoderma in dogs are pain, crusting, odour, and exudation of blood and pus. Erythema, swelling, ulceration, haemorrhagic crusts and bullae, hair loss, and draining tracts with sero-hemorrhagic or purulent exudate may also be seen. However, in juvenile cellulitis swelling of the eyelids, lips and muzzle are seen. Otitis externa is very common along with lymphadenopathy. Further, within 24- 48 hours, papules and pustules develop on the trunk, preputial and perianal areas.
- Pyoderma can occur at any age, whereas juvenile cellulitis is mainly observed at the younger age of less than 6 months.
- Pyoderma lesions are pruritic in contrast to juvenile cellulitis where the skin is painful but not pruritic.
- In pyoderma, the cytological examination reveals bacterial colonization, evidenced by the presence of healthy neutrophils, cocci and bacilli in the extracellular space along with degenerated neutrophils exhibiting phagocytosis (Carlotti, 2003). In juvenile cellulitis, the degenerated neutrophils are numerous indicating a granulomatous reaction, without engulfed bacteria.
- Culture can confirm the bacterial infection and permit sensitivity testing in case of pyoderma, whereas in juvenile cellulitis culture examination is sterile, unless there is bacterial infection from the unsanitized microenvironment.

B) Canine juvenile cellulitis, *cf.* dermatophytosis

Dermatophytosis is an infection of keratinized tissue skin, hair, and claws by one of the three genera of dermatophytes or fungi *Epidermophyton*, *Microsporum*, *Trichophyton* (Merchant, 1955) [19].

- Dermatophytosis can spread through contact with infected animals or contaminated objects such as furniture or grooming tools while in juvenile cellulitis transmission of the disease on contact with lesional tissues is not observed.
- In dermatophytosis regional or generalized folliculitis and furunculosis with papules and pustules are commonly seen on the face, ear tips, tail, and feet along with alopecic, scaly patches with broken hair, whereas in juvenile cellulitis the affected areas are oedematous and lesions on the muzzle, lips, chin, bridge of the nose, and periocular area typically progress to form fistulates,

drain-tracts and crusts.

- A focal nodular form of dermatophytosis in dogs is the kerion reaction, which is not seen in juvenile cellulitis.
- Dermatophytosis can be confirmed by fungal culture and wood lamp examination while juvenile cellulitis is confirmed by cytology, histopathology and negative bacterial culture.

C) Canine juvenile cellulitis, *cf.* angioedema

Angioedema, a type I hypersensitivity disorder (Anonymous, 2008) [1], is a common skin reaction to allergens which is clinically manifested as redish, raised bumps in the subcutaneous layer that cause conspicuous swelling and much discomfort to the patient.

- In angioedema, medium to large areas of redness and swelling around the muzzle, abdomen, and legs are observed, where as in juvenile cellulitis swelling along with papules and pustules remains confined to the facial region with concurrent sub-mandibular lymphadenopathy (Gross *et al.*, 2005) [10].
- In angioedema, swelling around the eyes causes them to close. However, no such optic abnormality is observed in juvenile cellulitis.
- The affected skin area is painful but not pruritic in juvenile cellulitis, while excessive scratching is observed in angioedema. Further, drooling occurs if the muzzle starts to swell abnormally, which is never observed in juvenile cellulitis.
- Angioedema is mainly caused by the adverse bioresponse to different allergens (Caliskaner *et al.*, 2007) [3]. However, in juvenile cellulitis the pathogenesis is elusive.

D) Canine juvenile cellulitis, *cf.* canine distemper

- Canine distemper (Hardpad disease) is caused by a single stranded RNA virus of the Paramyxoviridae family (Creedy, 2010) [5], while the aetiology of juvenile cellulitis remains unidentified.
- Transmission of canine distemper is through direct contact with the infected dog's saliva, blood or urine, or indirectly through the aerosol route (Deem *et al.*, 2000). Contact transmission of canine juvenile cellulitis has not been reported till date.
- In canine distemper, papules and pustules in the abdominal region are observed along with nasal discharge, vomiting and diarrhoea, tissue dehydration, excessive salivation, coughing and/or laboured breathing, anorexia and weight loss. However, no gastrointestinal symptoms are observed in juvenile cellulitis.

E) Canine juvenile cellulitis, *cf.* adverse cutaneous drug reaction

- The 'adverse cutaneous drug reaction' (Maddison and Page, 2010) [15] involves a triggering agent like vaccines, nonsteroidal anti-inflammatory drugs (NSAIDs), ectoparasiticides, anthelmintics, anaesthetics (Tizard, 1990) [31]. However, no such pathoclinical nexus exists in canine juvenile cellulitis.
- The typical clinical signs of hypersensitivity include frequent vomiting and diarrhoea, inappetence, lethargy, pyrexia, dermatitis, abdominal pain, anaphylactic shock leading to hypotension, angioedema, urticaria, erythema, pruritis, pharyngeal or bronchial oedema. However, in juvenile cellulitis localized sterile pustular lesions are

observed on the lips, muzzle, chin, bridge of the nose, and the periocular area. Otitis externa is common, and the ear pinnae are frequently indurated and oedematous.

F) Canine juvenile cellulitis, *cf.* canine juvenile demodicosis

- Juvenile demodicosis is a severe disease of young dogs with generalized lesions like erythema, papules, alopecia, oedema, hyperpigmentation and crusts that are usually aggravated by secondary bacterial infections (Dryden, 2010)^[7]. On the other hand, in juvenile cellulitis swelling of the eyelids, lips and muzzle are seen along with sterile papules and pustules. Further, otitis externa with lymphadenopathy is very common.
- Skin scrapping examination is a dependable differential diagnosis for juvenile demodicosis and juvenile cellulitis.

6. Prognosis

In canine juvenile cellulitis, the prognosis is favourable if adequate treatment is initiated early (Fonseca-Alves *et al.*, 2012; Miller *et al.*, 2013)^[9, 20] within 4-5 days (Dubey and Sarkar, 2013)^[8].

7. Treatment

The treatment of choice in canine juvenile cellulitis is

judicious use of the proven anti-inflammatory agent, glucocorticoid: Prednisolone, singly or in combination with broad-spectrum antibiotic in a well-planned oral therapeutic regimen. This effective line of treatment is based on the pertinent clinical reports. Efficacy of Prednisolone/Prednisone @ 2.0 mg/ kg OD, or Dexamethasone @ 0.2 mg/ kg OD, PO over the specified period is well-documented (Scott *et al.*, 2001; Medleau *et al.*, 2001; Hutchings, 2003; Rhodes, 2004 and Snead *et al.*, 2004)^[28, 12]. Treatment is usually given over a period of 2-3 weeks under clinical supervision (Simon *et al.*, 2017)^[29]. Relapses may occur if the treatment is stopped too soon.

To obviate chance bacterial infection, antibiotic: Cephalexin/ Cefadroxil/ Amoxicillin clavulanate should be given, concurrently. Systemic antibiotic alone is not effective (Medleau *et al.*, 2001; Scott *et al.*, 2001; Hutchings, 2003; Snead *et al.*, 2004; Bassett *et al.*, 2005)^[18, 28, 2, 12]. Topical therapy with wet soaks of aluminium acetate or magnesium sulphate is useful in ameliorating the discomfort through facilitated removal of the deleterious surface debris, with smoothening effect (Medleau *et al.*, 2001; Scott *et al.*, 2001)^[18, 28].

Other therapeutic options include an immuno-modulatory drug Griseofulvin @ 14.2 - 34 mg/ kg BID, PO effective within 3 weeks (Miura *et al.*, 2005; Park *et al.*, 2010)^[21].



Fig 4: Patient's gross appearance before and after treatment

7.1 Optimized home management

- Apply a hot pack on the dog's sore face two to three times daily.
- Do hot water sponging with a wash cloth, holding it against the dog's swollen throat in repeated cycles of on and off, each of five minutes duration.
- Soak and soften the crusted sores in the dog's face with warm water and then gently wipe with diluted betadine solution (5%) to sanitize the entire area.
- For abscessed lymph nodes, the areas should be cleaned 3-4 times daily with a warm, wet cloth, applied for 5-10 minutes.
- The companion dog's affected spots are very sensitiver, hence gentle handling is needed, otherwise the chances of scarring are greatly increased.

8. Conclusions

- Canine juvenile cellulitis, one of the challenging skin disorders affecting puppies from three weeks to six months of age is characterised by sterile granulomas and pustules, pyogranulomatous dermatitis and lymphadenitis.
- The cause and pathogenesis of the unique skin disorder remain unclear; special stains and high resolution electron microscopic examination of tissues do not reveal microorganisms, and cultures are negative.
- The diagnosis is based on the precise case history, nature and distribution of the cutaneous lesions, laboratory findings and response to immunosuppressive therapy.
- Prognosis is favourable if the remedial oral therapy is instituted within 4-5 days, primarily based on effective immunosuppression through glucocorticoid, generally with proven Prednisolone in combination with a potent broad-spectrum antibiotic, such as Cephalexin, Cefadroxil, or Amoxicillin clavulanate aimed to pre-empt or eliminate subclinical/ microbial infection.

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