



# Atypical eosinophilic granuloma in a dog. Case report

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## ABSTRACT

The eosinophilic granuloma is characterized by dense cellular infiltration of eosinophils, macrophages, and mast cells, in addition to collagenolysis foci. Canine eosinophilic granuloma is a rare inflammatory skin disease that affects the oral mucosa. However, the cutaneous form is more evident and can be in the scrotum, testicles, perineum, and flanks. The etiology of eosinophilic granuloma in dogs is not clear but allergic processes can originate granulomatous nodules or plaques. Affected dogs may experience itching, swelling, and, occasionally, pain. The histopathological analysis is necessary for definitive diagnosis. The present case report described a 12-year-old male dog, Poodle, with a history of swelling, itching, and pain in the scrotum. Complete clinical staging was performed through blood count, biochemistry analysis, thoracic radiographs, abdominal ultrasound, and electrocardiogram. The dog was submitted to surgical removal followed by histopathologic evaluation. Eosinophilic granuloma should be included in the differential diagnosis of solitary masses in the scrotal region.

**Keywords:** Canine; skin diseases; eosinophilia; pathology; mast cells; scrotum (*Source: MeSH*).

## RESUMEN

El granuloma eosinofílico se caracteriza por una infiltración celular densa de eosinófilos, macrófagos y mastocitos, además de focos de colagenólisis. El granuloma eosinofílico canino es una rara enfermedad inflamatoria de la piel que afecta la mucosa oral. Sin embargo, la forma cutánea es más evidente y puede estar en el escroto, los testículos, el perineo y los flancos. La etiología del granuloma eosinofílico en perros no está clara, pero los procesos alérgicos pueden originar nódulos o placas granulomatosas. Los perros afectados pueden presentar picazón, hinchazón y, ocasionalmente, dolor. El análisis histopatológico es necesario para el diagnóstico definitivo. El presente informe del caso describe un perro macho de 12 años, Poodle, con antecedentes de hinchazón, picazón y dolor en el escroto. La estadificación clínica completa se realizó mediante recuento sanguíneo, análisis bioquímico, radiografías torácicas, ultrasonido abdominal y electrocardiograma. El perro fue sometido

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a extracción quirúrgica seguida de evaluación histopatológica. El granuloma eosinofílico debe incluirse en el diagnóstico diferencial de las masas solitarias en la región escrotal.

**Palabras clave:** Canino; enfermedades de la piel; eosinofilia; patología; mastocitos; escroto (*Fuente: MeSH*).

## INTRODUCTION

In dogs, the eosinophilic granuloma is a rare inflammatory skin disease. The main characteristics are the presence of nodules or plaques in the mucosa of the oral cavity which may cause salivation, inappetence and dysphagia, however, in most cases, cutaneous regions such as flank, ventral area of the abdomen, and scrotal area can also be affected. The clinical and histopathological findings suggest a hypersensitivity reaction by arthropod bites in dogs with eosinophilic granuloma (1,2,3).

The breeds most affected by eosinophilic granuloma (oral form) are the Siberian Husky and Cavalier King Charles Spaniel. The breed predisposition has genetic bases as a probable etiology, however, in the cutaneous form does not seem to have a breed predisposition (3). The clinical signs can be the presence of ulcerated areas, itch, and pain in some dogs. The final diagnosis of eosinophilic granuloma requires histopathological analysis. The description can show eosinophilic debris coated in collagen fibers that may be degenerated. Differential diagnoses for eosinophilic granuloma must include reaction to foreign bodies, bacterial or fungal granulomatosis, and tumors (1,4).

The present case aimed to report a dog with eosinophilic granuloma addressing the clinical, and histopathological signs.

## ANAMNESIS

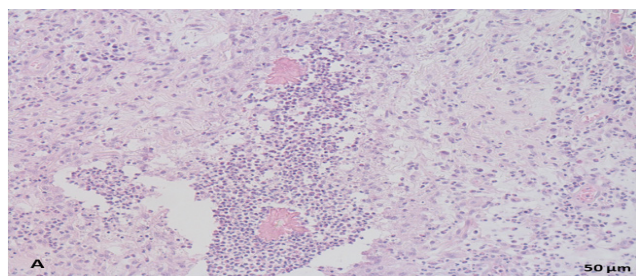
It was admitted a male dog, Poodle, 12 years old, weighing 5.8 kg. The client reported that a week ago the dog showed enlargement, itching and pain in the testicular area. Complementary tests were performed, such as blood count, biochemistry analysis, thoracic radiographs,

abdominal ultrasound, and electrocardiogram. The dog was referred for surgical removal and histopathological analysis.

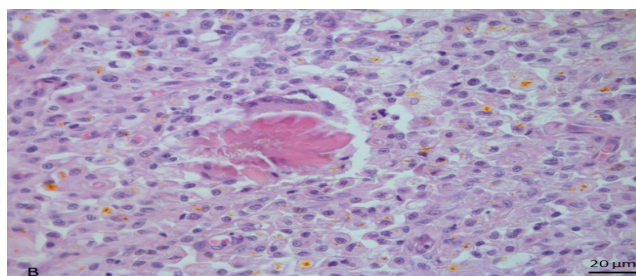
**Clinical exams findings.** The clinical examination revealed pain on palpation and the presence of a multilobulated nodule, with soft consistency located in the right scrotum. No other relevant findings were detected on the clinical examination.

**Diagnose aids used.** Blood count showed normochromic normocytic anemia (Hematocrit 33.4% [reference: 38-47%]), neutrophilic leukocytosis (total leukocytes:  $53.790 \times 10^3 / \mu\text{L}$  [reference:  $6-16 \times 10^3 / \mu\text{L}$ ]; segmented neutrophils 31% [reference: 55-80%]; eosinophils: 58% [reference: 1-9%]; monocytes: 1% [reference: 1-6%]; lymphocytes: 10% [reference: 13-40%], platelets  $170,000 \times 10^3 / \mu\text{L}$  [reference:  $200-500 \times 10^3 / \mu\text{L}$ ] (5), without morphological changes or haemoparasites. Biochemistry analysis were within normal ranges (alkaline phosphatase, urea, creatinine, total proteins, alanine aminotransferase - ALT, aspartate aminotransferase - AST, gamma glutamyltransferase - GGT). Thoracic radiographs in three projections (left and right latero and ventro-dorsal), abdominal ultrasound and electrocardiogram showed no alterations. Samples were collected for bacterial and fungal culture and the results were negative.

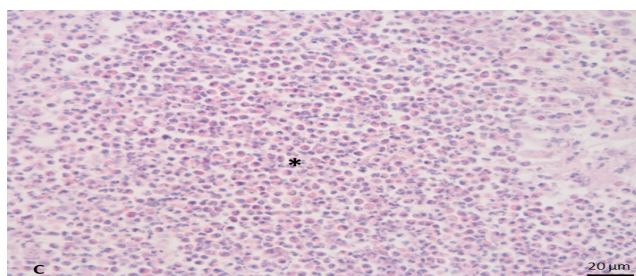
Histopathological sections of the skin from the scrotum showed multifocal areas of severe inflammatory infiltrate with macrophages, eosinophils, mast cells, and fewer lymphocytes and plasma cells. Some multifocal areas of collagen fiber necrosis surrounded by eosinophils degenerated eosinophils, and macrophages were associated (Figures 1, 2 and 3).



**Figure 1.** Note multifocal areas of necrosis surrounded by eosinophilic inflammation, macrophages, and proliferation of collagen fibers. Haematoxylin-Eosin stain, bar 50 µm, obj 20 x.



**Figure 2.** Note the focal necrosis surrounded by macrophages. Haematoxylin-Eosin stain, bar 20 µm, obj 40 x.



**Figure 3.** Note the intense eosinophilic inflammatory infiltrate (asterisks) associated with occasional macrophages and proliferation of collagen fibers. Haematoxylin-Eosin stain, bar 20 µm, obj 40 x.

Frequently, a yellowish granular pigment was seen filling the cytoplasm of macrophages and also binucleated macrophages.

There was a severe proliferation of collagen fibers separated by the inflammation, mainly around the enlargement of endothelium and blood vessels. In the superficial dermis, multifocal areas of mast cells were seen in rows. In the epidermis, there was a focal area of acanthosis and spongiosis associated with ulcers and degenerated neutrophils.

For differential diagnosis of mast cell tumor, the Blue Toluidine staining was performed, which revealed non-neoplastic mast cells with the cytoplasm filled with metachromatic granules. In association, the morphology of the lesion and the Blue Toluidine staining directed the diagnosis for eosinophilic granuloma.

**Treatment approach.** The treatment suggested was surgical removal (nodulectomy with wide margins). The medication prescribed was amoxicillin + potassium clavulanate (20mg/kg, PO, every 12 hours/10 days); metronidazole (20mg/kg, every 12 hours, PO, 5 days); meloxicam (0.1 mg/kg, every 24 hours, PO/4 days), and surgical wound dressing, every 12 hours, with chlorhexidine-based ointment (0.7g).

## DISCUSSION

The etiology of eosinophilic granuloma has not yet been clarified, but it is speculated that the cutaneous form is related to type I hypersensitivity reactions secondary to arthropod bites (mosquitoes and fleas), environmental allergens, food, intestinal parasites, infectious agents (bacterial, fungal and viral) and idiopathic (1, 4). In the dog's history, there was no report of the use of topic or systemic ectoparasitic products, which suggests the occurrence of a hypersensitivity reaction to the bite of ectoparasites, probably arthropods, leading to the formation of granuloma eosinophilic.

In dogs, although this condition is rare, it is reported affecting the oral cavity, and in the cutaneous form with similar histopathologic lesions (1).

In cats, the oral presentation of eosinophilic granuloma is more common when compared to the cutaneous form (2). In some dog breeds (Siberian Husky and Cavalier King Spaniel) the oral form is the most reported (1). Skin lesions can show multiple papules, nodules, or plaques in the digits, snout, axillary fingers, foreskin, and flanks. Other locations of granuloma eosinophilic include the eyelid and scrotum (1,3,6). These other locations were described in the patient mentioned in this case report.

The clinical signs, such as pain and itch may be present, however, some authors describe non-painful injuries (1). In this case, the patient revealed the same clinical signs described.

Usually, the inflammatory infiltrate of eosinophilic granuloma contains mainly macrophages and eosinophils associated with collagen, and necrosis surrounded by degenerate neutrophils (1). In general, the intense infiltrate of mast cells arranged in rows associated with eosinophilic granuloma can be seen, which is why the diagnosis can be mistaken for differentiated mast cell tumors (1,3).

Several idiopathic eosinophilic diseases (eosinophilic myositis, eosinophilic pneumonia, eosinophilic gastroenteritis) or neoplastic conditions (mast cell tumors), through the action of interleukin-5 (IL-5), can generate the sequestration of immature bone marrow eosinophils into the bloodstream or tissues causing eosinophilic inflammatory infiltrates (7). In this report, the blood count revealed leukocytosis due to eosinophilia, suggesting sequestration of immature bone marrow eosinophils into the bloodstream and eosinophilic infiltration in the scrotum. Considering this, the patient developed the clinical signs reported, which were itching, swelling, and painful sensitivity on palpation. The histopathologic evaluation showed a granulomatous pattern of nodules in the deep dermis similar to what has been reported by other authors.

The Toluidine Blue staining was efficient to exclude the diagnosis of mast cell tumors. It was observed an intense infiltrate of non-neoplastic mast cells with cytoplasm filled by metachromatic granules. Moreover, they were dispersed in the granuloma and lined up in the superficial dermis. However, it should be noted that the description above can elevate the reaction of mast cells. Consequently, diffuse and progressive infiltration of these cells can be seen (8). Other stains can be used to diagnose infectious agents such as

Ziehl-Neelsen and periodic acid from Schiff (PAS) since bacteria and fungi can cause similar granulomatous inflammations (8). Bacterial and fungal culture can also be useful diagnostic tools (1). However, in this case report, these tests were negative.

Besides mast cell tumors, the eosinophilic granuloma may have other differential diagnoses, such as T-cell epitheliotropic lymphoma (7). In non-differentiated tumors, the immunohistochemical panel in these cases would be efficient to exclude lymphoma as a differential diagnosis. However, in this case, the histopathological analysis was enough to guide the diagnosis correctly.

The medical therapies used to treat the eosinophilic granuloma consist in the administration of antibiotics and corticosteroids. These medications usually show partial responsiveness in reducing nodule size and improving clinical signs. More recently, the use of electrochemotherapy has been described as an alternative treatment to drug therapy, with excellent results, not only for eosinophilic granuloma, but for several tumors located in the cutaneous or subcutaneous region (9,10,11). In this case report, surgical removal and postoperative therapy were sufficient to promote the resolution of granuloma and related clinical signs. In addition, the dog has regained its quality of life since then.

In conclusion, the eosinophilic granuloma should be included in the differential diagnosis of solitary masses in the scrotum. Clinical history together with histopathologic evaluation was relevant to differentiate eosinophilic granuloma from a mast cell tumor in the scrotum; an anatomic site considered with unfavorable when affected by mast cell tumor, especially in old dogs.

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