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Case Report

Phenobarbital-Responsive Sialadenosis in Dogs: Case Series

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Phenobarbital-responsive sialadenosis (PRS) is a rare idiopathic disease in dogs. Vomiting, retching, and gulping with bilateral enlargement of the submandibular salivary glands are the more frequent clinical signs. A thorough diagnostic examination must be performed to rule out the most important systemic etiologies involved with chronic vomiting, as there is no specific test to diagnose PRS. Diagnosis is confirmed clinically by a rapid and dramatic improvement of clinical signs after instauration of phenobarbital treatment. The aim of this article is to describe the clinical presentation, diagnostic findings, and outcome of a case series of 4 dogs with presumptive PRS.

Introduction

Salivary gland pathology is uncommon in dogs and cats.[1,2] The most frequent diseases affecting the salivary glands are salivary neoplasms, edema, sialadenitis, sialoceles, salivary gland infarction, sialolithiasis, and sialadenosis.[2-6]

Sialadenosis is a bilateral, painless, noninflammatory, uniform, nonneoplastic enlargement of the salivary glands. In humans, this is a disease triggered by a secretory and metabolic disturbance of the acinar parenchyma and characterized by uniform hypertrophy of the functional acinar parenchyma.[4] The condition has been classified into 3 major groups: neurogenic, dystrophic, and metabolic or hormonal.[3] Dysfunction of the autonomous nervous system innervation of the salivary glands may be a unifying factor in all forms, in both dogs and humans. Sialadenosis can be seen in people with bulimia, anorexia nervosa, malnutrition, liver diseases, diabetes mellitus, and neoplasia.[1,7]

Sialadenosis is commonly recognized in laboratory mammals and has been reported secondary to some drugs, hormonal changes, salivary gland resection, or amputation of incisor teeth.[2] There are several reports describing idiopathic sialadenosis in dogs, but only a single presumptive case in cats.[3]

Phenobarbital-responsive sialadenosis (PRS), also known as idiopathic sialadenosis, is a rare, idiopathic disease in dogs that is characterized by a sudden onset of retching and gulping with bilateral enlargement of the salivary glands.[1-3,7-10]

Gagging, ptyalism, lip-smacking, weight loss, hyporexia or anorexia, and vomiting are commonly observed in dogs with PRS.[1-3,7-10] The etiology of this condition remains unclear, but it has been associated to an unusual form of limbic epilepsy.[1] The diagnosis of PRS involves careful exclusion of other diseases with similar clinical signs, including primary and secondary gastrointestinal disease, as there is no specific test available for definitive diagnosis. Diagnosis of PRS is confirmed clinically by a rapid and dramatic improvement of clinical signs after instauration of phenobarbital treatment.

The aim of this article is to describe the clinical presentation, diagnostic findings, and outcome of a case series of 4 dogs with presumptive PRS.

Materials and Methods

Case 1

A 9-month-old, intact female mongrel dog weighting 2 kg was presented with a 3-week history of vomiting, retching, lethargy, and weight loss. On physical examination, the dog was thin with a body condition score of 3 on 9, was moderately dehydrated, and presented with severe sialorrhea. The submandibular glands were enlarged. The dog showed signs of stress and vomiting during physical examination. Symptomatic treatment was initiated based on Fluidotherapy, metoclopramide, and ranitidine. Results of complete blood count (CBC) and serum biochemistry supported dehydration with a mild increase of the packed cell volume, total solids, and urea. The potassium level was moderately decreased likely because of vomiting. The result of the adrenocorticotropic hormone (ACTH) stimulation test was within normal limits. Findings on thoracic and abdominal radiographs and abdominal ultrasound were unremarkable. An exploratory laparotomy was

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performed, and samples of the liver, pancreas, stomach, small intestine, and salivary glands were obtained for histopathologic study. Uniquely, a mild intestinal eosinophilic inflammatory infiltrate was detected, and findings on histopathologic study of the salivary glands were normal. At that moment, the presumptive diagnostic was inflammatory bowel disease (IBD) or food allergy. A food trial based on hypoallergenic commercial food, prednisolone, and metoclopramide treatment was initiated. Gastrointestinal signs diminished initially, but 2 weeks later, severe clinical signs relapsed.

Brain and cervical computerized tomography and cerebrospinal fluid (CSF) analysis were performed, and no abnormalities were detected. A presumptive diagnosis of PRS was made. Supportive treatment with intravenous fluids and metoclopramide was administered, and intramuscular phenobarbital (6 mg/kg twice daily) was started. After 4 days, the dog was normal with no vomiting or sialorrhea. Phenobarbital dose was diminished to 2 mg/kg twice daily, orally. The dog remained clinically normal until it was lost to follow-up after 6 months.

Case 2

A 2.5-year-old nonspayed female mongrel dog weighing 5 kg was presented with a 10-day history of vomiting, retching, apathy, and anorexia. On physical examination, a moderate dehydration, body condition score of 4 on 9, sialorrhea, submandibular glands enlargement, and vomiting were observed. Immediate symptomatic treatment was initiated to rehydrate the patient. An extensive diagnostic workup was performed, including CBC, serum biochemistry, and a fine-needle aspiration of the enlarged salivary gland. Alterations observed on those tests were mild thrombocytopenia, slightly increased serum urea levels, and low potassium levels. Antibody titers for *Ehrlichia* spp. and *Leishmania* spp. were negative. The result of the ACTH stimulation test was within normal limits. Findings on thoracic and abdominal radiographs and abdominal ultrasound were unremarkable. The following diagnostic investigations were made under anesthesia: oropharynx exploration, endoscopy, intestinal biopsies, and CSF analysis. The unique alteration was the presence of a mild to moderate lymphoplasmacytic enteritis. Thus, a presumptive diagnosis of IBD was made, and treatment with prednisolone was established. After 10 days of treatment with corticosteroids, no clinical improvement was noted. PRS was suspected, and phenobarbital was prescribed. After 3 days, there was a remarkable improvement regarding gastrointestinal clinical signs and the size of the salivary gland. Based on the favorable response, a PRS diagnosis was made. The dog was clinically healthy after 6 months of treatment.

Case 3

A 2.5-year-old nonspayed female bull terrier dog weighing 16 kg was presented with chronic vomiting, regurgitation, and anorexia. Enlargement of the submandibular salivary glands was the unique abnormality seen on physical examination. The referring veterinarian prescribed amoxicillin-clavulanic acid, nonsteroidal anti-inflammatory drugs, and metoclopramide, obtaining a partial clinical response.

A thorough diagnostic workup was performed including CBC, serum biochemistry, thoracic X-rays, abdominal ultrasound, and ACTH stimulation test. All the results were within normal limits. To rule out gastrointestinal causes of vomiting, a histopathology study should have been done, but the owners refused to perform further test owing to economic concerns. A therapeutic trial with phenobarbital was initiated because of a suspicion of PRS.

After 5 days, the owner was contacted by phone and it was confirmed that the dog had a complete remission of gastrointestinal signs (vomiting, sialorrhea, and retching) after phenobarbital treatment. The dog remained without any clinical signs 6 months later, and phenobarbital treatment was gradually tapered without suffering any relapse.

Case 4

A 4-year-old nonspayed male bull terrier dog weighing 23 kg was presented with a long-term history of vomiting. The dog had been treated unsuccessfully for 3 months with almagate, omeprazole, metoclopramide, amoxicillin-clavulanate, and metronidazole. A combination of commercial and house-made digestive diets was prescribed. An endoscopic diagnosis of hiatus hernia and gastric ulceration had been obtained at the referring veterinary clinic. According to the owner, the dog had daily vomiting episodes and also showed exercise intolerance. The only abnormality noticed on general physical examination was bilateral enlargement of the submandibular salivary glands. General blood workup was initiated. The results for canine pancreatic lipase immunoreactivity and antibody titers for *Leishmania* spp. were negative. The result of the ACTH test was within normal limits. Findings on thoracic radiographs and abdomen ultrasound were unremarkable. Owing to economic restraint, the owner declined to perform further tests. A presumptive diagnosis of PRS was made, and treatment with phenobarbital was initiated at 2.5 mg/kg twice daily. Over a phone call made a week later, it was found that the dog had completely recovered without clinical signs (no vomiting or retching).

After 3 months, the owner decided to withdraw treatment and regurgitation and retching episodes relapsed. The owner also noted a seizurelike episode, with a postictal period of 2-day duration. Symptomatic treatment was started, and phenobarbital was reinitiated at the same dosage. Findings on biochemistry and CBC analysis were unremarkable. Phenobarbital plasma level monitored 2 weeks later was within therapeutic range. A month later, retching and vomiting relapsed. The dog was referred to the neurology service, and pacing during gait was detected. Magnetic resonance imaging and CSF analysis were performed, and no abnormalities were found. As there was suspicion of a hiatus hernia initially, an endoscopic study was performed and a dynamic hiatal hernia was observed. Biopsies obtained revealed moderate atrophy and fibrosis of the gastric mucous and mild lymphoplasmacytic enteritis. Phenobarbital treatment was continued and prednisone (1 mg/kg once daily) was added to treat inflammatory enteritis. After an initial partial response, this dog was lost to follow-up. The dog responded completely to phenobarbital during 3 months, but afterwards, the response was partial.

Discussion

PRS is a rare idiopathic disease in dogs. Similar to the cases previously described, retching and gulping with bilateral enlargement of the submandibular salivary glands are the more frequent clinical signs. Gagging, ptyalism, lip-smacking, weight loss, decreased appetite, and vomiting have also been reported.[1-3,7-10] This form of sialadenosis has been proposed to be a form of limbic epilepsy based on the response to antiepileptic drugs (i.e., phenobarbital and potassium bromide) and on the electroencephalographic tracings consistent with seizure activity.[1] Interestingly, a dramatic response to anticonvulsive drugs can be observed even before obtaining therapeutic phenobarbital plasma levels.[8]

A total of 4 cases compatible with PRS were presented at our center. Although 75% of our cases were female and 50% were bull terrier dogs, the number of patients included was too small to determine a sexual or breed predisposition. The retrospective