



IDIOPATHIC PHENOBARBITAL-RESPONSIVE SIALADENOSIS

Case Report
Mark C. Fuller, DVM

REVIEWED BY
TODD DEPPE, DVM, DACVIM

Signalment:

“Willie”

2-year-old MN Shih Tzu-X
4/9 BCS

History:

Willie was referred for a 2 week history of progressive vomiting, regurgitation, ptyalism and anorexia with sublingual abscessation and bilateral enlargement of the mandibular salivary glands. His symptoms developed after general anesthesia for a medial patellar luxation repair. Complete blood work showed an inflammatory leukogram and was otherwise unremarkable. Cytologic analysis of mandibular salivary gland fine needle aspirates was unremarkable. Upper gastrointestinal endoscopy revealed mild tonsillar, pharyngeal and esophageal erythema, along with severe gastric ulceration. Serial cervical radiographs were unremarkable. Histopathology of mandibular salivary gland tru-cut biopsies was pending. Willie was managed with intravenous fluids, esophagostomy tube feedings, broad-spectrum antibiotics, corticosteroids, and gastro-therapeutics, though his symptoms continued to progress.

Clinical Exam:

On examination Willie was depressed, hypersalivating, tachypneic with increased respiratory effort; he had poor perfusion parameters and was minimally responsive. Marked mandibular salivary gland enlargement was present bilaterally. Palpation of his mandibular salivary glands did not appear painful, but would evoke a gagging response followed by continued vocalization. A patent esophagostomy tube was present in his left mid-cervical region.

Laboratory Findings:

SpO₂: 79% on presentation.

Complete Blood Count: marked leukocytosis (37,800 cells/ul), characterized by a mature neutrophilia (33,264 cells/ul) and monocytosis (1890 cells/ul).

Serum Biochemistry: mild increase in AST (85 u/l), decreased amylase (395 u/l), low BUN (4 mg/dl),

T4: <0.4 ug/dl

i-STAT EC8+: moderate hypokalemia (2.7 mmol/l), mild metabolic alkalosis (pH 7.438, pCO₂ 38.7 mmHg, HCO₃ 26.2 mmol/l)

Diagnostic Imaging:

Radiography: Cervical and thoracic radiographs were performed. Mild subcutaneous emphysema was present at the thoracic inlet; the remainder of the study was unremarkable.

Histopathology:

Mandibular salivary glands: Normal salivary histopathology.

Sublingual tissue: Severe focally extensive, ulcerative, suppurative sublingual stomatitis with bacterial colonization.

Diagnosis:

Idiopathic sialadenosis, bacterial stomatitis, tonsillitis, pharyngitis, esophagitis, ulcerative gastritis.

Treatment/Management:

Willie was hospitalized for a 5 day period. He was initially managed with a 20ml/kg bolus of Normosol R IV, followed by Normosol R qs 40 mEq/L KCl IV at 2x maintenance over the following 2 days to correct for his hypokalemia, hypovolemia and dehydration. His IV fluids were switched to 0.9% saline on the 3rd day, as he became hyperkalemic and progressively more hyponatremic. Supplemental oxygen was provided via an oxygen chamber at FiO₂ at 40% for the first 2 days of hospitalization until his SpO₂ improved to greater than 95% on room air. His medical management consisted of enrofloxacin (5mg/kg IV q12hr for 4 days, PO for an additional 6 days), clindamycin (11mg/kg IV q12hr for 4 days, PO for an additional 6 days), famotidine (1.0 mg/kg IV q12hr for 2 days), omeprazole (0.8mg/kg PO q24hr for an additional 10 days), sucralfate (150mg/kg PO q6hr for 12 days), misoprostal (4mcg/kg PO q8hr for 13 days), metoclopramide CRI (1mg/kg/day for 24hrs), Cerenia (1mg/kg SQ q24hr for 1 day and 2mg/kg PO q24hr for 4 days), dolasetron (0.5mg/kg IV 12hr for 3 days), theophylline (8mg/kg PO q12hr for 2 days), and buprenorphine (10mcg/kg IV q6hr for 3 days). Prior to the histopathology results, phenobarbital was started on the 2nd day of hospitalization (2mg/kg IV q12hr, followed by 2.4mg/kg PO q12hr) on the suspicion of idiopathic sialadenosis. Over the first 2 days Willie's vital parameters improved significantly, though he continued to hypersalivate, regurgitate, vomit and frequently vocalize in discomfort. His salivary gland swelling remained unchanged. Chlorpromazine was added as an additional antiemetic on the 3rd-day of treatment (0.3mg/kg SQ q8hr

for 10 days). He was offered free choice water on the 3rd day of hospitalization, followed by esophagostomy tube feedings at 1/3 of his daily requirements spread over 4 feedings. Over the final 3-days of hospitalization his symptoms slowly improved, and his salivary gland swelling improved mildly. At the time of discharge he was regurgitating and vocalizing much less frequently.

Follow-up care:

At the time of discharge, Willie still required intense medical management. His owner was dedicated to monitor him closely and continue with the above treatment plan, along with staged increases in his esophagostomy tube feedings. His symptoms slowly improved at home, and his general attitude improved. Four days post-discharge, he regurgitated his esophagostomy tube, which had to be removed prematurely. Over the next 2 days his symptoms improved dramatically, and his appetite, so his feeding tube was not replaced. Eighteen days post-discharge, the owner reported that he had completely recovered, with no residual symptoms. He was weaned off phenobarbital 1.5 months after discharge and only had occasional regurgitation. Phone discussion 5 months after the time of discharge revealed that Willie's symptoms completely and was not currently receiving any treatment.

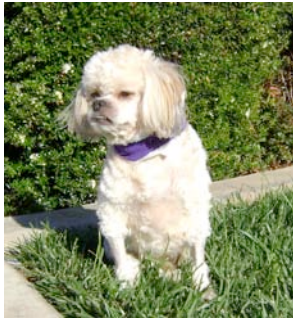


Figure 1

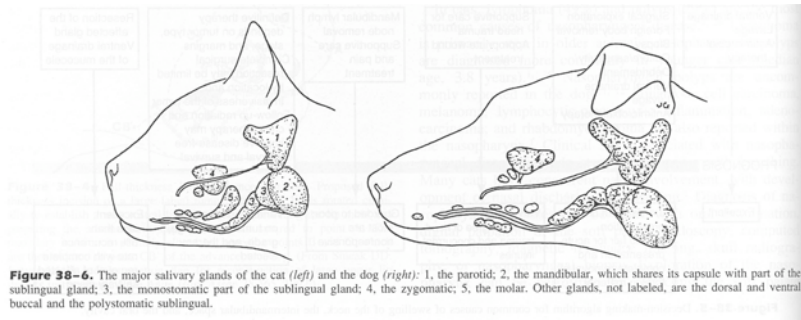


Figure 38-6. The major salivary glands of the cat (left) and the dog (right): 1, the parotid; 2, the mandibular, which shares its capsule with part of the sublingual gland; 3, the monostomatic part of the sublingual gland; 4, the zygomatic; 5, the molar. Other glands, not labeled, are the dorsal and ventral buccal and the polystomatic sublingual.

Figure 2

Discussion:

Enlargement of salivary glands is rarely seen in small animal practice [1, 2]. Common causes of salivary gland enlargement include neoplasia, sialadenitis, sialoceles, infarction, sialolithiasis and edema [1].

Over the past 30 years, sialadenosis has become a recognized disorder in dogs and cats. Currently, over forty canine cases and one feline case have been reported in the literature [2, 3]. The term sialadenosis has been used in dogs to characterize reports of non-painful, often bilateral, mandibular salivary gland enlargement, where no significant abnormalities are found cytologically or histologically [6]. There are, however, a larger number of reported cases with similar clinical symptoms, physical findings and treatment response that have variable inflammatory or necrotic findings microscopically. Sialadenosis in dogs and cats remains an ill defined and minimally discussed disorder, highlighted by the limited discussion in the current internal medicine and surgery textbooks, along with its exclusion in a large case series describing salivary gland disorders in dogs and cats [1, 4, 5].

In humans sialadenosis comprises 6% of salivary disorders and is characterized as bilateral, non-painful, non-inflammatory enlargement of the salivary glands [6]. The parotid glands are most commonly affected. Sialadenosis as a result of physiologic hypertrophy has been seen in patients with compulsive eating disorders and acromegaly, though in other cases the etiology remains unknown. Vomiting is a common symptom of this disorder in people, and salivary gland enlargement appears to be directly correlated with the frequency of vomiting. Sialadenosis has also been seen in people with diabetes mellitus and with the administration of various drugs.

The reported cases of canine salivary gland enlargement were often accompanied with hypersialism, and with varying degrees of gagging, vomiting, decreased appetite and weight loss [3,7]. Palpation of the enlarged salivary glands does not appear painful, though it can exacerbate the clinical signs. Diagnostic work-up has included routine hematology, serum biochemistry and urinalysis, skull, cervical and thoracic radiographs, salivary ultrasound, upper gastrointestinal endoscopy, fine needle aspirate and/or biopsies of the enlarged salivary glands, and electroencephalography. In over 50% of reported cases, no additional associated disorders have been identified. In the remainder of cases, concurrent gastritis, esophagitis and or megaesophagus have been identified. In a case series from South Africa 14 of the dogs had concurrent esophageal disease from *Spirocerca lupi* infections [3]. Cytology and histopathology of the enlarged salivary glands is often unremarkable, though, as mentioned above, a number of cases have shown evidence of necrosis, ductal hyperplasia or inflammation [3]. It is currently unknown whether cases with and without histopathologic lesions represent the same or different disorders [3]. Currently, the etiology in dogs, as in humans, remains obscure. In all cases of mandibular salivary gland enlargement, dogs were not responsive to sialoadenectomy, antibiotics or immunosuppressive therapy [3]. Oddly, the majority of cases respond to long-term phenobarbital or other anticonvulsants [3, 6, 7, 8]. The clinical symptoms usually decrease within 24-36 hours, and salivary gland enlargement decreases within 2 weeks [6]. Some dogs can be tapered off anticonvulsant medication around 6 months, though others relapse and require life-long therapy. Given the strong response to phenobarbital, it has been postulated that this syndrome is an unusual form of limbic epilepsy [3, 6, 7, 8]. Electroencephalography has been performed in a few patients, but the results have been inconclusive [3].

References:

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- 2) Boydell P, Pike R, Crossley D. Presumptive sialadenosis in a cat. *J Small Anim Pract* 41(12): 573-574, 2000.
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- 4) Smith MM. Oral and Salivary Gland Disorders. In Ettinger SJ, Feldman EC: *Textbook of Veterinary Internal Medicine*, 6th ed. Elsevier Saunders, St. Louis, MO, 2000, p 1295-1297.
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- 6) Boydell P, Pike R, Crossley D, Whitbread T. Sialadenosis in dogs. *J Am Vet Med Assoc* 216(6): 872-874, 2000.
- 7) Stonehewer J, Mackin AJ, Tasker S, Simpson JW, Mayhew IG. Idiopathic Phenobarbital-responsive hypersialosis in the dog: an unusual form of limbic epilepsy? *J Small Anim Pract* 41(9): 416-21, 2000.
- 8) Chapman BL, Malik R. Phenobarbitone responsive hypersialism in two dogs. *J Small Anim Pract* 33(11): 549-552, 1992.

Figures:

- 1) Willie at the time of discharge
- 2) Anatomic salivary gland arrangement. See reference 5.