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Evaluation of an anal sac adenocarcinoma tumor in a Spitz dog

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PEER REVIEW

Peer reviewer

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Comments

This is a good study in which the authors evaluate an anal sac adenocarcinoma tumor in a Spitz dog and provided treatment and prevention for future studies. The results of this report in Iran was for the first time in this breed dog. And the results are very interesting. This paper was recommended because it was considered as substantial by means of being the first case reported in a Spitz dog.

(Details on Page 77)

ABSTRACT

A 9-year-old emasculated male Spitz with tenesmus and constipation had a subcutaneous mass at the left ventral aspect of the anus with history of polyuria and polydipsia. A complete blood count, serum biochemistry panel, and urinalysis (cystocentesis sample) were evaluated. Abnormalities in the serum biochemistry panel included a mildly elevated serum cholesterol concentration (7.28 mmol/L; reference interval, 2.70–5.94 mmol/L), increased serum alkaline phosphatase activity (184 U/L; reference interval, 9–90 U/L), alanine transaminase (122 U/L; reference interval, 5–60 U/L) activity and aspartate aminotransferase (80 U/L; reference interval, 5–55 U/L) activity, severe increased total calcium concentration (16.3 mg/dL; reference interval, 8.2–12.4 mg/dL or 9.3–11.4 mg/dL), and decreased total calcium concentration (3.4 mg/dL, reference interval, 2.5–5.6mg/dL). Furthermore, testing revealed an increased intact parathyroid hormone concentration (38.6 pmol/L; reference interval, 3–17 pmol/L). On cytologic and histopathologic examinations, various types of cells were observed. Most of the cells were oval to polygonal and had elliptical or elongate nuclei and a moderate amount of pale to basophilic cytoplasm. The remaining cells had round to oval nuclei and pale to basophilic cytoplasm. Cells of both types were loosely adhered to each other and were arranged in rosette-like structures. Both neoplastic cell types had fine homogenous chromatin and either a small indistinct nucleolus or no visible nucleolus. Mild anisokaryosis and anisocytosis were observed. Histologically, the mass consists of glandular structures formed by cuboidal cells admixed with bundles of spindle cells. Based on location and histologic features, the final diagnosis was adenocarcinoma of the apocrine gland of the anal sac, which should be included as a cytologic differential diagnosis when spindle cells and typical epithelial cells are observed in masses in the region of the anal sac of dogs.

KEYWORDS

Anal tumors, Histopathology, Dog, Surgery, Cytology

1. Introduction

Anal sac adenocarcinoma is a malignant tumor originated from apocrine gland epitheliums^[1–3]. The tumor is seen between 5–12 years old in different breeds of dogs. It is more frequently seen on neutered female and castrated male^[4–6]. The tumor is metastasized (90%) to regional lymph nodes and 40% to visceral^[7]. The most affected breeds are English Cocker Spaniel, English springer spaniel, German Shepherds and subsequently Golden Retriever and Boxer^[4]. Anal tumors of the anal sacs are uncommon in dogs and very rare in cats^[8]. The anal sacs are paired glands found on either side of the anus, which are similar to the scent glands found in skunks^[9–11]. Apocrine gland adenocarcinoma of the anal sacs occurs

at relatively low frequency in the dog, representing 17% of all perianal tumors and 2% of all skin tumors^[11–13]. Apocrine gland adenocarcinoma is the most common malignancy in this area in older female dog^[4,5,14]. As with most tumors in animals and people, we do not know what causes them to occur. Malignant neoplasms that are usually related with humoral hypercalcemia of malignancy in animals are: the adenocarcinoma originating from apocrine glands of the anal sac in dogs, some T-cell lymphomas in dogs, myelomas and miscellaneous carcinomas^[13,14]. Inordinate secretion of parathyroid hormone related protein is the main reason of hypercalcemia in most forms of humoral hypercalcemia of malignancy^[15,16]. The purpose of the study is to describe clinical and patomorphological findings of anal sac carcinoma

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in a Spitz dog.

2. Case report

In July 2012, a 9-year-old, 7 kg, castrated male white Spitz dog was presented to the clinics with a growing mass around anus and defecation problems related to the mass, and euthanasia was applied upon the owner's request and also taking into consideration the age of the animal and the size of the mass. The mass spreading into sub acute is of left hind leg out from the ventro-lateral of anus, was of 3.2×2.8 cm size and 185 g weight. A complete blood cell count and biochemical profile showed an elevated total calcium of 16.3 mg/dL or 4.0 mmol/L (reference ranges: 8.2–12.4 mg/dL or 9.3–11.4 mg/dL respectively), but no other significant abnormalities were found. Upon presentation to the university of Tehran Veterinary Teaching Hospital, the dog was bright, alert, and responsive. A firm, fixed mass, measuring approximately 3 cm at its longest diameter was palpated in the region of the left anal sac. The remainder of the physical examination was unremarkable. An ionized calcium of 1.91 mmol/L (reference range, 1.1–1.3 mmol/L) confirmed hypercalcemia. Thoracic radiographs, abdominal radiographs, and an abdominal ultrasound were performed. No abnormalities were noted on thoracic radiographs; Abdominal ultrasound suggested these structures were medial iliac lymph nodes, ranging in size from 1.5 cm to 3.4 cm. No additional sonographic abnormalities were noted. Cytology of these presumed lymph nodes was indicative of epithelial neoplasia consistent with anal sac adenocarcinoma (ASAC); Hypercalcemia has been attributed to production of a parathyroid hormone-related protein by the neoplastic cells, and although its documented incidence is variable, it has been reported in up to 51% of dogs with anal sac gland carcinoma^[13].

Table 1

Serum biochemical parameters of a spitz dog with ASAC.

	Result	Normal
Color	Yellow	
Appearance	Clear	
Specific Gravity	1/005	
PH	8/0	
Protein	2+	
RBC	0–1	
WBC	2–3	
Epithelial Cells	Many	
Bacteria	Many	
Total Protein (TP)	7.5	(5.1–7.8)
Albumin (g/dL)	2.6	(2.6–4.3)
Globulin (g/dL)	3.5	(2.3–4.5)
Glucose (mg/dL)	83	(60–125)
Triglycerides (mg/dL)	103	(20–150)
Cholesterol (mg/dL)	212	(129–330)
BUN (mg/dL)	120 H	(8–29)
Creatinine (mg/dL)	2 H	(0.4–1.8)
Urea (mg/dL)	60.7	(35–70)
ALP (V/L)	184 H	(90–150)
AST/GOT (V/L)	80 H	(5–55)
ALT/GPT (V/L)	122 H	(5–60)
Ca (mg/dl)	16.3 H	(9.4–11.6)
P (mg/dl)	3.4 L	(2.5–5.6)

ALT: alanine aminotransferase, AST: aspartate aminotransferase, ALP: Alkaline phosphatase.

2.1. Clinical signs

The most common clinical signs in dogs with ASAC included polyuria, polydipsia, lethargy, weakness that were related to hypercalcemia, local irritation (which may result in bleeding and licking of the anus), tenesmus or constipation associated with enlargement of the iliac lymph node.

2.2. Surgery technique (Closed technique)

At first the anal sacs were palpated to determine their location and extent by placing the middle finger in the rectum and thumb over the sac and evacuated the feces from the rectum. Then the preanal area was prepared for surgery. After atropine was injected (0.02–0.04 mg/kg *i.v.*) as premedication, thiopental (10–12 mg/kg *i.v.*) as induction and isoflurane as maintenance. First, a balloon-tip catheter was inserted into the orifice of the anal sac duct, after dissected against the anal sac through a curvilinear incision, the sac's outer part were separated from the internal, external and sphincter muscles surrounding it using a metzenbum. Also placed a ligature around the duct at the mucocutaneous junction with a 4-0 polydioxanone and polyglyconate, at last the anal sac was excised and ducted and closed the skin with 0-4 nylon sutures. Postoperatively, the dog recovered in the intensive care unit and was administered Normosol-R supplemented with 15 mEq potassium chloride (50 mL/kg/24 h), hetastarch (24 mL/kg/24 h), hydromorphone (0.1 mg/kg *i.v.* q 4 h), and metronidazole (15 mg/kg *per os* q 12 h) for post-operative stress colitis.

2.3. Cytological findings

Anisocytosis and anisokaryosis, hypercellularity, were increased nuclear to cytoplasmic ratio and prominent nucleoli round, shaped cells were observed which resembled hepatocytes and high number of cellular sheets, a mass of epithelial cells having a nucleus of coarse chromatin pattern, plenty of basophilic cytoplasm and cytoplasm vacuolation.

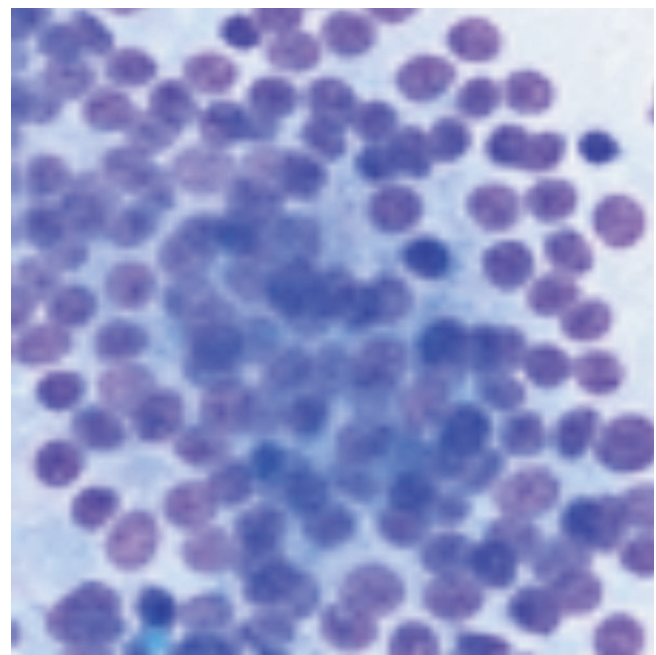


Figure 1. Cytology of an anal sac adenocarcinoma.

The cells typically are polyhedral and have uniform round nuclei at 1000×.

2.4. Ultrasound and radiography findings

There was a mass in left ventral region with a high vascularization pattern. No evidence of metastasis to other organs was noted by imaging. No evidence of pulmonary metastasis was noted on thoracic radiographs. Mild signs of bronchial pattern was seen which could be considered as a normal finding in this age. Also investigation spinal radiographs of the thoracolumbar region taken under general anesthesia, did not show any evidence of metastatic.

2.5. Micro and macroscopic findings

Histologic association with the anal sac and microscopic features of the neoplasm in this dog is consistent with a diagnosis of anal sac gland adenocarcinoma. It was covered with nodules varying from size to a chickpea. The cut section of tumoral mass was yellowish in color and containing cystic structures filled with a yellowish–red fluid. Tissue specimens were fixed in 10% formalin, processed routinely, embedded on paraffin, sectioned in 5 μ m and stained with haematoxylin–eosin (H&E). Oval or round shaped neoplastic cells with hyperchromatic nuclei, eosinophilic cytoplasm, showing solid distribution were observed microscopically. These structures were accompanied by a thin stroma consisting of capillaries and connective tissue, tumor cells were undifferentiated, multilobulated and polygonal, pleomorphism and hyperchromatic nuclei and invasive to surrounding glandular tissues, the primary tumor most commonly appeared as a deep–seated, firm, nodular perianal mass ventrolateral to the anus and involving, or within close proximity to the anal sac. Tumors were unilateral and typically 1–3 cm in diameter (range, 0.5–3 cm).

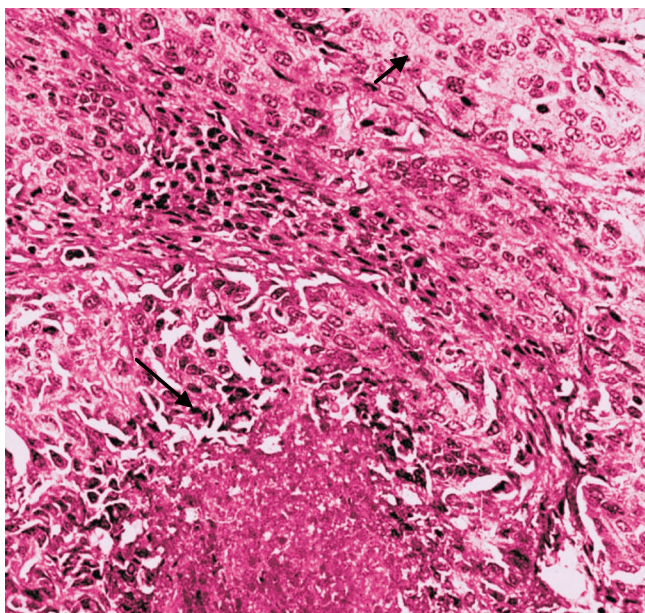


Figure 2. Histological appearance of the excised canine ASAC. The tumor was composed predominantly of solid nests (Small arrow) affected by multifocal necrosis (Arrow).

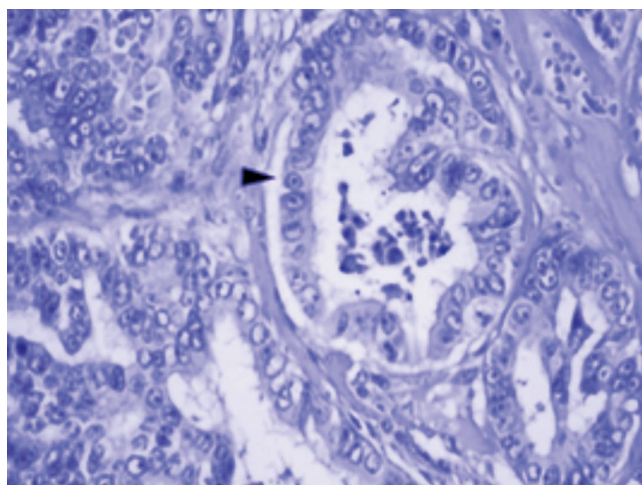


Figure 3. Lower magnification of the tumor showing irregular acini containing degenerate cellular debris (arrow head) and lined by a cuboidal epithelium exhibiting marked cellular pleomorphism (H&E).

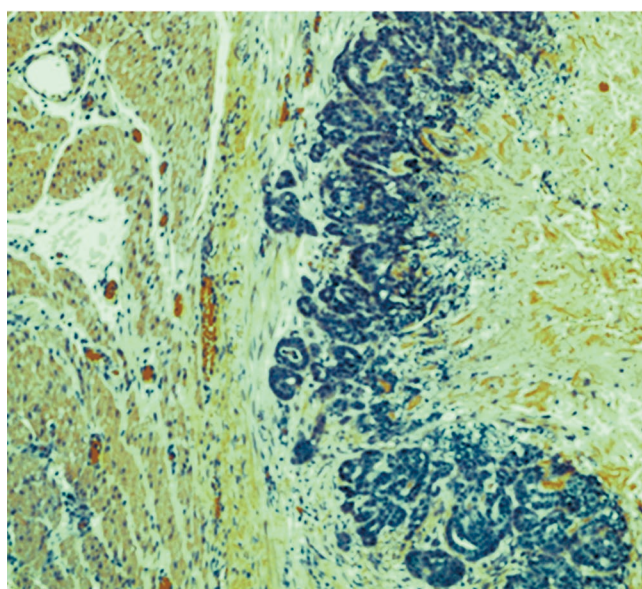


Figure 4. Anal sac apocrine adenocarcinoma in a dog. Higher magnification of the tumor showing nests of tubules, compression of the internal anal sphincter and necrosis on the right (H & E).

2.6. Care

Removal of tumor with surgical was treated. No dog was administered chemotherapy or radiation therapy, of course, calcium concentrations and clinical signs were controlled with prednisone.

3. Discussion

ASAC is a malignant tumor which originates from apocrine glands of the anal sac[3, 9, 11, 17]. Meuten *et al.* categorized the tumors into 3 types as solid, tubular and rosette[17]. Ogawa *et al.* reported the fourth types as a papillary[18]. ASAC was reported to demonstrate 2% of

all skin tumors and 17% of anal sac neoplasm's in dogs, despite it is an unusual neoplasm, it is locally invasive and has a high acceleration of metastasis to the draining iliac lymph nodes[19–22]. Anal sac adenocarcinomas can cause serious problems, because they have a tendency to metastasize to nearby tissues and organs, usually metastasize to sacral, iliac and lumbar lymph nodes by lymphatic drainage, and metastasize less to liver, lungs and spleen[8,10,21,23]. ASAC is the most common tumor of the anal sacs in dogs. These tumors are locally invasive and frequently metastasize to medial iliac lymph nodes early in the course of disease. Approximately 50% of cases develop regional nodal metastases at the time of diagnosis[24,25]. A multimodal therapeutic approach combining surgery, radiation therapy, and chemotherapy is often necessary for prolonged disease control[25,27]. Lymphadenectomy of metastatic lymph nodes is feasible at the time of primary tumor removal, and has been reported as a positive prognostic factor[8,17,24]. Normally, calcium homeostasis is regulated by parathyroid gland production of PTH and its effects on bone resorption, renal excretion and vitamin D metabolism. The ionized form of calcium is the biologically active form which is tightly maintained within a narrow normal range by a well-controlled negative feedback mechanism. During serum ionized calcium level is high, PTH production is inhibited, but when serum ionized calcium level is low, PTH production is stimulated. This tight regulation of calcium is extremely important to prevent clinical signs and adverse effects of hyper and hypocalcemia[25,27]. Hypercalcemia of malignancy is the most common cause of hypercalcemia in the dog[24,28] and is most often due to lymphosarcoma or apocrine gland adenocarcinoma of the anal sac[28]. It is less commonly present with other malignancies, including multiple myeloma and carcinomas[28]. In primary hyperparathyroidism, the most common tumors of the parathyroid glands are adenomas[29], whereas hyperplasia and parathyroid carcinoma are more infrequently diagnosed [24,29]. Clinical signs of hypercalcemia include polyuria, polydipsia, anorexia, listlessness, weakness and signs related to urinary tract stones or infection[16,30]. Diagnostic work-up for hypercalcemia should include a CBC, serum biochemistry profile, urinalysis and free calcium, iPTH, and parathyroid-related protein concentrations (PTH-rp). In this case, PTH-rp concentration was not measured, because the physical examination and plain film survey radiographs of the abdomen and thorax revealed no abnormalities, and primary hyperparathyroidism was considered to be the most likely diagnosis. Hypercalcemia has many etiologies, and a thorough diagnostic work-up is required to accurately ascertain such cause. If the cause is determined to be primary hyperparathyroidism, surgical excision provides both definitive diagnosis and therapy. As for this case, both solid and rosette types were observed.

For that reason, it is thought to be more appropriate to classify the tumor as mixed type. It is recorded that the tumor metastated 90% to the regional lymph nodes and 40% to the internal organs[7].

In conclusion, the tumor was diagnosed as anal sac adenocarcinoma in the light of clinical and pathomorphological findings. It was considered as substantial by means of being the first case reported in a Spitz dog.

Conflict of interest statement

We declare that we have no conflict of interest.

Comments

Background

Anal Gland Adenocarcinoma is a cancer of the apocrine gland, located inside of the anal sac. Canine anal glands are scent glands that produce an oily secretion. They are found on either side of the dog's anus between the internal and external sphincter. These tumors tend to be locally invasive and can metastasize early. However, this cancer is associated with a prolonged clinical course. Breeds more commonly affected include English Cocker Spaniels, Cavalier King Charles Spaniels, German Shepherds and English Springer Spaniels. Both genders of dogs are equally affected. The cause of this tumor is unknown.

Research frontiers

A 9-year-old, 7kg, castrated male white Spitz dog was presented to the clinics with a growing mass around anus and defecation problems related to the mass and euthanasia was applied upon the owner's request and also taking into consideration the age of the animal and the size of the mass. The mass spreading in to sub acute is of left hind leg out from the ventro-lateral.

Related reports

Our study nearly agreement with Akhtardanesh Baharak *et al.*, 2012. Metastatic apocrine sweat gland adenocarcinoma in a terrier dog, but our research focuses more on anal sac adenocarcinoma that is rare in dogs in these areas than in other tumor.

Innovations and breakthroughs

Data regarding: Emphasis on tumor incidence, Diagnosis, Considering spitz dog breed. Due to ASAC rarity and severe metastasis to lymph nodes around it importance study is most in dog breed, reports of ASAC are limited in the veterinary literature. There is some conflicting information regarding gender predisposition. In this report, dog with ASAC was male. Based on, reporting of Iran can

an effective step for treatment and prevention for future studies to provide.

Applications

It is significant to know the distribution of ASAC in dogs. The results of the present study suggest that the tumor was diagnosed as anal sac adenocarcinoma in the light of clinical and pathomorphological findings. It was considered as substantial by means of being the first case reported in a Spitz dog.

Peer review

This is a good study in which the authors evaluate an anal sac adenocarcinoma tumor in a Spitz dog and provided treatment and prevention for future studies. The results of this report in Iran was for the first time in this breed dog. And the results are very interesting. This paper was recommended because it was considered as substantial by means of being the first case reported in a Spitz dog.

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