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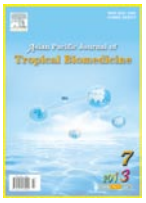

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An overall assessment of circumanal gland adenoma in a terrier mix breed dog

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PEER REVIEW

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Comments
This is a good study in which the authors evaluated a circumanal gland adenoma in a terrier mix breed dog and provided treatment and prevention for future studies. This paper is important because it is the first case reported in a terrier mix breed dog in Iran. And the results are very interesting.
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ABSTRACT

In September 2012, a 10-year-old, intact male, terrier mix breed dog was evaluated because of multiple, 0.5 to 1.2 cm in diameter, round, intradermal nodules around the anus. It had surgery to excise a firm, painful swelling in the left ventrolateral perianal region and the excision part was observed under light microscopy. The mass spreading in to sub acute was of left hind leg out from the ventro-lateral of anus, 1.2 cm×1 cm/ 0 cm×0.5 cm in size and 125 g in weight. A complete blood cell count, serum biochemistry panel, and urinalysis (cystocentesis sample) were evaluated. Significant laboratory data demonstrated microcytic anemia (hemoglobin of 6.4 mg/dL) and normal coagulation times. No remarkable abnormalities were found in the complete blood count and an ionized calcium of 1.91 mmol/L (reference range, 1.1-1.3 mmol/L) was confirmed hypercalcemia. On cytologic and histopathologic examinations, evaluation of the aspirate revealed a prominent population of round-to-polygonal nucleated cells arranged as cohesive groups with isolated individual cells. A mild degree of anisocytosis and anisokaryosis was observed. In addition, smaller reserve type cells, with darker cytoplasm and a higher nucleocytoplasmic ratio. The adenomas generally retain the lobular architecture, but some may contain focal areas of cellular pleomorphism. These changes may suggest malignant transformation and have led to discordant interpretations, the well-developed stroma surrounding the lobules and hepatoid cells was noted. Ulceration, hemorrhage, necrosis and secondary infection with inflammatory cell infiltrates are common. These cytology and histopathology features are consistent with hepatoid gland adenoma.

KEYWORDS
Hepatoid gland adenoma, Cytology, Histopathology, Dog, Blood cell count

1. Introduction

The perianal region of dogs contains multiple glands, some of which are unique to the area. These are the perianal or circumanal gland (hepatoid) glands, the anal sac glands and the anal glands[1,2]. The perianal glands, unique into the dog and marsupials, are non-secretory abortive sebaceous glands situated around the anus in a uniform circle up to 2 cm from the anal orifice, and scattered areas on the prepuce, tail, hind legs, and trunk[3]. At birth these glands are small but continue to enlarge throughout life until senility[4]. The anal sac glands are apocrine, tubular mural glands of the anal sac, while the anal glands are modified tubuloalveolar sweat glands located in the submucosa of the anal sac[5]. Three types of glandular tumors, namely perianal gland (or circumanal or hepatoid) tumor, apocrine gland tumor of the anal sac, and apocrine gland tumor commonly occur in the perianal area of the dog[6-8]. The biological behavior of each

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type varies considerably. Most perianal gland swellings are focal hyperplasia and the benign proliferative form (adenoma), while their malignant counterparts (adenocarcinoma) are uncommon[9,10]. The aim of our study was to evaluate histopathological, clinical and pathomorphological features in tissue specimens from canine hepatoid gland adenoma.

2. Case report

In September 2012, a 10-year-old, intact male, terrier mix breed dog was evaluated because of multiple, 0.5 to 1.2 cm in diameter, round, intradermal nodule around the anus. The mass spreading in to sub acute was of left hind leg out from the ventro-lateral of anus. It was of 1.2 cm×1 cm / 0 cm×0.5 cm in size and 125 g in weight. There was a history of intermittent hematochezia and perianal nodule causing perianal pain and colorectal obstruction with tenesmus. On physical examination, the lesion of the perianal area was ulcerated. The remainder of the physical examination was un remarkable, and also perianal visual and digital examination showed a blood-covered 2 cm×1 cm pedunculated mass protruding from the anus by a stalk. Significant laboratory data demonstrated microcytic anemia (hemoglobin of 6.4 mg/dL) and normal coagulation times and no remarkable abnormalities were found in the complete blood count (red blood cell count: 5.93 $\times 10^6/\mu L$; hematocrit: 41.7%; mean corpuscular volume: 59.9 fL; mean corpuscular hemoglobin: 21.5 pg; mean corpuscular hemoglobin concentration: 35.7 g/dL; platelet count: $281\times 10^3/\mu L$; total white blood cell count: $12.6\times 10^3/\mu L$; lymphocytes: 3.3 $\times 10^3/\mu L$; eosinophils: $0.5\times 10^3/\mu L$; or other white blood cells: 8.7 $\times 10^3/\mu L$), serum biochemistry (glucose: 112 mg/dL; blood urea nitrogen: 11.8 mg/dL; total cholesterol: 242 mg/dL; aspartate aminotransferase: 21 U/L alanine aminotransferase: 61 U/L; 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. Radiography showed prostatomegaly with a mildly compressed rectum. Ultrasonographic examination revealed a diffuse, symmetrically enlarged prostate gland. A perianal gland adenoma was diagnosed based on histopathological examination, which revealed hepatoid epithelial cells with round nuclei with 1 or 2 prominent nucleoli, and moderately dense light eosinophilic granular cytoplasm. At the completion of the treatment all clinical signs including pain and tenesmus had disappeared. The size of the mass around the anus had remained moderately decreased. Cryosurgery is an effective method for treatment of perianal gland′ adenoma. Sedation for cryosurgical treatment was maintained by administration of xylazine hydrochloride. Perianal region was cleaned and prepared for cryosurgery. Before starting procedure biopsy material obtained from the tumor site. Subsequently, the freezing procedure was performed by means of insertion of the cryoprobe, which is in an appropriate shape and size for the lesion, and subsequent rapid cooling. The freeze-thawing process was repeated twice, and the freezing temperature was adjusted between minus 30 °C and minus 80 °C. Special attention was paid to protect the rectum during the performance of the application. 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 Ⅳ q 4 h), and metronidazole (15 mg/kg *per os q* 12 h) for post-operative stress colitis. Cytologic evaluation of the aspirate revealed a prominent population of round-to-polygonal nucleated cells arranged as cohesive groups with isolated individual cells. A mild degree of anisocytosis and anisokaryosis was observed. In addition, smaller reserve type cells, with darker cytoplasm and a higher nucleocytoplasmic ratio, were present along the margins of some clusters (Figure 1). These cytologic findings were consistent with a well-differentiated circumanal gland tumor, also referred to as perianal tumor or hepatoid gland tumor. The perianal tumor was surgically removed. Histologic evaluation of the biopsied tissue verified the cytologic diagnosis and confirmed that the circumanal gland adenoma was completely excised. Histopathologically, perianal gland adenoma was clearly observed. In addition, the well-developed stroma surrounding the lobules and hepatoid cells was noted. Ulceration, hemorrhage, necrosis and secondary infection with inflammatory cell infiltrates are common. Surrounded by a connective tissue capsul, small basophilic reserve cells are found at the periphery of the tumor lobules (Figure 2). The hepatoid cells had a vacuolated cytoplasm, large nucleus with single prominent nuclei, white-eosinophilic cytoplasm and no mitotic figure (Figure 1). This was further evaluated under anesthesia and complete excision of distal anal tissue was performed. Our report is the first describing of a hepatoid gland adenoma in the Iran.

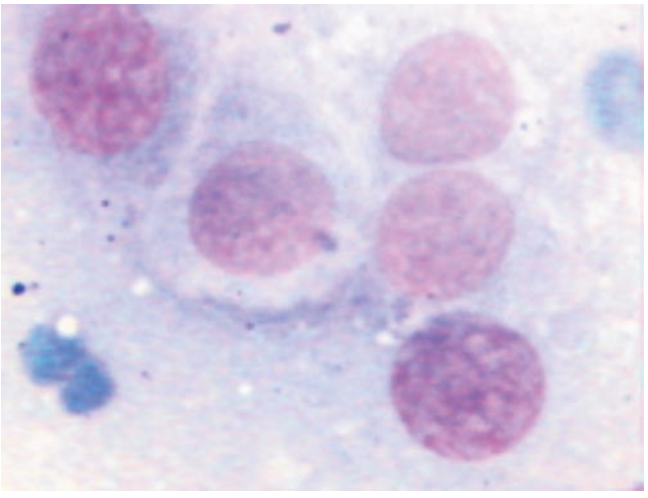

Figure 1. These cytologic findings were consistent with a well-differentiated circumanal gland tumor; Cumulative epithelial cells with nuclear of coarse chromatin pattern and abundant basophilic cytoplasm. In addition, smaller reserve type cells, with darker cytoplasm and a higher nucleocytoplasmic ratio.

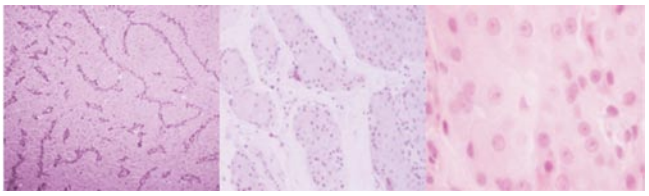

Figure 2. Histopathologically, hepatoid gland adenoma with well-differentiated glandular tissue arranged in cords and limited from surrounding tissue with a fibrous capsule. Reserve cells are scarce and located at the periphery of the cords. The well-developed stroma surrounding the lobules and Circumanal cells was noted.

3. Discussion

Benign tumours are typically slow-growing, and may remain small, discrete and clinically asymptomatic for long periods. Nevertheless, periods of rapid growth are not uncommon and adenomas can attain a considerable size in some case. Their average diameter is 0.5-3.0 cm and the lesions are generally well circumscribed. Benign lesions may ulcerate and become infected, possibly resulting in their acute presentation but are rarely adherent or fixed to surrounding structures[11,12]. The canine perianal region has different kinds of glands, such as sebaceous glands, perianal (hepatoid) glands, and apocrine glands of the anal sac. The anal sacs are paired cutaneous anal diverticula that are lined by cornified, stratified squamous epithelium, and located within the ventrolateral perianal region of carnivores and many rodents[13]. Goldschmidt and Shofer reported this tumor involving 9% of skin tumors. Perianal gland tumors are rarely found in the cat.The tumor arises from modified sebaceous gland epithelium within the dermis that is lined by small basophilic reserve cells[14]. Perianal gland adenomas are a common tumor in dogs. Our study demonstrates that the tumor's location and distinctive cytologic appearance are often sufficient for a histologic and cytologic diagnosis. Cytologically, sheets of mature, round hepatoid cells predominate characterized vy abundant, finely granular, pinkish-blue cytoplasm. Nuclei resemble those of normal hepatocytes, appearing round with an often single or multiple, prominent, nucleolus. Cytologically and hisopathologically diagnosis of a perianal gland adenoma is critical in order to differentiate this benign perianal tumor from anal sac adenocarcinoma, which characteristically has significant malignant potential in dogs. Our study demonstrates that cryosurgical therapy of primary perianal adenoma in dog, especially hepatoid adenoma is a highly effective treatment. The advantages of cryosurgical therapy in perianal region are reported to include low rate of recurrence, healing without any complication, ease of performance, no risk of haemorrhage, and prognosis ranging from good to excellent. According to the results from evaluation of case in this clinical study, cryosurgery was revealed to be a more preferable option for the treatment of perianal gland adenoma tumor, when compared to surgical methods. 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 the cause. If the cause is determined to be primary hyperparathyroidism, surgical excision provides both definitive diagnosis and therapy[15,16].

Although this study has several limitations, many of which were unavoidable given the retrospective nature of the investigation and the multiple primary care veterinary practices involved (*e.g.* limited clinical investigation, lack of archived case records and necropsy findings), it has yielded useful information about the clinical manifestations and biological behavior of perianal gland adenoma in the dog and raises awareness of this condition. On the basis of the cases in this study, a guarded to poor prognosis seems appropriate, depending on early detection and completeness of excision. This report provides evidence that, although rare, perianal gland adenoma should be recognized as a distinct clinical entity in the dog and should be included in the differential diagnosis for older dogs with clinical signs of anal sac disease.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

The authors are deeply grateful to Mr. Reza Samani for his excellent technical assistance in preparing the histological specimen.

Comments

Background

The perianal region of dogs contains multiple glands, some of which are unique to the area. These are the perianal or circumanal gland (hepatoid) glands, the anal sac glands and the anal glands. Anal sac adenoma accounts for about 17% of perianal tumors in dogs. Most affected dogs are older (average age, 10 to 11 years), and some, though not all, studies reported a predisposition in females. Clinical signs may include tenesmus or perineal swelling, although the mass may be an incidental finding in one-third of

animals. A suspected diagnosis of anal sac adenoma is based on a palpable thickening of the anal sac or a mass in that region, particularly in dogs with hypercalcemia or sublumbar lymph node enlargement. A definitive diagnosis is based on cytologic examination of an aspirate or histologic examination of a biopsy sample.

Research frontiers

A 10-year-old, intact male, terrier mix breed dog was evaluated because of multiple, 0.5 to 1.2 cm in diameter, round, intradermal nodule around the anus. The mass spreading in to sub acute was of left hind leg out from the ventro-lateral of anus and the mass was of 125 g weight. There was a history of intermittent hematochezia and perianal nodule causing perianal pain and colorectal obstruction with tenesmus. On physical examination, the lesion of the perianal area was ulcerated. The remainder of the physical examination was unremarkable, and also perianal visual and digital examination showed a blood-covered 2×1 cm pedunculated mass protruding from the anus by a stalk.

Related reports

This study nearly agrees with Andreasen, 1988 that reported the cytologic and histologic diagnosis of canine skin and soft tissue tumors. Forthermore, Meuten, 1981, reported hypercalcemia was associated with an adenocarcinoma derived from the apocrine glands of the anal sac. But this research focuses more on a complete circumanal gland adenoma of the anal sac identified to be associated with multiple perianal anomalies of unknown aetiology. That is rare in dogs in these areas than in other circumanal gland adenoma.

Innovations and breakthroughs

This study emphases on anal sac adenoma incidence and diagnosis due to its rarity in dogs, while this disease could be more often found in horse. The report provide an effective way for treatment and prevention in future studies in Iran.

Applications

It is important to know the distribution of anal sac adenoma in dogs. The results of the present study suggest that the anal sac adenoma was diagnosed as anal sac in the light of clinical and pathomorphological findings. It was considered as substantial because it is the first case reported in a terrier mix breed dog in Iran.

Peer review

This is a good study in which the authors evaluated a circumanal gland adenoma in a terrier mix breed dog and provided treatment and prevention for future studies. This paper is important because it is the first case reported in a terrier mix breed dog in Iran. And the results are very interesting.

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