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Radiographic assessment of canine transmissible venereal tumor metastases

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Abstract

Transmissible Venereal Tumor (TVT) is a common genital and extra-genital tumor of dogs that has been reported to metastasize to distant organs, however very little has been reported about the radiographic assessment of metastasis of the tumor. This study describes the use of radiography in assessing canine transmissible venereal tumor metastasis. The clinical records and thoracic and abdominal radiographs of 15 dogs diagnosed with either genital, and/or extra-genital, TVTs were reviewed to evaluate the role of radiography in the recognition of TVT metastasis. In addition, the necropsy records of four of the dogs that died, or were euthanized due to recurrence, were also reviewed. The median age of the dogs in this study was 5 years (age range = 6 months to 9 years). Nine of the dogs were females and six were males. Four dogs

showed radiographic evidence of tumor metastasis. Tumor evidence was noticed on the thoracic radiographs of three dogs, while one dog had evidence of tumors on the abdominal radiograph. In addition, two dogs each showed evidence of tumor metastasis to the mammary gland and the popliteal lymph nodes, while two other dogs each had metastasis to the uterus and cutaneous nodules, respectively. Tumor presence on the abdominal radiographs of one dog was evident as an enlarged sub-lumbar lymph node. Tumor metastases were seen in the liver and spleen of two dogs at necropsy. All tumor metastases were either confirmed by cytology of impression smear or by histology. Radiographic detection of tumor metastasis appeared to be better on the thoracic radiographs than the abdominal radiographs. It is therefore concluded that both thoracic and abdominal radiographs should be included in the diagnostic protocol of canine transmissible venereal tumor.

Introduction

Transmissible Venereal Tumor (TVT) is a sexually transmissible, contagious, reticulo-endothelial tumor of the dog that mainly affects the external genitalia and occasionally the internal genitalia[1]. Although the tumor is cosmopolitan in distribution, it is most frequently seen in tropical and subtropical regions[1,2,3]. Implantation of the tumor is facilitated by loss of mucosal integrity or a mucosal lesion. Once tumor cells are implanted, primary growth appears 15 to 60 days later[2]. The rate of tumor spread depends on the immune system of the host. Tumor growth is rapid in young or immuno-compromised dogs, and metastasis as been shown to be more frequent in males than females[4,5].

The exact cytogenic origin of TVT is unknown; however, reports have supported the hypothesis of histocytic origin[6]. Phylogenetic analyses indicated that TVTs most likely originated from a wolf or an East Asian breed of dog between 200 and 2500 years ago[7]. The tumor is highly aneuploid, with chromosome number ranging from 57 to 64 but with a remarkable stable genotype. Metastases of TVTs have been reported in less than 5-17% of the cases[2]. The most common metastatic site is the regional lymph node, but distant nodes outside the expected lymphatic drainage pattern can also be involved[1,2]. Other metastatic sites include the skin and sub-cutaneous tissue, lips, oral mucous membrane, eye, liver, spleen, lung and central nervous tissue[1,2,5]. In addition, the tumor may spread directly to involve the cervix, uterus and oviduct[5].

Most reports of canine TVT have been isolated case reports[8,9,10,11] (8 - 11).There is dearth of information on the radiographic pattern of metastasis and recurrence of TVTs. This study reviewed the radiographic assessment of metastasis and recurrence in 15 cases of TVT presented at the Veterinary Teaching Hospital, University of Ibadan, Ibadan and Veterinary Teaching Hospital, University of Agriculture, Abeokuta between 2001 and 2007.

Case Histories:

Records of 15 dogs of different breeds diagnosed with TVTs at the Veterinary Teaching Hospital, University of Ibadan, Ibadan and Veterinary Teaching Hospital, University of Agriculture, Abeokuta between 2001 and 2007 were reviewed. Routine diagnostic procedures included complete blood counts and cytological examination of fine needle aspirates of the primary tumor, and the superficial lymph nodes (pre-scapular and popliteal). In five of the dogs, histological examinations of incisional biopsies or excised masses were performed to confirm the diagnosis. In addition, lateral and ventro-dorsal, thoracic and abdominal radiographs were obtained to assess tumor metastasis.

In all the cases of TVT reviewed, the tumors were treated with four weekly intravenous injections of vincristine sulphate at the rate of 0.025mg/kg. Tumor recurrences were observed in four dogs between seven to nine months after the initial tumor remission. During tumor recurrence, masses were observed grossly and confirmed either by cytology or histology, in the mammary gland and the popliteal lymph nodes of four dogs and in ventral subcutaneous tissue of two dogs. In the dogs where tumor recurrences were observed, 50mg/kg intravenous injection of cyclophosphamide injection was combined with vincristine sulphate to achieve tumor remission. In one dog, ovariohysterectomy was performed immediately after the completion of the antitumor chemotherapy to prevent recurrence. A post mortem examination was performed in one dog that died one week after the initiation of chemotherapy and in three dogs that were euthanized due to poor anti-tumor chemotherapy response following tumor recurrence.

Results

The median age of the dogs in this study was five years (6 months to 9 years). Nine of the dogs were females and six were males. Twelve of the dogs were exotic breeds {Alsatian (7), Doberman (2), Ridgeback (1) and Rottweiler (2)}, while three were local breeds (Table 1). In the female dogs, the primary tumors were found in the peri-vulva area (7) (Fig. 1), and vagina (2) while the metastases were found in the mammary gland (2) (Fig. 2), popliteal lymph node (5), uterus (2), lungs (3) and skin nodules (1). In the male, the primary tumors were found on the prepuce (3), penis (2) and subcutaneous ventral abdomen (1). Tumors on the peri-vulva areas were fibrous in appearance and measured about 3 to 5 cm and in some areas were necrotic or dry. Tumors in the vagina were smaller (1 to 3 cm) and occasionally protruded out of the vulva. Mammary tumors were large masses with varying degree of ulcerations. The subcutaneous tumor was characterized by numerous large nodules measuring between 1 to 5 cm in length. The cutaneous nodules were diffuse and measured between 2 to 4 mm in diameter. Tumors in the prepuce were observed around the preputial orifice, had a cauliflower-like in appearance, and measured about 0.5 to 2 cm; whereas the penile tumors were diffuse.

Four dogs showed radiographic evidences of tumor metastasis. Tumor evidence was observed on the thoracic radiographs of three dogs, while one dog had evidence of tumor presence on the abdominal radiograph. Tumor presence on the thoracic radiographs was characterized by multiple, nodular, radiopaque, pulmonary masses of varying sizes (Fig. 3), while, on the abdominal radiograph, metastasis was evident as a sub-lumbar lymphadenopathy between the

fifth and sixth lumbar vertebrae (Fig. 4). Five dogs had evidence of TVT in the cytology of the fine needle aspirate of the popliteal lymph nodes.

In all dogs, a complete tumor disappearance was observed by the end of the fourth weekly injection of vincristine, however, in four dogs tumor re-growth was observed about seven to nine months after initiation of therapy. In two dogs, tumor re-growth was reported about two weeks after the bitches whelped. In the dog that had an ovariohystectomy performed after the end of antitumor chemotherapy, nodules of about 2 mm in diameter were observed on the mucosal surface of the uterine horns.

Post mortem examination confirmed tumor metastasis in the middle lung lobes of three dogs, as well as enlarged sublumbar lymph nodes in one dog. In addition tumor evidence was observed in the liver in two dogs and the spleen, kidney and pancreas in another dog. All tumor metastases were confirmed either by cytology of an impression smear of the tissue or by histopathology.

Table 1: **Case distribution of transmissible venereal tumors in seen in dogs at the** Veterinary Teaching Hospital, University of Ibadan, Ibadan and Veterinary Teaching Hospital, University of Agriculture, Abeokuta

S/N	Breed	SEX (M/F)	AGE (Years)	Site Of Primary Tumor	Radiographic Evidence Of Metastasis	Outcome
1	Rottweiler	M	7	Ventral Abdomen	Sublumbar Lymph Node	Died After First Vincristine Injection
2	Alsatian	F	5	Peri-Vulva	None	Complete Cure
3	Alsatian	M	6	Penis	None	Complete Cure
4	Alsatian	F	5	Peri-Vulva	Pulmonary Nodules	Recurred After Initial Treatment
5	Local Dog	F	0.5	Vulva	None	Complete Cure
6	Ridgeback	M	4.5	Prepuce	None	Complete Cure
7	Alsatian	F	5	Vagina	Pulmonary Nodules	Recurred After Parturition
8	Local Dog	F	9	Vulva	Pulmonary Nodules	Recurred After Initial Treatment
9	Doberman	M	5	Penis	None	Complete Cure
10	Alsatian	F	4	Vulva & Vagina	None	Complete Cure
11	Alsatian	F	5	Peri-Vulva	None	Complete Cure
12	Local Dog	M	6	Penis	None	Complete Cure
13	Doberman	F	4	Vagina	None	Recurred After Initial Treatment
14	Rottweiler	F	7	Peri-Vulva	None	Complete Cure
15	Alsatian	M	3	Prepuce	None	Complete Cure

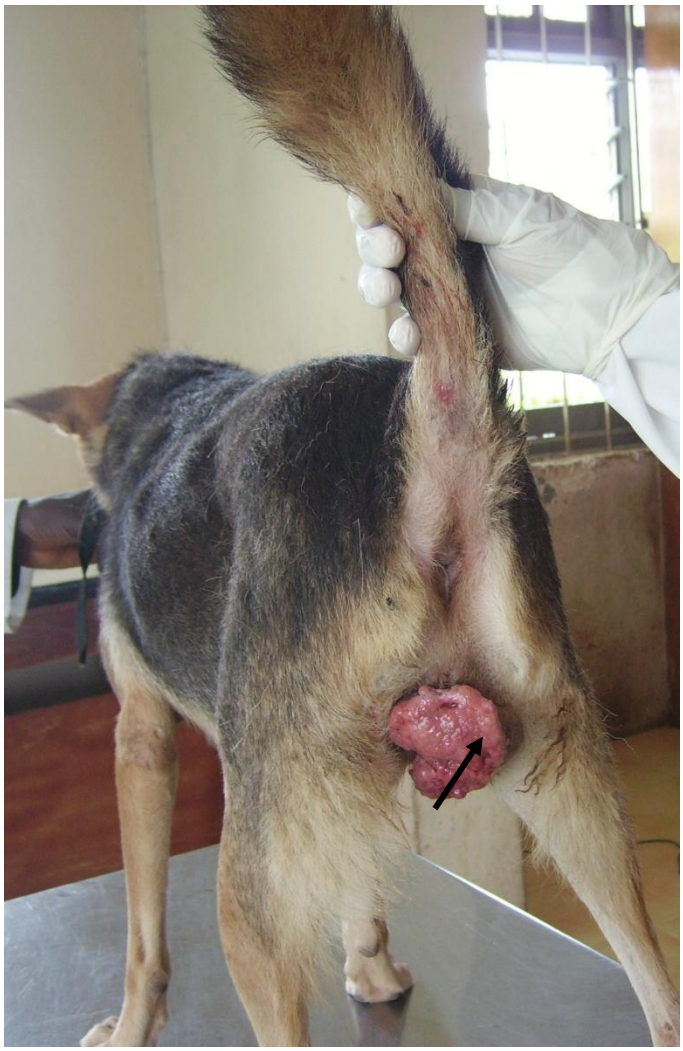

Fig 1: **Caudal view of a 4 year old female Alsatian dog with extensive vulvular transmissible venereal tumor.**

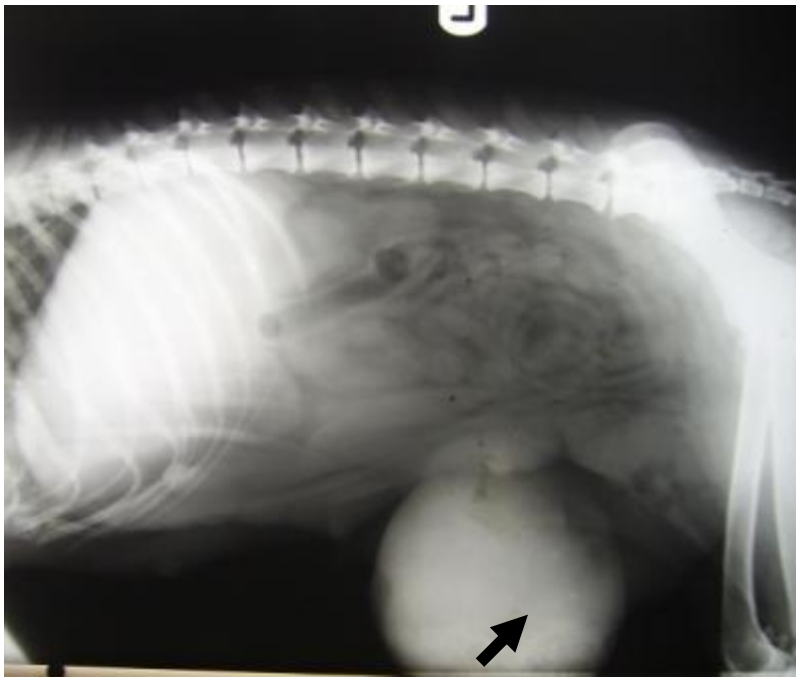

Fig.2: **Lateral radiograph of the abdomen of an adult female mongrel with an enlarged caudal abdominal mammary gland (arrow) secondary to metastatic genital TVT.**

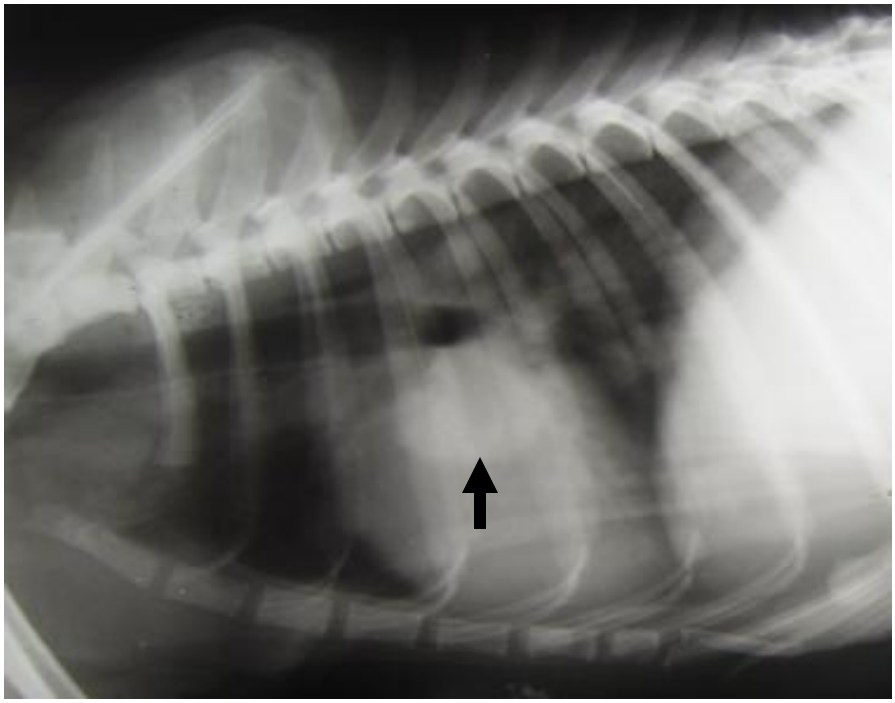

Fig. 3: **Lateral thoracic radiograph of the dog in Fig. 2 with a solitary pulmonary mass (arrow)**.

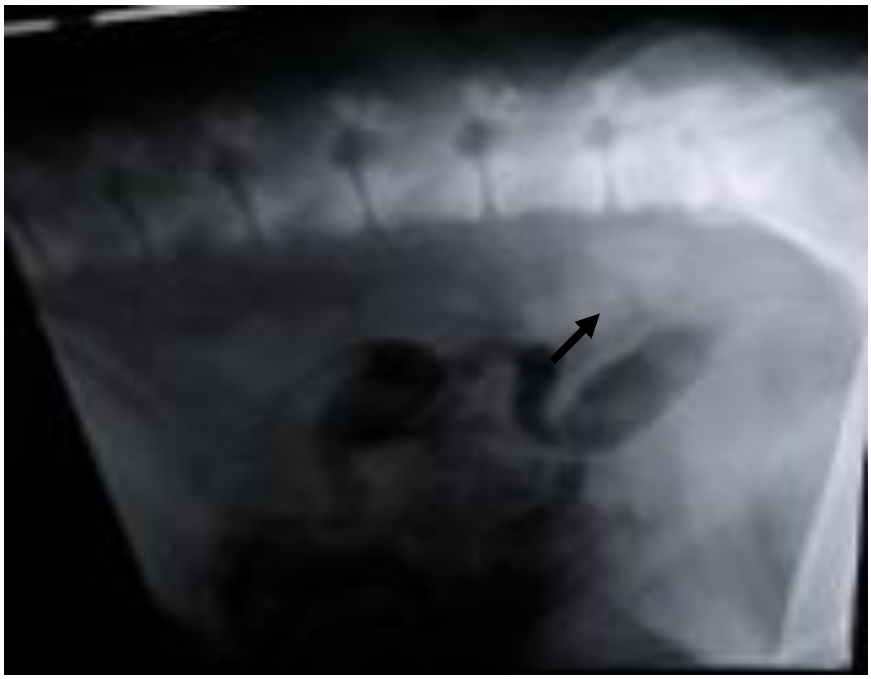

Fig. 4: Lateral abdominal radiograph of a 7 year old male Rottweiler with enlarged sub-lumbar lymph nodes (arrow) secondary to cutaneous TVT.

Discussion

Transmissible Venereal Tumor is the most prevalent neoplasm of the external genitalia of the dog in the tropical and sub-tropical areas. In one report, TVT was reported to occur in young sexually mature dogs, although no age predilection was given[2]. In the present study, the median age of the dogs was 5 years (6 months to 9 years) and did not differ from earlier reports. In the present study female dogs were more affected than the male, contrary to earlier reports[2,3,4], although this is not statistically significant. This might be because the existence of a mass in the female genital tract can easily be detected by the owners. For example, the common location for TVT in the vagino-vestibular area predisposes to its protrusion through the vulvar labia when the tumor grows, thus making it easier to recognize than in the male where the penile growth might be covered by the prepuce. Similarly, more exotic breeds were affected than the local dogs, while the Alsatian dogs appeared to be more affected than other breeds. The reason may be due to people's preference for the breed because of their perceived economic values. It is also possible that owners of local dogs will not seek veterinary attention owing to the cost of treatment.

In addition to the previously reported predilection sites of TVT[3,8,9,10,11], two dogs in this study had TVT tumors affecting the mammary gland. The dogs that had mammary recurrence had tumors observed 5 to 9 months after the initial anti-tumor chemotherapy. It might have been that the mammary gland is a metastatic site of the original genital tumor that did not resolve completely at the end of the initial anti-tumor chemotherapy. Another reason might be that tumor recurrence was due to a new infection following mating with an infected dog, with subsequent dissemination of the neoplastic cells into the mammary gland through lymphatic drainage.

The exact mechanism for tumor recurrence following clinical remission of the primary tumor has not been described. In this study, tumor recurrence was observed in two dogs five to six months after the initial clinical remission. These dogs were mated during the subsequent estrous cycle following the completion of anti-tumor chemotherapy. Mammary masses were observed two weeks after parturition in these dogs and the masses continued to increase in size until the bitches weaned the puppies. Progesterone has been reported to induce proliferation of mammary epithelium and induce local biosynthesis of growth hormones[12,13]. The high progesterone concentration during pregnancy might have contributed to the development of mammary growth in these dogs, however the role of progesterone in the pathogenesis of TVT should be determined in a controlled study.

Radiography has been the mainstay of veterinary imaging for decades and is unlikely to change, even with the increasing availability of more sophisticated imaging modalities[14]. With regard to oncologic imaging, radiography is used mainly for metastasis screening and assessment of bone tumors. The sensitivity of radiography for pulmonary metastasis has been estimated to be between 65 to 97 %[15], however, there appear to be no reports about the sensitivity of radiography for abdominal metastasis. There is one report using radiography and scintigraphy to assess canine TVT[16]. In that study, recognition of pulmonary metastasis was better than abdominal metastasis. Recognition of secondary, metastatic tumor in the abdomen largely depended on the ability of the tumor to produce an appreciable change in organ size as to cause the displacement of the adjacent structures. This may explain why sub-lumbar lymph node enlargement secondary to an infiltrating tumor was the apparent radiographic sign in the abdominal radiographs, however; using contrast techniques might enhance secondary tumor recognition in the abdominal cavity, although this might not be feasible in routine tumor staging. The use of ultrasound might improve the detection of metastatic tumors in the abdomen. For instance, small uterine nodules can easily be recognized by ultrasound, whereas the same lesion in the uterus might remain undetected using radiography until surgery or necropsy, as observed in this study. Although other imaging techniques such as scintigraphy and computed tomography can be employed to detect the presence of metastasis in organs such as the spleen and the liver, high cost and limited availability, make the routine use of these techniques in staging TVT unrealistic.

Recognition of secondary tumors in the thoracic radiographs is characterized by solitary masses or nodular pulmonary lesions. Most common solitary nodules in dogs are primary tumors, while most common multiple nodules are pulmonary metastases[17]. Distinguishing the various causes of pulmonary nodules radiographically is impossible because of the similar appearance of tumors, granulomas and abscesses. In the current study evidence of metastasis was characterized by either solitary masses or multiple nodules and was commonly observed around the middle lung lobe.

Radiographically visualized abdominal organs include liver, spleen, stomach, bladder, intestine, colon and the kidney and their visualization is dependent on the size, shape, location and the density. Considerations for generalized hepatomegaly are numerous and radiography alone is insufficient to narrow the list[18]. Conversely, excretory urography may be required to recognize a diffuse enlarged irregularly shaped and sized kidney[19]. This might explain the low recognition of tumor metastases in the abdominal cavity using survey radiographs compared to that observed at post mortem

Finally, metastasis in TVT has been reported to be less than 5-17% of cases[2,20] (2 and 20), however, in this study distant metastasis accounted for 26.7% of the cases while popliteal lymph node involvement was observed in 33.3% of cases. It may be that the actual metastatic rate of TVT is higher than earlier reported, because in most cases of TVT tumor staging is not often done. In conclusion, metastases of TVTs appeared to be higher than previously reported. Routine staging of all TVT cases using cytology of the fine needle regional lymph node aspirate, as well as thoracic and abdominal radiography and /or ultrasonography should be done to accurately assess the degree of spread. Also, a controlled study aimed at determining the role of female hormones on the metastasis and recurrence of TVT is suggested in order to determine the role of adjunct ovariohystectomy in the control of the tumor.

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