Interobserver Variation in the Morphopathological Diagnosis of Canine Mammary Gland Tumor Among Veterinary Pathologists

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ABSTRACT

Because morphopathological diagnosis of tumors plays a key role in prognosis and therapeutic decisions, the reproducibility and coherence among pathologists is important. To determine the level of inter-observer variation among veterinary pathologists for the diagnosis of canine mammary gland tumors, 15 canine mammary gland tumor slides were coded and evaluated independently by 10 veterinary pathologists. The pathologists designated whether the canine mammary gland tumors are benign or malignant. Kappa, interpreted as the proportion of agreement among raters, showed varying degrees of agreement among the 10 veterinary pathologists with kappa values ranged between 0 (no agreement) and 1 (complete agreement). Overall, we found only moderate inter-observer agreement among veterinary pathologists (mean kappa=0.43). Therefore, internationally accepted pathological diagnostic criteria of canine mammary gland tumors would assist veterinary pathologists in making more accurate diagnosis of canine mammary gland tumors.

INTRODUCTION

Pathologists, human or veterinary, play a key role in the diagnosis of tumor or tumor-related lesions. Mammary gland tumors (MGTs) are the most common neoplasms in female dogs, and are known for their complex pathological features.[1] The histological classification of canine MGTs has been a subject of debate, and a number of different classifications system have been proposed.[2-5] Currently, the World Health Organization/ Armed Forces Institute of Pathology (WHO/ AFIP) classification for canine MGTs, published in 1999, is the most widely used system worldwide.[6]

Inter-observer variations of the pathological diagnosis of human breast lesions among pathologists have been reported.[7-9] However, through years of efforts, little diagnostic inconsistency exists among pathologists on human breast tumors nowadays.

On the contrary, little consensus had been reached among veterinary patholo-

Table 1. *Kappa values among the ten veterinary pathologists.*

	DVM1	DVM2	DVM3	DVM4	DVM5	DVM6	DVM7	DVM8	DVM9	DVM10
DVM1	--	0.53	0.82	0.41	0.02	0.39	0.82	0.66	0.66	0.15
DVM2	0.53	--	0.67	0.29	0.31	0.50	0.67	0.53	0.53	0
DVM3	0.82	0.67	--	0.55	0.17	0.29	1	0.82	0.82	0.05
DVM4	0.41	0.29	0.55	--	0.39	0.11	0.55	0.71	0.71	0.10
DVM5	0.02	0.31	0.17	0.39	--	0.12	0.17	0.23	0.23	0.12
DVM6	0.39	0.50	0.29	0.11	0.12	--	0.29	0.39	0.39	0.44
DVM7	0.82	0.67	1	0.55	0.17	0.29	--	0.82	0.82	0.05
DVM8	0.66	0.53	0.82	0.71	0.23	0.39	0.82	--	1	0.15
DVM9	0.66	0.53	0.82	0.71	0.23	0.39	0.82	1	--	0.15
DVM10	0.15	0	0.05	0.10	0.12	0.44	0.05	0.15	0.15	--

DVM *Doctor of Veterinary Medicine*

gists on canine MGTs. In clinical practice, pathological examination relies on a certain degree of subjective interpretation by observers and inevitably results in interobserver variation. The purpose of this study is to assess the inter-observer variation among the veterinary pathologists in the diagnosis of canine MGT.

MATERIALS AND METHODS

Canine MGTs

Fifteen randomly selected slides of benign or malignant canine MGTs diagnosed between 2001 and 2008 were selected from the archives of the pathological files of the School of Veterinary Medicine, National Taiwan University, Taiwan. All tumors were surgically resected and provided adequate amount of tissue to evaluate detailed pathological changes. Each slide was cut from a formalin-fixed, paraffin-embedded tissue block and stained with hematoxylin-eosin.

Raters

A total of 10 veterinary pathologists examined the randomly selected canine MGTs. The participated pathologists were from the following institutions in Taiwan: the School of Veterinary Medicine, National Taiwan University; College of Veterinary Medicine, National Chung Hsing University; Graduate Institute of Veterinary Medicine, National Chiayi University; National Laboratory Animal Center; Animal Technology Institute Taiwan. All 10 participating pathologists have been actively practicing veterinary pathology for at least 10 years and have regularly evaluated canine mammary tissue. All pathologists scored the coded slides and knew that their diagnoses were going to be compared with those of others, but they reviewed the slides independently without discussing with each other during this study.

Pathological Iinterpretation

All of the pathologists diagnosed these slides as only benign or malignant mammary lesions without further classification. Any reference books could be consulted during the slides reviewing process, and there was no time and place restriction for them to finish these works.

Statistical Analysis

The inter-observer variation among pathologists was assessed by calculation of Kappa(κ) value, which is a widely used parameter of agreement. The Kappa statistics measures level of agreement adjusted for agreement expected to occur by chance alone. The Kappa value ranges from -1 to 1. The Kappa values less than 0 indicate poor agreement, 0-0.20 slight agreement, 0.21-0.40 fair agreement, 0.41-0.60 moderate agreement, 0.61-0.80 substantial agreement, and 0.81-1.00 excellent or almost perfect agreement.

RESULTS

Ten well-experienced and active academic and clinical veterinary pathologists in Taiwan participated in the study and classified all fifteen cases of canine MGT. The results showed varying degrees of agreement among the 10 veterinary pathologists with kappa values ranged from 0 (no agreement) and 1 (complete agreement) (Table 1). Between all pairs of observers, the mean kappa for agreement was 0.43. Despite the fact that all ten participants are among the most experienced veterinary pathologists in Taiwan, only moderate agreement was achieved. Of the 45 pairs, the diagnosis in only eight pairs of pathologists reached excellent or almost perfect agreement (kappa between 0.81-1.00) in which two pairs (DVM3 and DVM7, DVM8 and DVM9) made the exact same diagnosis in all 15 cases. Six pairs showed substantial agreement (κ= 0.61 -0.80), 8 showed moderate agreement (κ= 0.41-0.60), 10 showed fair agreement (κ= 0.21-0.40), and 13 pairs were in poor agreement (κ= 0-0.20).

DISCUSSION

Correct diagnosis is the prerequisite for adequate therapy, which is a crucial determinant of survival in patients with cancer. Kappa statistics have been applied in the assessment of inter-observer variations in many fields of clinical medicine. Although many inter-observer variation studies have been conducted in human pathology to make the pathological diagnosis more consistent, no similar study related to tumor diagnosis has been performed in veterinary pathology.

The present study showed that veterinary pathologists have only moderate agreement in the diagnosis of canine MGTs. This moderate consistency in the diagnosis of canine MGT raises doubts concerning the robustness of the current diagnostic criteria.

Our finding suggest that diagnosis of canine MGT is associated with substantial variation depending on the pathologist. Several factors may have contributed to this inter-observer variation. First and most importantly is the complexity of histological architecture of canine MGTs. For veterinary pathologists, nuclear atypia, increased mitotic activity and infiltrative border are important factors that master their final judgment. Nuclear atypia is sometimes the result of reactive reaction rather than malignant change. Increased mitotic activity is also not a diagnostic indicator of malignant tumors.

Furthermore, infiltrative nests of cells are occasionally hard to be differentiated from entrapped mammary glands. The observer variability found is unlikely to be associated with the qualification of the participating veterinary pathologists since all 10 participants are active veterinary pathologists and well-experienced.

Currently, many veterinary pathologists assign MGT types according to the WHO/AFIP histological classification of canine MGTs. Despite its tremendous contributions to the veterinary pathology over the years, this reference contains relatively short definitions and descriptions on canine MGT and only several black photos. On the contrary, better definitions and detailed descriptions, and nearly 2 hundred colorful illustrations are presented in the book of WHO tumor classification for human breast for human pathologists for reference. Therefore, based on the results of the present study, we believe that inadequate reference might be a major factor that contributed to the inter-observer variation among the veterinary pathologists in the diagnosis of canine MGTs.

The limitation of our study, by its design, was the lack of a "gold standard diagnosis" by a board of experienced veterinary pathologists against which individual diagnosis could be compared. However, each of the 10 participating veterinary pathologists in this study was highly experienced and have regularly evaluated canine mammary tissue.

CONCLUSION

The present study suggests that there is a considerable inter-observer variation in the morphopathological diagnosis of canine MGT among veterinary pathologists, and one of the reasons that might have contrib-

uted to this variation is the lack of adequate reference or guidelines to which the diagnoses can be based on more accurately and consistently. Thus, more robust, internationally agreed criteria for making these diagnoses are required.

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