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Implication of CA 15-3, CEA and mammary gland temperature in diagnosis and management of canine mammary tumor

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This study was conducted to explore the diagnostic potential of serum biomarkers such as CA 15-3 and CEA, along with mammary tissue infrared temperature in canine mammary tumor (CMT). Total thirty five suspected cases of CMTs were evaluated by histopathology. Further CA 15-3, CEA, and mammary tissue infrared temperature value was figured out and correlated with clinical picture of CMTs. Mammary tissue infrared temperature as well as CA 15-3 and CEA values were significantly higher in dogs with CMTs than healthy dogs. These values were also higher in malignant cases as compared to benign cases. Diagnostic sensitivity of CA 15-3, CEA and infrared thermography were 94.29%, 54.28% and 88.57%, whereas specificity were 87.5%, 87.5% and 100%, respectively for CMTs. CA 15-3 stronglyassociated with tumor progression, malignancy, CEA level, mammary tissue temperature, number of mammary gland involvement, ulceration, tumor size and tumor weight. Post-surgery reduction in serum concentration of tumor markers and mammary gland temperature were recorded in recovered animals. Thus, expression of CA 15-3 and CEA tumor markers along with mammary tissue infrared temperature could provide valuable diagnostic significance regarding nature of tumor and start of treatment regimen in CMTs.

Keywords: Canine mammary tumor, CA 15-3, CEA, Infrared mammary temperature, Surgico-chemotherapeutic management

Canine mammary tumors (CMTs) represent a very diverse group of tumors and therefore different treatment approaches may be required. In female dogs, mammary tumors may be either malignant or benign that accounts for approximately 50% of the all neoplasms[1,2].Due to high malignancy rate, CMTs have a bad prognosis and therefore, early diagnosis is crucial for effective management[3].Currently, no screening method can predict the presence of a malignant tumor with 100% accuracy. The only reliable diagnostic method is a biopsy, which is recognized as the gold standard for diagnosing canine cancer[4]. World Health Organization (WHO) approved the official histological classification for CMTs based on its morphology and cell type[5].CMTs may be adenomas or carcinomas of epithelial cell origin, fibrosarcomas, fibroadenomas (mesenchymal origin), or mixed tumors of both epithelial and myoepithelial tissue.Histopathological assessment requires thorough knowledge, technical skill and vast experience; therefore, it can be variable and subjective.

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Recently, new diagnostic options have emerged, including a new cytological grading system for CMTs, B-mode ultrasound, the Doppler technique, contrast-enhanced ultrasound, and real-time elastography, which may be useful in pre-surgical evaluation. However, to detect malignancies before macroscopic changes are visible, evaluating serum and tissue biomarkers may be considered effective. Canine mammary tumors have heterogeneous morphology and biology that makes it difficult to choose the most appropriate biomarkers for its diagnosis. However, studies have shown similarity in gene transcription of breast cancer in women and female dogs[6].Therefore, serum tumor markers have emerged as an effective tool to determine prognosis and treatment efficiency in different cancer types. CA 15-3 is a *MUC1* gene-coded glycoprotein expressed on the surface of various epithelial cell types and over-expressed in 90% of breast cancer cases[7].CEA is expressed in the majority of human lung, pancreatic, and gastric cancers, in addition to breast carcinoma.CA 15-3 and CEA permit the early identification of up to 60-80% of breast cancer patient metastasis in human[7,8].In addition to this, thermography, an older screeningtechnique which measures mammary tissue temperature

and demonstrate variation in temperature with the tumor tissues surrounding the breast shows high accuracy and a cost-effective diagnostic tool[8,9].

Surgical resection is standard therapy for mammary tumors in dogs and single most effective method to attain local tumor control except for inflammatory carcinoma or presence of distal metastases[10]. Chemotherapy with vincristine sulphate is effective in the treatment of mammary tumor and venereal granuloma in dogs as compared to doxorubicin therapy[11]. The present study was therefore undertaken to evaluate the clinical significance of serum CA 15-3 and CEA tumor markers, thermography and gross morphology in diagnosis of CMTs. Further, response of CMTs to different management approaches was also evaluated.

Materials and Methods

Screening of canine mammary tumor

Current investigation screened dog population (n=235) in and around Durg district of Chhattisgarh, India. Dogs suspected of having mammary tumors clinical symptoms such as swelling at mammary gland were recorded.

Clinical observation

Canine mammary tumors were examined clinically through visual findings and palpation of entire mammary glands. Size of tumor (cm), condition of tumor and weight of tumor (g) were recorded.

Infrared thermography

Mammary tissue surface temperature of dogs was recorded, from 3 cm distance with the help of infrared thermometer (Pristyn care thermometer IR, Beat XP) and was expressed in °C.

Histopathology

The biopsy samples of mammary tumor were collected in 10% neutral buffered formalin and then processed for histopathological studies. The formalin-fixed tissues were cut into small pieces of 2-3mm thickness and washed thoroughly in tap water overnight, dehydrated in graded alcohol or acetone series, cleared with graded xylene and embedded in paraffin wax. The paraffin-embedded tissue was cut in 4µ thickness. The sections were deparaffinised in xylene and stained with hematoxylin and eosin (H&E) and mounted with DPX[12]. Stained sections were examined under 100× and 400× magnifications.

Detection of CA 15-3 and CEA in serum

Serum sample was collected from each of the suspected cases of CMTs. CA 15-3 estimation in serum was analyzed by semi-automated CLIA (Chemiluminescence Immuno Assay) plate analyzer (Radiance, Tosoh India Pvt.Ltd.) using CA 15-3 reagent kits (AccuLite, Tosoh India Pvt.Ltd.) at MEDCIS labs, Hyderabad according to the manufacturer′s instruction and was expressed in IU/mL. CEA estimation in serum was performed by semiautomated ECLIA (Electro Chemiluminescence Immuno Assay) plate analyzer (ECLIA –IIM chemiluminescence immune analyzer, Life science instrument and equipment) using CEA reagent kits at MEDCIS labs, Hyderabad according to the manufacturer′s instruction and was expressed in ng/mL.

Briefly, the patient serum and horse radish peroxidase (HRP) were added to the white opaque microporous plate coated with streptavidin and exogenously biotinylated monoclonal antibodies. The molecule to be tested in the serum was specifically bound to enzyme labeled polyclonal antibody (the conjugate of horse radish peroxidase enzyme and the antibody) on the solid phase carrier to form immobilized sandwich complex. Separation and washing of unreacted free components was done after equilibrium attained. Then luminol luminescent substrate was added and the antibody-bound fraction was excited by the free energy released from the chemical reaction, and the energy was released in the form of photons from ground state to excited state. At this time, the microporous plate is placed into the analyzer, and the number of photons passing through each hole is read out by photon counter through three-dimensional transmission systems inside the instrument. The molecular concentration in the sample was quantitatively analyzed according to mathematical model established using standard sample.

Management of canine mammary tumor

Considering the histopathology report as inferential observation, the tumors were broadly categorized as benign and malignant. Accordingly experimental design was made to study the efficacy of surgico-chemotherapeutic management of canine mammary tumors as shown in Table 1.

After premedication with atropine sulphate @0.04 mg/kgbody weight intramuscularly, dogs were sedated using injection xylazine @1 mg/kgbody weight intramuscularly. General anaesthesiawas induced and

Table 1 — Experimental design for surgico-chemotherapeutic management of canine mammary tumor

Group	Particulars	Number of animals	Management strategy
I	Healthy animals	8	Nil
II	Benign mammary tumour	8	Surgical intervention only (as described below)
III	Malignant mammary tumour	8	Surgery with injection vincristine sulphate @0.025 mg/kg body weight I/V at weekly interval for three weeks

maintained by ketamine hydrochloride @5 mg/kgbody weight intravenously. The surgical technique of lumpectomy and simple mastectomy were performed for the management of mammary tumors[13].Thetumor mass was weighed and preserved in 10% formalin for histopathological examination. Animals were treated with cefotaxime@25 mg/kgbody weight intramuscularly for 5 days and meloxicam @ 0.5 mg/ kgbody weight intramuscularly for 3 days post operatively. The surgical wound was cleaned with povidone iodine liquid and dressed daily with ointment silverex for 10 days. The owner was advised to feed milk on first day and to resume normal feeding from second day onwards. The skin sutures were removed based on the wound healing condition. Each dog was observed for any recurrence up to 2 months after surgery. Sera samples were collected from each of the recovered dogs after treatment for estimation of CA 15-3 and CEA antigen levels. Mammary tissue temperature was also recorded after recovery.

Statistical analysis

Data were presented as Mean ± S.E. Analysis of variance (ANOVA) was performed to compare measurable variables such as CA 15-3, CEA, temperature, tumor weight and tumor size between groups. *Chi-square* test was used to compare tumor condition (ulcerative/non ulcerative) between groups. *P*-values were determined to interpret significant level. To assess and compare the diagnostic performance of biomarker, best cut-off value for CA 15-3, CEA and infrared temperature was estimated to maximize the sum of sensitivity and specificity to diagnose an animal with mammary gland tumors. Cut-off value was calculated by determining 95% Confidence Interval (mean value in healthy dog′s ±2SD). Pearson correlation coefficient test was done to illustrate an association between variables or agreement between two methods. Variables are said to be directly related if the coefficient has positive number (between 0 and 1) and variables are inversely related if the coefficient is negative number (between 0 and -1). Considering the inferential results of histopathology, diagnostic sensitivity and specificity of serum tumor markers and thermography was calculated as below:

Diagnostic Sensitivity = (true positives tested) / (true positives tested +false negatives tested)

Diagnostic Specificity = (true negatives tested)/ (true negatives tested +false positives tested)

Results

Prevalence of CMT

Canine mammary tumorswere characterized by localized swelling, hard texture, painless, itch less of the mammary gland and surrounding subcutaneous tissue, with varying sizes. Out of 235 female dogs screened, 35 dogs exhibited clinical signs suggestive of canine mammary tumors. Prevalence rate of canine mammary tumor was 14.89%.Out of 35 female dogs 15 (42.86%) were nulliparous followed by primiparous (n=10, 31.25%) and pluriparous (n=10, 31.25%). All the affected females were non-pregnant and non-spayed.

Clinical findings of CMT

Clinical presentations and different tumor markers of CMTs are depicted in Fig. 1 and Table 2.In a total of 26 dogs (74.29%), single mammary gland was involved whereas in 9 dogs (25.71%) more than two mammary glands were affected. There was involvement of only one teat in each of the benign cases whereas more than one mammary gland was affected in 64.28% of the malignant tumor cases. The size of tumor recorded in affected female dogs ranged between 1 and 19 cm. Malignant tumors (13.91 ± 0.77cm) were significantly bigger than benign ones (4.83 ± 0.54cm). Thirteen malignant tumor cases (37.14%) were ulcerated while condition was nonulcerative in remaining cases. 95.24% of benign tumors were nonulcerative while only one showed ulceration (Fig. 1). The maximum weight of mammary tumor was 4500 g while the lightest one was 20 g. malignant tumors (1497.14±91.22 g) weighs significantly more than benign tumor (229.52±45.96).

Histopathological categorization of tumors

Microscopic examination of tissue biopsy categorized CMT into benign (n=21, 60%) and malignant tumor (n=14, 40%).Various histologcaltypes ofCMT are

Table 2 — Comparison of various markers and clinical findings of CMTs

Markers/clinical findings	Group	Mean Value	*P*-Value
CA 15-3	Benign	4.47±0.28	
	Malignant	8.31±0.20	0.0001**
	Healthy	1.36±0.07	
CEA	Benign	0.31±0.01	
	Malignant	0.39±0.004	0.0001**
	Healthy	0.23±0.03	
Temperature	Benign	36.47±0.29	
	Malignant	38.81±0.24	0.0001**
	Healthy	33.53±0.27	
Tumor size	Benign	4.83±0.54	0.0001**
	Malignant	13.91±0.77	
Tumor weight	Benign	229.52±45.96	0.0003**
	Malignant	1497.14±91.22	
Tumor condition			0.001**

Note: One way ANOVA was performed to compare CA 15-3, CEA, Temperature, Tumor size and Tumor weight between groups whereas *chi-square* test was performed to compare tumor condition between groups.

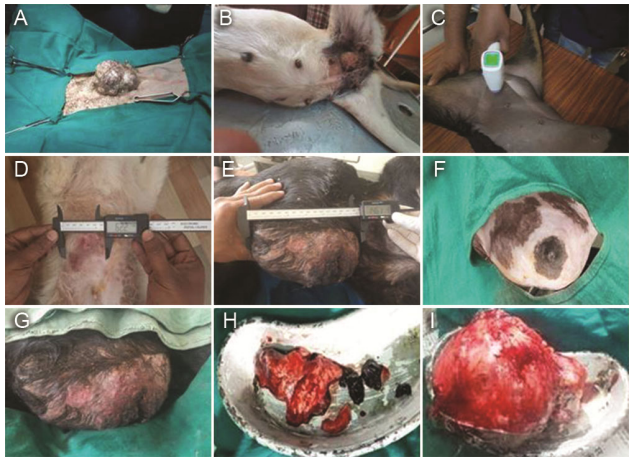

Fig. 1 — Clinical presentation of CMTs- (A) Single mammary gland involvement (B) Involvement of more than one mammary gland (C) Recording infrared surface temperature of mammary gland (D) Small-sized (6.2 cm) tumor (E) Large sized (14.5 cm) tumor (F) Large-sized non-ulcerated pedunculated tumor (G) Large-sized ulcerated tumor (H) Small-sized tumor measuring 50 g (I) Large-sized tumor measuring 950 g.

illustrated in Table 3 and Fig. 2. Histological types in benign tumours were fibroadenoma and haemangio sarcoma. Fibroadenoma was characterized by tubules lined by cuboidal or columnar cells, with nuclei that were round and uniform whereas haemangio sarcoma consisted of blood-filled channels and spaces.Malignant tumors were tubular adenocarcinoma (transform cells arranged in a tubular fashion), papillary adenocarcinoma (neoplastic tubules arranged in a sessile or pedunculated papillary fashion), comedo carcinoma (necrotic areas within the center of the neoplastic cells aggregates), squamous cell carcinoma (epithelial cells with the keratin pearls), solid carcinoma (cells arranged in solid masses without lumina), cribiform carcinoma (epithelial cells forming a sieve-like arrangement), intraductal carcinoma (well demarcated nodules) and lipid rich carcinoma (sheets of cells with inconspicuous fibrovascular trabeculae and foci of necrosis).

Surface temperature of mammary gland (ºC)

The values of infrared temperature in affected mammary tissue were significantly higher than healthy mammary tissue of dogs. The infrared temperature of mammary tumor ranged from 34ºC to 40.10ºC. The values of infrared temperature of affected mammary tissue (37.41±0.28ºC) were significantly higher than healthy mammary tissue (33.54±0.28 ºC) of dogs. The results showed significantly higher infrared temperature in dogs with malignant mammary tumor (38.81±0.24ºC) than that of benign tumor (36.47±0.29ºC). Association of size of tumors, weight of tumors and temperature was determined (Table 4). Size and weight of benign tumors were positively correlated with temperature. In case of malignancy tumor weight was positively correlated with temperature however slight negative correlation was reported between tumor size and temperature.

Level of CA 15-3 and CEA in serum

The CA 15-3 (IU/mL) and CEA (ng/mL) values in healthy dogs were 1.36±0.07 and 0.23±0.03, respectively which were significantly higher in dogs affected with mammary tumor. CA 15-3 and CEA values were significantly higher in malignant tumor cases (8.31±0.2and 0.39±0. 004, respectively) than that of benign tumor patients (4.47±0.28 and 0.31±0.01, respectively). CA 15-3 value ranged between 1.38 and 5.90 in benign cases and between 6.13 and 9.10 in malignant cases whereas CEA value were 0.26-0.39 in benign and 0.37-0.40 in malignant cases.

Surgico-chemotherapeutic management of canine mammary tumor

During present investigation, after two months follow up, the combination of surgery along with chemotherapy was found to be more effective for the management of malignant cases of CMTs with success rate of 87.5%. 12.5 percent recurrence was

Table 3 — Histological typing of CMT

S. No.	Tumor Type	Histological type	No. of dogs	Prevalence (%)
1	Benign	Fibroadenoma	17	48.57
2		Haemangiosarcoma	4	11.43
Total			21	60.00
1	Malignant	Tubular adenocarcinoma	2	5.71
2		Papillary adenocarcinoma	1	2.86
3		Comedocarcinoma	1	2.86
4		Sqaumous cell carcinoma	3	8.57
5		Solid carcinoma	1	2.86
6		Cribiform adenocarcinoma	4	11.43
7		Intraductal carcinoma	1	2.86
8		Lipid rich carcinoma	1	2.86
Total			14	40.00
Grand Total			35	

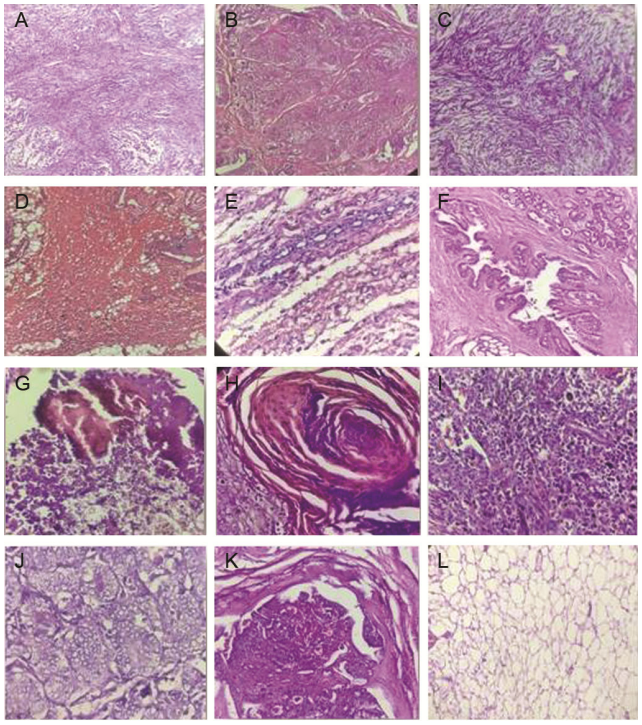

Fig. 2 — Histopathological typing of CMTs- (A) fibroadenoma showing fibrosis (B) fibroadenoma showing extensive fibrosis with mitotic figures (C) fibroadenoma showing stroma of loose connective tissue (D) haemangiosarcoma showing blood filled channels and spaces (E) tubular adenocarcinoma showing neoplastic cells arranged in tubular fashion (F) papillary adenocarcinoma indicating neoplastic tubules arranged in pedunculated papillary fashion (G) comedocarcinoma with area of necrosis within neoplastic aggregates (H) squamous cell carcinoma showing keratin pearls like structure (I) solid carcinoma showing compact neoplastic cells, hyperchromatic nuclei, with poorly differentiated lobules (J) cribiform carcinoma showing sieve like arrangement of epithelial cells (K) intraductal carcinoma showing layer of transform cells within the ducts (L) lipid rich carcinoma showing nuclei at periphery with a single large lipid vacuole.

seen in group III dogs. Side effects like alopecia, vomition and anorexia were commonly observed in group III dogs, while in group II, the use of surgical excision was found to be an effective line of treatment with overall success rate of 100%. Although CA 15-3, CEA and mammary temperature values in recovered animals of group II and III were higher but it did not vary significantly with group I animals (Table 5). Pre and post treatment CA 15-3 and CEA values differed significantly (P<0.001) in group II and III.

Diagnostic sensitivity and specificity of CA 15-3, CEA and infrared thermography

Maximum cut-off value for CA 15-3, CEA and infrared temperature in healthy dogs was calculated as 1.71, 0.38 and 35.12, respectively. Dogs showing values above these cut-off values were considered positive for CMTs. Considering the histopathology results inferetive for CMT cases, diagnostic sensitivity and specificity of serum tumor markers and thermography were determined. Diagnostic sensitivity of CA 15-3, CEA and infrared thermography were 94.29%, 54.28% and 88.57%, whereas diagnostic specificity were 87.5%, 87.5% and 100%, respectively for CMTs.

Correlation of CA 15-3 with other diagnostic tool for CMT

When 35 CMTs were examined for correlation (Table 4) it was observed that CA 15-3 level was positively correlated with malignancy, CEA, mammary tumors tissue temperature, number of mammary gland involvement , ulceration, tumor size and tumor weight.

Discussion

CMTs have substantial significance in veterinary medicine as it is common neoplastic disease among female dogs, representing over half of all tumor types

diagnosed among entire female dogs[14]. Before proceeding for treatment it is necessary to understand the nature and possible outcome of CMTs. The heterogeneity of mammary tumors makes them highly variable in their biological behaviour, which generates the necessity of identifying factors with prognostic or therapeutic value for each particular patient and type of tumors. However, no consistent efforts have been made to automate the diagnosis of CMTs. Variation in incidence during current study supports the earlier observation that incidence of CMTs differs between regions[15].Previous studies also recorded similar prevalence of CMTs in dogs[16,17]. The mammary gland tumors are hormone-dependent. The higher incidence of mammary gland tumors in intact dogs might be due to estrogen and progesterone hormone which is attributing factor[10].Higher prevalence CMTs in non pregnant dogs suggests the inhibitory effect of pregnancy on the development of mammary tumors[18].

Clinical picture of tumors such as size, depth, and pathological heterogeneous nature facilitate distinguishing malignancy from benign mass. Current study aligns with previous studies and reported 40-50% prevalence of malignant mammary tumors in female dogs[10,19]. On the contrary, some studies reported higher incidence of malignant CMTs[15,20]. Similar histopathological types and conditions of benign and malignant mammary tumor in dog was reported in previous studies[17,18-21].Although histopathology is a gold-standard technique in classifying CMTs but it is a time-consuming process and affected by high inter-observer variability that essensiates exploration of a rapid and noninvasive alternative technique.

Multiple tumors involving more than one gland in female dogs are very common[10].Large sized tumor with involvement of multiple mammary glands is more painful and warm. Therefore size and weight of tumor could be directly correlated with prognosis of CMTs. Earlier study also reported that benign tumors are usually smaller than malignant tumors and their prognosis may be better than that of large tumors[10,18,22].The benign mammary tumors in dogs commonly tend to become encapsulated and are freely movable where as malignant tumors invade, encroach and become fixed in tissue in which they are situated and also penetrate skin and get ulcerated[23].The ulceration on the skin over the tumor mass might be due to the malignant nature of the tumor, which produces tremendous inflammation and ultimately becomes ulcerated[18]. Tumorsize above 5 cm is usually considered malignant while benign tumors are smaller[24].Tumors weight with a verge of more than 400 grams could be considered as malignant cases[25].Wide variation in weight of tumor masses ranging from 30g to 2kg has been reported[26].In present study we observed higher incidence of large-sized malignant tumor. As malignant canine tumors grow, they may become firmer because intratumoral necrotic tissue enlarges due to hypoxia or intratumoral pressure is increased due to compression between surrounding tissues such as muscle and fascia[27-29].Usually benign tumors are slow-growing and don't spread to other areas of your body but a large benign tumors may press on nearby tissue and organs and may show ulceration as shown in one benign tumor (8.5 cm, 620 g) in present study.

Variation in infrared temperature between tumor and healthy tissue attributed to differences in metabolic energy released from healthy and carcinogenic cells[30].To meet oxygen requirement in cancerous cells blood flow increases and leading to

Table 4 — Association between tumor size, tumor weight and surface temperature in CMT cases

Group	Tumor size	Tumor weight	Temperature
Benign			
Tumor size	1	0.95	0.75
Tumor weight	0.95	1	0.74
Temperature	0.75	0.74	1
Malignant			
Tumor size	1	0.90	-0.12
Tumor weight	0.90	1	0.13
Temperature	-0.12	0.13	1

[Given values represent the correlation coefficient (r)]

Table 5 — Post recovery record of CA 15-3, CEA and mammary gland temperature

Tumor markers	Group I		Group II		Group III	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
CA 15-3 (IU/mL)	1.36±0.07	1.33±0.12	4.75±0.34	1.48±0.30	8.57±0.09	1.70±0.48
CEA (ng/mL)	0.23±0.03	0.22±0.07	0.33±0.02	0.28±0.07	0.38±0.002	0.36±0.07
Mammary tissue temperature (ºC)	33.53±0.28	33.36±0.10	36.55±0.48	34.72±0.12	39.18±0.19	35.12±0.09

[Pre and post-treatment values of CA 15-3, CEA and mammary tissue temperature within Group II and III significantly ($P<0.05$)]

rise in temperature of cancerous cells. It is preferred over other methods as it is painless and noninvasive. Positive correlation of temperature with tumor weight and size as tumor cells liberate nitric oxide into the bloodstream that also improves blood circulation and ultimately rise in temperature occurs[31]. Therefore, evaluating these differences in temperature would be useful in detection of the malignant region in the breast.

In reference to CA 15-3 and CEA level in serum of dogs CMT dogs; our finding supports the earlier observations[18,32-33].CA15-3 directly correlates with the progression of tumor and metastasis[7]. Therefore CA 15-3 marker can be used for detection of mammary tumor and also to monitor the response to the treatment in female dogs. CEA is a glycoprotein and a broad-spectrum tumors marker which is mainly used in the diagnosis of adenocarcinoma[8,34]. CEA is one of the first identified tumor markers of human breast cancer which is associated with tumor progression[35].

Present study reported that diagnostic sensitivity of CA 15-3 was higher followed by infrared thermograpgy and CEA. Although the sensitivity of CEA was lower but specificity was similar to that of CA15-3. Mammary thermography with 100% specificity and 88% sensitivity could be employed as a screening method followed by detection of CA 15-3.Earlier studies have suggested CA 15-3 as good biomarker of CMTs[7-8,36]. To avoid any chance of errors, CA 15-3 should not be used alone for diagnosis of CMTs.Combined detection of CA 15-3, CEA and mammary thermography would be more efficient and confirmative for the diagnosis of CMTs. Typically use of more than one technique is emphasized for detection of CMTs[37].Tumor marker CA15-3 is considered as an important concern in the realm of CMTs. No reference ranges for CA 15-3 suggested till date, and thus reference ranges need be established for future assessments. Based on the results of present study, CA15-3 serum level $\geq$6 IU/mL in dogs could be considered at risk of malignancy. However, in a report serum cut-off value for CA 15-3 was established at 1.5 IU/mL with 100% sensitivity and specificityin diagnosis of CMTs[38].

Present study demonstrated strong association of CA15-3 and malignancy in CMTs. CA 15-3 is proved to be efficient as a prognostic monitoring marker than CEA and reveals a positive correlation between surgico-chemotherapeutic management and malignancy, with increased observability in early stage. Post-surgery decreased serum concentration of CA 15-3, suggesting that an increase in their value after mastectomy can be used as evaluation of tumor recurrence. Affected dogs with largest tumor and malignancy exhibit significantly higher concentration of CA 15-3. As previously stated, the number of nodules, tumor size, ulceration, histopathological types and clinical staging are all associated with worst prognosis in female dogs with CMTs[39,40].Likewise, higher serum level of CA 15-3 was reported in ulcerated tumors of previous study[10].Although there is lack of sensitivity of CEA antigen, but it may be used in adjunction with CA 15-3 to increase the diagnostic accuracy to detect CMTs, given its strong association with CA 15-3, as determined in the present study.

Conclusion

Increased incidence of malignancy has been observed in canine mammary tumor (CMT). Early diagnosis of CMTs increases the success of treatment. However, early diagnosis of the disease is a challenging task in dogs especially in country like India where periodic visit of dog owners to a veterinarian is not a regular practice. None of the diagnostic tool alone could bring out definitive diagnosis of CMTs but the use of set of biomarkers together that includes CA 15-3, CEA and mammary gland temperature would improve follow-up monitoring of CMTs.

Conflict of interest

The authors declare no competing interests.

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