Proceedings of the 8th International Symposium on Canine and Feline Reproduction
ISCFR

June 22-25, 2016
Paris, France

In a joint meeting with the XIX EVSSAR Congress

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Growth hormone immunoactivity in canine adenomas and adenocarcinomas
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Growth hormone (GH) of pituitary origin is an important global regulator of mammary gland development, as it induces insulin-like growth factor-1 in the mammary stroma and epithelium to stimulate ductal branching [1]. In dogs, GH is also secreted by normal mammary tissue and may induce proliferation of mammary tumor cells [2]. It is now widely accepted in human medicine that GH functions in the mammary gland in an autocrine and paracrine manner as local growth factors in tumor formation [3]. Therefore, the aim of this study was to compare GH immunoactivity in archived canine mammary adenoma and adenocarcinoma submissions to histopathologic grading. We hypothesized that canine mammary adenocarcinomas would be more likely to be GH than canine mammary adenomas. 

Formalin-fixed specimens from spontaneously occurring mammary adenomas and adenocarcinomas from 24 female client-owned dogs were submitted to the Oregon State University Veterinary Diagnostic Laboratory for histopathologic diagnosis. Mammary tumors were histologically classified and morphologically described according to the World Health Organization system. Information pertaining to the reproductive status of the patient at the time of mammary tumor diagnosis was obtained from each of the submitting veterinarians. A canine anterior pituitary was used as a positive control for GH. Tissues were paraffin-embedded, and sectioned (6 µm) onto charged slides. All slides were deparaffinized and rehydrated. Endogenous peroxidase activity was inactivated with 3% H₂O₂ and nonspecific binding was blocked with DAKO serum-free protein block (X0909). Polyclonal rabbit anti-human GH antibody (DAKO A0570) was applied at a 1:200 dilution. A universal rabbit negative control (DAKO) (N1699) was used on pituitary and mammary tissues. Slides were then reacted with DAKO ENV™ with anti-rabbit horseradish peroxidase (K4003) followed by Nova Red Peroxidase substrate (#SK4800, Vector Laboratories). Slides were counter-stained with hematoxylin, dehydrated, and mounted. 

Tumor type and reproductive status at time of tumor diagnosis were compared individually between tumors that were negative or positive for GH using a two-tailed Fisher's exact test. Significance was defined as p < 0.05. Eight of the thirteen submissions with mammary adenocarcinoma were GH positive compared to six of the eleven submissions with mammary adenoma. There was also no significant relationship between tumor type and GH presence. Reproductive status (e.g. ovariohysterectomized versus intact) at the time of tumor removal was compared with GH expression in mammary neoplasia and found to be not significant. The mammary tumor GH immunoactivity in the current study (55%) is lower than that reported by van Garderen and colleagues (1999) (87%). However, in the van Garderen study, two of the GH negative samples were from progesterone-depleted castrated bitches, which led these authors to speculate that progestogens induced biosynthesis of mammary GH [2]. In the current study, nine of the fourteen bitches with GH positive mammary tumors were ovariohysterectomized at the time of diagnosis, meaning that factors other than progestogens contribute to biosynthesis of mammary GH. More research in this area is needed.