c-Kit gene mutations frequency in cutaneous and subcutaneous mast cell tumors in dogs

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Objectives: Mast cell tumors (MCT) are the most common malignant skin neoplasms in dogs, classified into cutaneous (ccMCT) and subcutaneous (scMCT). These tumors exhibit significant variability in their biological behavior, and there is still no consensus on reliable prognostic biomarkers. Mutations in the *c-Kit* gene, particularly in exons 8, 9, and 11, have been identified in MCTs and are considered potential prognostic indicators. This study aims to evaluate the frequency of these mutations in ccMCT and scMCT from a cohort with known clinical outcomes and to assess their prognostic potential.
Material and Methods: Paraffin-embedded samples from 59 tumors (29 ccMCT and 30 scMCT) from 57 dogs, all treated exclusively with surgical excision, were analyzed. Clinical outcome data were available for all dogs two years post-diagnosis. In the ccMCT group, 22 dogs were alive and 5 had died, while in the scMCT group, 20 dogs were alive and 10 had died. DNA was extracted from all samples, followed by conventional PCR to amplify *c-Kit* gene exons 8, 9, and 11. The PCR products were analyzed for mutations through agarose gel electrophoresis and sequencing.
Results: Mutations were identified in 5 ccMCT cases. An Internal Tandem Duplication (ITD) in exon 11 was found in 2 cases, while non-synonymous mutations were identified in exon 8 (2 cases) and exon 9 (3 cases). Two of these cases exhibited mutations in both exons 8 and 9. In the scMCT group, mutations were detected only in 1 dog (3.3%), which was an ITD in exon 11. Overall, non-synonymous mutations in exons 8 and 9 were either insertions or point mutations, with no ITDs observed. All dogs with non-synonymous or ITD mutations survived.
Conclusion: These findings indicate a higher prevalence of mutations in ccMCT compared to scMCT. Mutations in exon 8 identified in this study differed from the commonly reported ITDs. Exon 11 ITD mutations, previously associated with poor prognosis by others, were not linked to a negative outcome in our cohort.

Keywords: *c-Kit gene*, Dog, Exons, Mutations, Prognosis.
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