Scope of comparative oncology in India

Sir/Madam,

Dogs are the most preferable companion animal in biomedical research, and this is mostly due to their anatomical and physiological similarity with humans. Studies on dogs have opened a significant opportunity for translational research. The information obtained from these studies has a positive impact on advancing both human and animal health care. Therefore, in advanced countries aggressive collaborative efforts are being made to harness the benefits of comparative oncology studies. Unfortunately, the Indian cancer research and veterinary science communities have grossly ignored this field. Highlighting these issues the summary of a talk presented at the last Veterinary Pathology Congress, Bhubaneswar, India (November 21-23; 2013) and subsequent discussions are provided here.

Due to incidence of many spontaneous cancers in dogs, it has a long history in cancer research. Additionally, cancers in dogs have many other features which uniquely recapitulate human cancer progression. For example, canines/dogs are the only large mammals other than humans, which commonly suffer from spontaneous prostate cancer. Prostate cancer in dogs has many important similarities with that of prostate cancer in human: (i) spontaneous prostate cancer develops over a long period of time in an intact immunity set up, (ii) individual and intratumor heterogeneity in histology, genetic makeup and phenotypes are observed, (iii) cancer cells are locally invasive and metastasize to distant tissues like bone, (iv) incidence of prostatic intraepithelial neoplasia (PIN) is very commonly found in both the species, and (v) both have similar tumor genetics. Like prostate cancer, different other cancers of dogs (non-Hodgkin lymphoma, melanoma, osteosarcoma, and mammary tumor) have also strong similarities with corresponding human cancers with respect to histology, genetics, mode of progression and response to conventional therapies.

The canine genome sequence has recently been released. Preliminary analysis of the canine genome has shown a strong resemblance between dog and human than humans and rodents in terms of nucleotide divergence and rearrangements. Further, comparative genomic studies have shown substantial homology between diverse cancer-related genes like MET, mTOR, KIT, and IGFR1R both in dog and humans. Many mutations detected in canine cancers are also common in human cancers. Taken together, many clinical and experimental evidences have given the rationale for using dogs for human cancer studies.

Realizing the importance of comparative oncology, in 2003, the National Cancer Institutes’ Center for Cancer Research (CCR), USA has launched the Comparative Oncology Program (COP). The primary goal of this multidisciplinary approach is to use pet animals (mostly dog) for better understanding of human cancer biology and to evaluate the efficacy of novel treatments against different cancers by treating pet animals with spontaneous cancer. The COP has a well-established mechanism of designing and implementing different clinical trials in collaboration with different veterinary institutes of the USA. This program has become instrumental in understanding the environmental risk factors in cancer; examine genetic determinates of spontaneous cancer; evaluate novel therapeutics against cancers; and improve our understanding of cancer biology. Through Comparative Oncology Trials Consortium (COTC) nine clinical trials have already been completed, and two of the agents are currently in phase 1 human study. Currently, COTC is conducting a trial to evaluate proof-of-concept involving personalized medicine. This will help to understand the role of a tumor or a patient’s genetic makeup in the overall effectiveness of a therapy. The fact that the use of dogs as preclinical model will increase in future; on June 20, 2008, a meeting entitled the “Translation of new cancer treatments from canine to human cancer patients” was held and sponsored by the National Cancer Institute in Bethesda, USA. Members from pharmaceutical companies, academia, and regulatory agencies gathered in this forum to discuss the potential opportunity, risk, and outcome of an integrated and comparative drug development path. The summary of this meeting has been very nicely reviewed by Khanna et al., 2009. These kinds of forums have further added clarity on how to conduct and optimize translational studies with dogs. Unfortunately, in India the concept of comparative oncology study is in a very rudimentary stage.

Due to better economic status, nowadays many pet owners in India are interested to adopt improved therapeutics for their pets. However, the clinicians have limited suggestions for the deadly diseases like cancer. In many cases surgery is the only recommendation for solid tumors in dogs. There might be multiple reasons behind this, but the major reasons are: Chemotherapeutics or other anti-cancer treatments are very expensive and/or clinicians are less well informed about different novel recommended anti-cancer therapeutics in pets. Most cancer treatments for dogs are also used in humans. The first FDA-approved anticancer drug for dog is toceranib phosphate (Palladia), and it is very similar to the human drug sunitinib (Sutent). Both the drugs are effective against cancers with KIT oncprotein mutation. Therefore, a collaborative...

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approach like COP in India will not only help in advancing cancer research in India but also help veterinarians in adopting a better line of treatment. In addition, banking of tumor tissues and other bio-specimens through this program will help in the identification of novel diagnostic and therapeutic markers, which will be helpful to all. Importantly, the information obtained from these studies will not only help in the endpoint evaluation of therapeutics but also help in dissecting the molecular mechanisms involved in cancer initiation and/or progression and/or response to therapy.

Regarding the feasibility of a COP in India, most of us might be skeptical. Many obvious limitations that infuse such negative thoughts in our mind includes lack of a collaborative environment in India; lack of funding to support this kind of program; lack of facilities to execute such kind of multi institutional program; and difficulties to get animal ethical committee approval. However, we should not forget that “Rome wasn’t built in a day”. The current facilities in different clinical, academic and research facilities in India were never better than this. Computer and internet facilities in almost all sections have made data recording and sharing very quick and easy. Indeed, the major requirement that has not significantly improved is an environment toward collaborative research or studies. This might be due to lack of personal and/or institutional interest and efforts to address a question that is significant to both animal and human healthcare management. In the aforementioned programs, the veterinary clinicians and pathologists have a very significant contribution. Mostly, the contribution from veterinary pathologist is indispensable for the implementation of such kind of program. Indeed, initiating a multidisciplinary and multi institutional collaborative program might not be feasible for a single person or institute. Therefore, societies like “Indian Association of Veterinary Pathologist” might play a significant role in initiating such kind of efforts, and include members from different fields like research institutes, pharmaceuticals, policy makers, funding agencies, and other regulatory bodies like CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals).

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REFERENCES