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Renal Cell Carcinoma in Humans and Animals: A Brief Literature Review

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Abstract

Renal Cell Carcinoma (RCC) is the most common primary renal neoplasm in humans and domestic animals such as dogs, cats and horses. Various subtypes are recognized in both humans and animals. Advances in biomedical sciences have developed hitherto unprecedented extraordinary cancer therapeutic options varying from sophisticated surgery to immunotherapy and gene therapy. Treatment regimens employed, response to treatments and prognosis vary based on the subtypes of RCC, degree of malignancy, metastasis and stage of the neoplasm. Surgery is the main treatment for most RCCs. Drug resistance has long been a challenge in cancer treatment. New insights in cancer treatment such as molecular targeted therapy including nano-medicine against chemo-resistance are among the contemporary developments targeting cancers. This mini review highlights on the occurrence and significance of RCC in humans and animals, briefly summarizes the various subtypes reported and the treatment regimens executed.

Keywords: Animal; Human; Renal cell carcinoma; Review

Introduction

Malignant neoplasms (cancers) are among the major culprits of health in humans and animals particularly pet dogs in the developed world. About 12.7 million new cancer cases and 7.6 million cancer associated deaths are estimated to occur globally in 2008 [1]. Cancer in general is the second leading cause of mortality next to cardiac diseases in humans in the USA [2]. Neoplastic diseases in humans and dogs are very similar [3]. Malignant neoplasms are also among important diseases in various animals and are the major causes of death in pet dogs. Among domestic animals, canine cancer has become more prevalent in recent years because of increased life expectancy and greater attention to the health of pets [3]. About 58,000 and 13,000 new cases and death, respectively, are estimated in humans due to cancers of kidney and renal pelvis in 2010 [2]. Approximately 1 in 3 dogs (33%) will be diagnosed with cancer during its lifetime, and cancer currently accounts for about 50% of the deaths of all dogs older than 10 years [3].

Different types of treatment approaches have been instituted to cancer patients in humans and animals. Advances in science and medicine have developed hitherto unprecedented therapeutic approaches varying from surgery to immunotherapy and gene therapy. However, due to various forms of cancer with divers underlying genetic, environmental and other factors including chemo-resistance, cancer is still among the major causes of morbidity and mortality in humans and pet dogs in the developed world. In fact, the range of cancers observed in dogs is suggested to be as diverse as that reported in human patients, and despite more intensive therapeutic interventions, fatality rates remain unacceptably high in both species [3]. This brief review highlights on the occurrence and significance of renal cancers in humans as well as animals, summarizes the various types reported and the treatment regimens executed.

Renal Cell Carcinoma in Animals and Humans

Renal cell carcinoma in humans

The global incidence of Renal Cell Carcinoma (RCC) in humans varies substantially [4] and renal cancer is the fourteenth most common cancer worldwide, with an estimated 273,500 new cases diagnosed in 2008 [1]. The incidence is generally high in Europe and North America and low in Asia and South America [4]. Renal Cell Carcinoma (RCC) is the six most common renal neoplasm in humans in the USA [2,5,6] and accounts for about 2-3% of adult malignancies and 90% of renal cancers. The overall lifetime risk of developing the neoplasm in adults is about 1.6% [5,7]. The disease mostly occurs sporadically and the risk is higher in men than in women [5]. It is a heterogeneous disease comprised of different histological variants that show distinct clinical course, genetics and response to systemic treatment [6]. In the USA, over 50,000 new cases were diagnosed in 2010, and approximately 13,000 deaths were related to RCC [2]. These statistics include both renal cell carcinomas and transitional cell carcinomas of the renal pelvis. Renal cancer is very uncommon in people younger than age 45. Most often, it affects elders 55 years and older with an average age at diagnosis being 64[5].

Renal cell carcinoma in animals

The incidence of primary renal neoplasm in animals is quite low [8] as compared to humans. Among renal neoplasms, RCC is uncommon aggressive tumor in domestic animals [9,10]. However, it is the most common primary malignant renal neoplasm in dogs, horses, and cattle. There are sporadic reports on its occurrence in cats, sheep and pigs [8,9,11-13].

Primary malignant renal neoplasms (except Nephroblastoma) are most commonly observed in mature middle-aged to older animals [10,13,14], which apparently are at higher risk [15]. Nephroblastoma, which is morphologically identical to Wilms' tumor in children, is almost always a benign tumor in animals and is encountered in young pigs, puppies and calves [11]. Thus, owing to its middle- to old-age associated occurrence the incidence of RCC is relatively low in some species. Due to increased life expectancy, the incidence is higher in pet dogs than in any other animal species. The average age of affected dogs is approximately 8 years although the tumor has been reported in dogs less than two years of age. It is relatively common in male than female dogs. This is in contrast to the overwhelming higher occurrence in cows, likely because of a preponderance of females in the aged cattle population [13].

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In humans, RCC appears to be more observed in Europe and North America with relatively higher risk in African Americans [4,5]. There is no obvious breed predisposition to renal neoplasms in dogs [15,16] except for heritable predilection for bilateral, multifocal cystoadenocarcinomas in German Shepherds, generally between 5-11 years of age [14,17,18].

In both humans and dogs, males [5,13,15] appear to be more susceptible than females, indicating a possible role of androgens in the development or maintenance of the tumors [15]. Male dogs and men are affected about twice as often as bitches and women, respectively [13,19]. However, currently detailed studies and scientific evidence are lacking to determine the role of androgen in the initiation and development of RCC in male canines. Other risk factors are not described for RCC in animals.

Renal cell tumors are rare in other species and sporadic cases of RCC are reported in various animal species including a greater kudu (*Tragelaphus strepsiceros*), an Owl Monkey (*Aotus trivirgatus*), Sinai desert cobra (*Walterinnesia aegyptia*), Cape coral snakes (*Aspidelaps lubricus lubricus),* reticulated python, camel, boa constrictor, and laboratory rabbit [8,20-26]. Various types of renal neoplasms of tubular epithelial origin including RCC are reported in non-human primates [27], and captive coypus [28].

RCC is reported to occur as spontaneous as well as experimental disease in mice and rats [29-33] and as inherited genetic disease in Wistar rats [34]. Various renal tubular tumors including RCC are reported and described as familial in laboratory rat, Long-Evans derived Eker rats and the Nihon rat [35-40]. Furthermore, familial renal cell tumors are also suspected in F344 and Sprague-Dawley rats [41-43]. RCC is also reported in association with specific virus infections in frogs [44], chicken [45] and squirrels [46].

Classification (subtypes) of Renal Cell Carcinomas (RCCs)

Classification of RCC in humans

Renal epithelial neoplasms in humans are classified according to their histopathologic and molecular biologic characteristics [47,48]. Malignant renal cell tumors according to the 2004 WHO classification include: Clear cell RCC, multilocular clear cell RCC, papillary RCC, chromophobe RCC, carcinoma of the collecting ducts of Bellini, renal medullary carcinoma, Xp11 translocation carcinomas, carcinoma associated with neuroblastoma, mucinous tubular, granular, spindle cell, cyst-associated and RCC-unclassified [48-51]. This classification is based on current genetic knowledge, correlates with recognizable histological findings, and is applicable to routine diagnostic procedures and clinical management of the patient [48-50]. The clear cell histologic subtype is by far the most common RCC, comprising 75% -80 % of all cases [48,52]. Other less common subtypes include papillary RCC, unclassified RCC, chromophobe RCC, and collecting duct RCC, representing 10%, 4-6%, 5% and 1% of all RCCs, respectively [48]. Among renal tumors, Collecting Duct Carcinoma (CDC) is the most aggressive subtype [53].

A subset of RCC mainly affecting children and young adults has been designated as RCC associated with Xp11.2 translocations/*TFE3* gene fusions (Xp11.2 RCC) [54-57]. A variant of renal neoplasm, sarcomatoid RCC, previously believed to represent a primary renal sarcoma, is now considered a form of dedifferentiated carcinoma and not a distinct histologic entity. It is defined as any subtype containing foci of pleomorphic spindle cells and is observed at the end-stages of disease progression in high grade RCCs. Sarcomatoid differentiation is an uncommon finding reported to occur in approximately 1-8% of RCCs [58], and constitutes only 1.5% of primary renal tumors in general [59-61]. The chromophobe subtype is most frequently associated with a sarcomatoid component [62]. When present, sarcomatoid RCC is indicative of an aggressive tumor as demonstrated by rapid growth and poor prognosis [63]. Other type of renal carcinoma, Transitional Cell Carcinomas (TCC) also known as urothelial carcinoma, which originates from renal pelvis accounts for 5-10% of renal cancers [5].

Classification of RCC in animals

Several types of primary renal neoplasms have been reported in animals. Renal neoplasms usually are grouped according to the cell of origin into epithelial tumors of the renal parenchyma, epithelial tumors of the renal pelvis, nephroblastic tumors and mesenchymal tumors [16]. RCC is the most common histologic type of neoplasm in the kidney.

Spontaneous RCCs are relatively common and more studied in pet dogs than in any other animal species. In animals, RCCs are classified into several subtypes, based on their histologic (papillary, tubular, and solid type) and cytologic (chromophobic, eosinophilic, and clear cell type) patterns [64]. Other names such as malignant nephroma, hypernephroma and Grawitz tumor [9,10] were also used to denote malignant renal tumors. Although these tumors are subdivided into histological and cytological types, there is no known difference in their biological behavior, which remains to be elucidated [64]. Tubular RCC is the most common variant observed in domestic animals [61]. Nielsen et al. [11] reported that RCC is usually papillary in the dog. Clear cell variants are reported more frequently in laboratory animals and humans but are rarely observed in cattle and dogs as the predominant types [65]. Other rare variants such as sarcomatoid RCC in dogs [15] as well as cats [66,67] and canine renal neoplasm with morphologic, histochemical, and immunohistochemical characteristics consistent with human Collecting Duct Carcinoma (CDC) [68] were described. The oncocytic form of renal carcinoma has been reported infrequently in rats and dogs [13]. Generally, the neoplastic cells in renal carcinomas varied greatly in form and structure both among different tumors and within the same tumor [16].

Malignancy and Metastasis

Determination of a primary renal versus metastatic neoplasm and benign versus malignant can be challenging. Renal carcinomas in animals invariably arise in the cortex and lesions observed in the medulla favor a metastatic tumor. Foci of clear cells are consistent with renal origin [65]. It is difficult to decide if a small tumor is benign or malignant [16,69]. Classification by histological or cytological subtype is not predictive of biological behavior in domestic animals [65]. In dogs, variations of cellular and histological morphology seem to be acceptable predictors of malignancy. A high mitotic index, necrosis, invasion, and cellular atypia are characteristics of carcinoma, but metastasis from well-differentiated tumors occurs. Therefore, differentiation between well differentiated carcinomas and adenomas need to be proven since the two can make clear distinction difficult. In most cases, by the time renal tumors are clinically detectable in dogs, cats and horses, the tumor is advanced and malignant [16,69]. If a renal tumor metastasizes to the opposite kidney, there are invariably metastases in other organs [65].

Ninety percent (90%) of canine renal epithelial tumors are classified as malignant and metastases are detected in 50-60% of the

cases [69]. Although 90% of the epithelial neoplasms are classified as malignant based on light microscopy or gross size greater than 2 cm, this distinction is arbitrary and may have led to overclassification of carcinomas. Multiplicity of primary renal cell tumors is a feature in dogs, cattle and humans. It occurs in 33% of canine and 95% of bovine cases. In dogs, metastases occur much more frequently than is reported in cattle with renal cell tumors [65].

Rarely, RCC infiltrate through the retroperitoneal space and spread by implantation metastasis through the abdomen [65]. In dogs, it shows a marked propensity for vascular invasion, penetration of posterior vena cava, and subsequent pulmonary metastasis [11]. Metastatic disease can be detected with thoracic radiographs in approximately 50% of dogs with renal carcinomas at initial presentation. Generally, renal carcinomas metastasize early to various organs; and the opposite kidney, lungs, liver, and adrenals are involved most commonly [14]. In dogs, the most likely metastases sites are lungs, regional lymph node, liver, serosal surfaces, ipsilateral adrenal gland, but occasionally also to the brain, and skin [13,16,65,69].

The rate of metastasis in RCC is variable in other species of animals in which the neoplasm is reported. In cattle, metastasis rates are much lower than is reported in canine RCC [12,65], but multiplicity of primary RCC with bilateral renal involvement explained by multiple de novo development and less by intrarenal metastasis, is common [13]. Renal cell tumors are considered malignant in horses and cats; however, unlike in dogs, relatively few cases have been studied [65]. Metastases are common in horses and are widely disseminated often to the lungs and liver [70,71]. There is a report of clear cell renal carcinoma in a horse manifesting initially as an aggressive metastatic oral tumor [13]. Renal carcinomas are rarely diagnosed in cats, but typically occur unilaterally, in older cats, with no sex or breed predilection and with only sporadic metastases. Bilateral de novo development has also been documented [13]. In nonhuman primates, few RCCs have shown evidence of metastasis [27] as is in cattle which exhibit low rate of metastasis [12].

A high rate of metastasis from RCCs has been documented in humans similar as in dogs [19,65,72]. In humans, RCC has a great propensity for metastasis with 30% of patients already showing metastasis at the time of diagnosis. Metastatic RCC is a highly fatal disease, and clear cell RCC (ccRCC) accounts for most cases of metastatic disease [19]. Approximately, 10-28% of RCC develop a local recurrence or distant metastasis after curative nephrectomy [72].

Clinical Signs

Clinical signs are variable depending on the extent of renal involvement and parenchymal tissue damage. It may reflect the functional derangement of other tissues and organs to which RCC metastasized in cases of metastatic RCC.

In humans, unlike a decade ago, now it is known that RCC is not a single disease. As acknowledged by the 2004 WHO classification of adult kidney tumors, biological and clinical properties define a number of entities whose recognition is of value in daily clinical practice. Different subtypes have different clinical outcomes and show different response to therapy [48]. Some of the neoplastic masses are clinically observed only after enlargement to a noticeable size, but most are found before metastasis to distant organs occurs. Often they are detected on CT scans or ultrasounds done for other diseases than renal cancer [5]. An early stage renal cancer usually has no symptoms. Symptoms that may develop as the tumor progresses include blood in the urine, a pain or lump in the lower back or abdomen, fatigue, weight loss, fever, or swelling in the legs and ankles [5,7]. The aggressive behavior of sarcomatoid RCC results in nonspecific symptoms in 89% of patients, most commonly pain [73].

In nonhuman primates, anorexia, lethargy, weight loss, depression, and dehydration are the most frequent clinical signs associated with renal neoplasms including RCC [27]. Dogs with malignant neoplasms are typically presented with a history of a palpable abdominal mass, weight loss and occasional hematuria [13,74], similar to the classical triad of hematuria, palpable mass and abdominal pain reported in humans [74]. Clinically, hematuria is the most common symptom of canine renal tumors and has been observed in 32% of the cases [75]. Polycythemia associated with excessive erythropoietin production is very rare in animals; but paraneoplastic erythrocytosis occurs in 1-5% of humans with renal adenocarcinoma. Polycythemia typically resolves after removal of the tumor. Hypertrophic osteopathy may be present in cases of canine renal carcinoma with pulmonary metastases. Disseminated intravascular coagulation, extreme neutrophilic leukocytosis, leukemoid blood response and bone infarcts are additional rare canine renal adenocarcinoma-associated paraneoplastic syndromes [13]. In ruminants, the tumors are usually asymptomatic, or at least undetected antemortem. Several authors indicated that horses may be asymptomatic or may be presented with colic, weight loss, hematuria, ascites, hemoperitoneum and edema [65].

Risk Factors Associated with RCC

Generally, it is recognized that cancer is a genetic disease and genomic cellular damage underlies virtually all neoplasms, despite the fact that neoplasms arise in a broad variety of tissues and that diverse agents such as viruses, mutagenic chemicals and radiation induce their growth [76]. Several risk factors are associated with RCC in humans. Smoking or tobacco use is among strong risk factors for renal cancer, with the largest increased risk for cancer of the renal pelvis, particularly for heavy smokers. Additional risk factors for RCC include obesity [5,52], to which an estimated 20- 30% of cases can be attributed [5]. High blood pressure, chronic renal failure, occupational exposure to certain substances such as asbestos, cadmium, some herbicides, benzene, organic solvents, trichloroethylene, chemical additive and analgesic abuse have also been implicated in the etiology of RCC [5,7,52].

Genetic or familial predisposition to renal cancers is observed in some individuals. A small proportion of RCCs are associated with rare hereditary conditions [5]. Several inherited disorders including hereditary papillary renal cancer, hereditary leiomyoma-renal cell carcinoma syndrome, Von Hippel–Lindau (VHL) disease, and Birt–Hogg–Dubé syndrome predispose to a higher risk of developing RCC [5,52]. Patients with familial renal cancer due to defects in the genes SDHB and SDHD, succinate dehydrogenase subunit B and D, respectively, tend to develop renal cancer in both kidneys before age 40. Other risk factors suggested to be associated with renal cancer include family history of kidney cancer, certain medicines such as Phenacetin, advanced other kidney disease, as well as gender and race with respective increased tendency in men and African Americans in the USA [5].

Risk factors for RCC in animals are not definitely known, except an apparent age predisposition and increased incidence in male subjects. Apparently some animals are genetically predisposed to certain neoplasms. Renal neoplasm is reported to be an inherited genetic disease in various species of rats [35-43]. Hereditary renal cystadenocarcinoma is reported in German shepherd dogs [17]. However, from experiences

in human medicine and similarities of neoplastic diseases in humans and dogs [3], it would be plausible to consider that exposure to various chemical carcinogens and obesity may play some role in the incidence of cancer in pet dogs.

Treatment

Several subtypes of RCC with various biological behaviors, degrees of malignancy, metastasis and invasion are recognized in both humans and animals. Therefore, response to treatment is protean depending on the nature of a specific neoplasm. Each subtype of renal tumor thus requires a specific therapeutic regimen [77]. Determining the subtype of RCC can be a factor in deciding treatment of choices and would also help to rule out if specific cancer is associated with an inherited genetic syndrome. Like most cancers, RCC is difficult to treat and rarely cured once it has metastasized; and current therapies have limited efficacy. Various approaches and options for treatment of RCC include: surgery, ablation and other local therapies, radiation therapy, molecular targeted therapy, immunotherapy (biologic therapy), and chemotherapy. The stage of renal cancer and the general health status of the patient determine the treatment of choice [5].

Renal cancer tends to be resistant to both traditional chemotherapy and radiation therapy**.** Traditional or laparoscopic surgery is the main treatment for most RCC. The chances of surviving a renal cell cancer without surgery are small [5]. Many cases of RCC have been successfully treated by surgical resection at the early stages of the disease; this has been facilitated by advances in radiologic imaging [78]. Patients that are not surgical candidates may be subjected to ablation therapy [5]. Despite the emergence of molecular targeted systemic therapy for metastatic RCC, cure is uncommonly achieved in the absence of surgical resection. A proportion of patients with RCC will achieve long-term survival with aggressive surgical resection [79]. Radiation therapy can be used if the general health status of the patient is unsuitable for surgical intervention. However, because kidney cancers are not very sensitive to radiation, radiation therapy is more often used to palliate, or ease cancer associated symptoms such as pain, bleeding, or other symptoms consequent to metastasis especially to the bones or brain [5].

Various drugs (chemotherapy) and biologic therapy (immunotherapy) using proteins such as cytokines are used to treat and manage different subtypes of renal and other cancers [5]. Among cytokines, treatments with interferon-α (IFN-α) and interleukin-2 (IL-2) have shown poor response rates (<15%), with only reasonable improvement in overall survival [80]. Unfortunately, renal cancer cells are usually resistant to chemotherapy, and hence chemotherapy is not a standard treatment for kidney cancer. Some drugs, such as vinblastine, floxuridine, 5-fluorouracil (5-FU), capecitabine, and gemcitabine have been shown to help a small number of patients [5]. The Food and Drug Administration of the USA (FDA) has approved seven new drugs over the past few years, heralding the unprecedented drug development now being undertaken for the management of RCC. Axitinib is the most recent drug to have received FDA approval and is indicated for the treatment of advanced RCC after failure of one prior systemic therapy [52]. Notwithstanding significant advances in RCC-therapeutics in the past decade, no standard treatment has been identified for advanced chromophobe RCC [6]. An effective therapy has also not been established for human Collecting Duct Carcinoma CDC [65], which is known to have an unfavorable prognosis due to high frequency of postoperative recurrences and distant metastases [78]. Multimodal therapy including surgery should be considered for patients with metastatic RCC [79].

The range of cancers in dogs is as diverse as that in human patients, and irrespective of more intensive therapeutic interventions, fatality rates remain unacceptably high in both species [3]. Development of improved strategies for the diagnosis and treatment of sporadic cancers in animals such as dogs and cats presents the same fundamental problem as for humans: target selection, drug delivery and relapse or resistance. In spite of significant clinical advances over the past decade, numerous challenges remain in treating cancer in veterinary patients [81]. In animals, treatment of all renal neoplasms except lymphosarcoma involves surgical removal; unilateral nephrectomy is usually required [13,14]. Various chemotherapeutic interventions have been implemented in the control of canine cancers. Commonly, many conventional anticancer drugs used to treat human cancers such as doxorubicin are also used to treat animal patients [81]. However, chemotherapy is generally ineffective against renal tumors in animals [14] and chemo-resistance remains a challenge in cancer therapy. Improvements in detecting the molecular mechanisms of neoplasia have provided the means to develop more effective therapies. Recently, newer therapeutic approaches, such as the use of tyrosine kinase inhibitors and melanoma vaccination, for molecular targeting of canine and feline cancers, are brought forward. Generally, molecular targeted treatments of cancer have resulted in markedly improved response rates in some tumors [81].

New concepts which involve contribution of Cancer Stem Cells (CSCs) for chemo-resistance are proposed [82]. Cancer is becoming more recognized as a heterogeneous disease with hierarchies of cellular populations that demonstrate a range of differentiation phenotypes. The majority of cells in bulk tumors may be non-tumorigenic end-cells, and only a small subpopulation of cells (cancer stem cells) within tumors is responsible for tumor initiation, growth, and recurrence [82-84]. Cancer Stem Cells (CSCs) are more resistant to treatment than bulk cells and the CSC-hypothesis suggests that the therapeutic resistance of CSCs in tumors might underlie tumor chemo-resistance. Because CSCs in the same type of tumor are phenotypically and functionally heterogeneous and CSCs are protected by multiple resistance mechanisms that make them less susceptible to conventional therapies, Nanoparticle-based drugs have the potential to enhance treatments by overcoming chemo-resistance or targeting CSCs. Nano-medicine offers an innovative approach to reverse chemo-resistance by targeting CSCs. Nano-scale drug-delivery systems transport therapeutically active molecules, prolong circulation, improve bio-distribution in the body, and may allow more effective and specific therapies to address the challenges posed by CSCs [82].

Prognosis of patients with RCC varies with the specific subtype and degree of metastasis. The presence of sarcomatoid differentiation in a patient with RCC portends a much worse prognosis than those without it [63]. Surgical management has been the mainstay of treatment for RCC but does not improve the prognosis in those with sarcomatoid differentiation. This has prompted the use of chemotherapy in combination with nephrectomy resulting in promise in prolonging survival [85]. DNA or RNA genomic signature differences have recently been exploited to personalize medicine and chemo-resistant CSCs, facilitating individual-specific nano-medicine and dose selection for better cancer treatment efficacy and prognoses [82].

Prevention

Various environmental factors, exposure to chemical and physical agents, life style, nutrition, infections as well as genetic predisposition in some animals and humans are reported to be risk factors associated with cancer in general. It is difficult to incriminate or definitely associate

a specific cause to a given spontaneous cancer and thus propose specific preventive measure in most cases. However, various options have been suggested and implemented to avoid or minimize the occurrence of cancer. Avoiding or reducing cigarette smoking, controlling high blood pressure, regular exercise to maintain a healthy weight, and avoiding exposure to potential carcinogens may reduce the risk of developing cancer [5].

Dietary components are considered very important in carcinogenesis [3]. A number of dietary phytochemicals found in plant products such as fruits, vegetables, beverages, herbs, and spices, are reported to inhibit tumorigenesis in experimental animals and/or exhibit potent biologic properties [86]. Eepidemiologic studies show that human populations consuming foods rich in specific phytochemicals have lowered incidence of cancer, heart disease, and osteoporosis. Veterinary research addressing anticancer effects of dietary compounds in domestic animals is scarce. A few reports indicate that flavonoids may have impact on arrest of cell growth in canine cancer cell lines. However, these lack the mechanistic and clinical studies for broad use [3].

Cancer chemoprevention that may prevent, arrest, or reverse either the initiation phase of carcinogenesis or the progression of neoplastic cells to malignancy is an important means of confronting cancer. It is widely used and readily accepted as a strategy to minimize the risk for cancer. Currently, effective chemopreventive agents studied and used in humans include Non-Steroidal Anti-Inflammatory Ddrugs (NSAIDs), Peroxisome Proliferator-Activated Receptor-c (PPARc) ligands, and dietary compounds. Chemo-preventive agents, either alone or in combination with each other, can delay processes leading to invasive cancer. Carprofen, piroxicam, and meloxicam are the most common NSAIDs prescribed in dogs [3]. Tumor vaccination holds great promise for the treatment of cancer. The veterinary melanoma vaccine (Oncept™) and Provenge® for the treatment of prostate cancer in men established tumor vaccination as a valid treatment modality for cancer. Although the results with vaccines in general are promising, there are still some hurdles to overcome [87].

Conclusion

Cancer has been incriminated as a cause of disease in humans and animals since prehistoric times and is currently among the major causes of death in humans and pet dogs. Various types of cancers including RCC are identified and different types of treatment methods have been implemented to treat and manage cancer. However, there are protean responses to the different methods of treatment executed based on the type of cancer, degree of malignancy and metastasis. Chemo-resistance remained a challenge to cancer therapy. New insights in cancer treatment such as molecular target therapy including nano-medicine against chemo-resistance are among the contemporary developments targeting cancers. However, due to incessant genetic changes and mutations underlying initiation and development of cancers, undoubtedly a lot has to be done in the future to further prevent, treat and control cancers in both humans and animals.

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