CANINE CANCER CHEMOTHERAPY – AN OVERVIEW

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The shift of 'pets' to 'companions' increases the life span of canines and thereby chances of diseases like cancer. Cancer is an abnormal growth of cells which tend to proliferate in an uncontrolled way; and in some cases show metastasis destroying healthy tissues. It is a leading cause of death in dogs and cats. Dogs develop cancer twice as frequently as humans, but cats only half as frequently. The signs of cancer range from an abnormal swelling that persists or continues to grow, a sore that does not heal, weight less, bleeding or discharge from any body opening, reluctance to exercise, a loss of stamina or difficulty in breathing, urination or defecation.

Benign tumours have many common characteristics. They do not spread or invade organs. They compress nearby body organs due to their size. Surgical removal is curative. Malignant tumours show rapid irregular growth. These tumours can invade normal, local tissues as well as spread to other tissues. Remission denotes a decrease in tumour size over a period of time. Remission time is the duration of time in which the tumour is under control. The treatment of cancer in animals can often result in fairly long remission times.

Diagnosis can be done by biopsy, imaging techniques, and CT scans. Biopsy is the surgical removal of a small piece of tissue and its examination under microscope. An aspiration can also be made by a needle attached to the syringe for microscopic analysis. Tumours are assigned to high, intermediate and low grades based on microscopic evaluation, radiography using positive or negative contrast (iodinated agents), ultrasound, X-ray, Computed Tomography (CT), Magnetic Resonance Imaging (MRI) and Nuclear Scintigraphy. A CT scan or an MRI may elucidate a brain tumour that would not be apparent on skull radiographs.

Breed susceptibility

The incidence and type of tumour is related to breed and probably controlled by single or multiple genes. Specific tumours with high breed risks are

- Benign mammary tumour- Basset Hound, Poodle, York Shire Terrier, Chihuahua, Maltese
- 2) Malignant mammary tumour- English Setter, Chihuahua, Poodle, Afghan Hound
- Multiple dermal fibroma, Renal cystadenocarcinoma, Uterine leiomyoma-German shepherd
- 4) Trichoepithelioma-Basset Hound
- 5) Pilomaticoma- Kerry Blue Terrier
- 6) Anal sac gland carcinoma- English Cocker Spaniel
- 7) Subungual squamous cell carcinoma: Giant Schnauzer and Gordon Setter
- 8) Subungual malignant melanoma: Scottish Terrier
- 9) Melanocytoma: Vizsla and Miniature Schnauzer
- 10) Liposarcoma: Shetland sheepdog
- 11) Mast cell tumor: Boxer and Pug
- 12) Cutaneous plasmacytoma: Cocker Spaniel

Cancer – the Line of Treatment

There are three ways to treat cancer-surgery, radiography and chemotherapy

Surgery: Surgical removal of tumor is a very common and valuable approach for solid tissue tumors. It can be used for soft tissue as well as for bone tumors.

Radiotherapy: Radiation therapy consists of the use of a radioactive beam to damage and/or kill malignant cells in a localized area. It can offer good

quality remission times for many types of tumors, but usually do not give a complete cure. Animals are surprisingly tolerant to radiation therapy

Chemotherapy: It is the use of certain drugs alone, or in combination with surgery/ radiotherapy, to control tumour growth. All the drugs currently given to animals are human anti-cancer drugs. Fortunately, many of the negative consequences of their use in human medicine are not experienced in veterinary medicine. Chemotherapy and/or surgery are the two most important treatment modalities in veterinary cancer medicine. A combination of therapies may also be indicated in certain cancers.

Combination therapy in animals

The decision to use antineoplastic chemotherapy in animals depends on several factors such as type of tumour, stage of malignancy, condition of animal and financial constraints. Chemotherapy is generally used as an adjunct to surgery or irradiation. In most of the cases neoplastic burden is initially reduced either by surgery or irradiation followed by chemotherapy. In many cases chemotherapy may also be used as primary treatment especially when neoplasms are disseminated and not amenable to surgery or irradiation. Due to low therapeutic index of antineoplastic drugs, the protocols of various combination dosages in veterinary medicine are generally designed to cause minimal toxicity to patients and are calculated based on body surface area rather than body mass.

Surtace area in square meters = Body weight ^{0.67} x K/10⁴, when body weight is given in grams. For dogs and cats K is constant with value of 10.0 and 10.1 respectively

The Scope Of Chemotherapy

Chemotherapy is the name given to cancer treatment using cytotoxic chemical agents. Cytotoxic agents kill cells. Unfortunately it kills all cells, both cancer and healthy cells. However, the particular chemicals chosen tend to be more toxic to cancer cells than they are to normal cells. The duration of chemotherapy depends on the type of cancer and the extent of disease. Some animals need chemotherapy for the rest of their lives. In others, treatment may be spread out or discontinued after a period of weeks to months provided there is remission. The drugs of this group is classified under 3

Type of Tumor	Type of Tumor	
Lymphoma	Chemotherapy (several drugs available)	
Mast Cell Tumors	Chemotherapy, Surgery (+/-radiation)	
Fibrosarcomas	Chemotherapy, Surgery (+/-radiation)	
Oral Cancers	Surgical, with reconstruction	
Mammary Tumors	Surgical (+/-chemotherapy follow-up)	
Osteosarcomas (bone)	Surgical + chemotherapy follow-up	
Hemangiosarcomas	Surgical + chemotherapy	
Skin Tumors	Surgical +/- chemotherapy, radiation	
Transitional Cell Carcinomas	Surgical + chemotherapy	
Undifferentiated Sarcomas	Surgical +/-chemotherapy, radiation	

TABLE.I. SELECTION OF THERAPY

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TABLE II: DRUG ACTIONS AND USE

Drug	Mechanism of action	Dose
Mechlorethamine	Alkylation of DNA inhibits	Dogs-5mg/m ² IV
	translation and transcription	bogo olingilii 1V
Cyclophosphamide	- do -	Dogs and cats:50m g/m ²
		PO on alternate days
		1 0 on allemate days
		$100, 200 \text{ m s/m}^2$ $10/2$ m s/m
Melnhalan	- do -	Deep and estave tracility
		bogs and cats.o. mig/kg
Chlorambucil		Po daily for 7 days
	- 00 -	Dogs and cats:2-5mg/m
Ruculabaa		PO for 1-2 days
busuphan	Cell cycle phase non specific	Dogs and cats:3-4mg/m*
	arkylation agent	
		Once daily
		2
I THO TEPA	Cytotoxic agent	Dogs and cats:9mg/m*
		Single dose
Loniustine	- 00 -	Dogs and cats:60mg/m1
		PO Once in 7weeks
Carmustine	- do -	Dogs and cats:50mg/m ²
	· · · · · · · · · · · · · · · · · · ·	IV Once in 6 weeks
Decarbazine	- do -	Dogs and cats:200-
		250mg/m²
		IV Once daily for 5days
Methotrexate	Stimulate folic acid, inhibit	Dogs and cats:2-5mg/m ²
	UNA and RNA synthesis	
		PO or IV Once daily
6-mercaptopurine	Stimulate purine, inhibit cell	Dogs and cats:150-
	division	200mg/m IV every 7 days
5-flurouracil	Cell cycle phase non-	Dogs and cats: 75-100mg/m ²
Culture bin a	specific cytotoxic agent	IV daily for 2 days
Cytarabine	Cell cycle phase specific	Dogs and cats: 0.5-0.75
		mg/m*IV every week
	with action on S phase	
Vinceinting		· · · · · · · · · · · · · · · · · · ·
vincestine	Block mitosis in metaphase	Dogs and cats: 2-2.5mg/m ²
Viphlostins		IV every week (For all vinca)
Viii blastine	- do -	- do -
Dactinom yem	intercalate between GC pair	Dogs and cats: 0.5mg/m²
Deverybiein		1
Doxorubicin	Intercalation of DNA and	Dogs and cats: 30 mg/m ²
Diservirie	Generation of free radicles	IV every 3 weeks
BIBOMYCIN	Oxidative damage to	Dogs and cats:10-20 unit/m ²
	deoxyribose	IV every week
L-asparaginase	G phase specific drug	Dogs and cats: 10000-20000
0		unit/m ² IV,SC,IM every week
Cispiastin	Binds to Guanine of DNA	Dogs and cats:60-70 mg/m ²
		IV for 20 minutes every 3
		week

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CANINE CANCER CHEMOTHERAPY AN OVERVIEW
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JABLE III: TRADE PREPARATIONS AVAILABLE IN INDIA

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Drug	Trade preparations	
Cyclophosphamide	Cyclophosphamide Inj. (500mg), Cyphos Inj (1g,	
	200mg, 500mg), eldamide (50mg, 100mg, 200mg,	
	500mg), oncophos (1g, 200mg, 500mg)	
Dactinomycin	Casmegen vial (500mcg), Dacmozen Inj (0.5mg)	
Daunorubicin	Daunocin Inj (20mg), Daunomycin (20mg), Daunocide	
	(20mg)	
Chlorambucil	Leukeran Tab (2mg, 5mg)	
Cisplastin	Blastolem Inj (10mg, 50mg), Cisplan Inj (10mg, 5mg)	
	Cisteen Inj (10mg, 50mg)	
Busulphan	Busulphan Tab (2mg), Mylephan (2mg), Myleran Tab	
	(2mg)	
Bleomycin	Bledmax Inj. (15mg), Bleocin Inj (15mg), Bleocip Inj	
	(15mg)	
Asparaginase	Leucoginase Inj (5000 IU), Oncoginase (6000 IU)	
Cytatarbine	Arasid Inj (1g, 100 mg, 500mg), Cytabin Inj (100mg,	
	500mg,1000mg)	
Doxorubicin	Adrim Inj (2mg), Adrosal Inj (10mg), Cadria Inj (10mg),	
	Doxolem Inj (10mg), Oncodox Inj (10mg)	
Etoposide	5FU-CBC (250mg, 500mg), Fivocil (250mg, 500mg),	
	Florac (50 mg)	
Flurouracil	FU-CBC (250mg, 500mg), Fivocil (250mg, 500mg),	
	Florac (50 mg)	
Interferon alpha	Alferon Inj (3MIU), Intalfa Inj (3MIU, 5MIU)	
Lomustine	Lomtil Cap (40 mg), Lomustine (40mg)	
Vinblastine	Cytoblastin !nj 10 mg, Vblastin (10mg)	
Vincristine	Alcrsit (1mg vial), Cytocristin (1mg), VCR Inj (1mg/ml)	

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headings - Cytotoxic drugs, Immunosuppressants and Sex hormones

A. Cytotoxic drugs

- Alkylating agents
 - a) Nitrogen mustards eg: Mechlorethamine, Cyclophosphamide, Melphalan, Chlorambucil and Efusfmide
 - b) Alkyl sulphonates eg: Busulphan
 - c) Ethylenemines and methylmelamines eg: Thio TEPA and Hexamethylmelamine
 - d) Nitrosoureas eg: Lomustine, Carmustine, Semustine and Streptozocine
 - e) Triazenes eg: Decarbazine and Temozolamide
- 2). Antimetabolites
 - a) Folic acid analogres eg: Methotrexate
 - b) Purine analogues eg: 6-mercaptopurine, Azathioprine, fludarabine
 - c) Pyrimidine analogues eg: 5-flurouracil, Floxuridine, Cytarabine and Gemcitabine
- 3) Mitotic inhibitors
 - a) Vinca alkaloids eg: Vincristine and Vinblastine
 - b) Taxanes eg: Paclitaxel and Docetaxel
- 4) Antitumour antibiotics
 - a) Actinomycins eg: Dactinomycin
 - b) Anthracycline antibiotics eg: Doxorubicin, Epirubicin, Idarubicin, Daunorubicin
 - c) Other antibiotics eg: Bleomycin, Mitoxanthrone, Mitomycine and Mithramycine
- 5) Epipodophyllotoxins eg: Etoposide and Tenioposide
- 6) Enzymes eg: L-asparaginase and Pegapargase
- Miscellaneous eg: Cisplastin, Carboplastin, Hydroxyurea, Procarbazine, Mitotane, Aminoglutethamide

B. Immunomodulators

eg: Corticosteroids, Azathioprine and Interferons

C. Sex hormones and its antagonists

eg: Oestrogens, Antioestrogens (Tamoxyfen), Androgens, Antiandrogens (Flutemide), Progestogens and GnRH analogues. The dose rates are given in Table II.

Trade Preparations

Mainly drugs like immunosuppressants and anti sex hormones are available in the veterinary field. Other preparations are given in Table III Side Effects

Compared to people who receive chemotherapy, animals experience fewer side effects because of the lower dose of drugs and less use of combination therapy. The tissues that are typically more sensitive to chemotherapy are the intestinal lining, bone marrow and hair follicles. Toxic effects are responsible for decreased apetite, vomiting and diarrhea. Suppression of the bone marrow by chemotherapeutic agents may cause a drop in white blood count, red blood cell count etc. So there shouid be a regular check for these parameters. Hair follicle in dogs that are wire haired and non-shedding may be particularly susceptible to chemotherapy, however the hair re-grows once chemotherapy is

A dog with cancer requires adequate water, calories, proteins, vitamins and minerals as a supportive measure. In many cases we are unable to cure veterinary cancer patients. Our goal is therefore to improve the quality of life of pets.

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