

Gold Nanorods Assisted With Near Infrared Laser Irradiation in Treatment of Breast Cancers in Pet Animals

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Mammary tumors (or breast cancers) are common in female dogs but rare in male dogs and cats. Mammary tumors are more common in female dogs that are not spayed or were spayed after 2 years of age. The risk of a dog depending mammary tumor is 0.5% in spayed before their first heat. In cats spaying at any age reduces the risk of mammary tumors by 40 to 60%. In female dogs 50% of mammary tumors are benign and 50% are malignant. In contrast over 85% of mammary tumors in cats are malignant and most of these have an aggressive biological behavior (highly invasive and metastatic).

The most common clinical sign of a malignant mammary tumor is one or more palpable masses underneath the skin of the abdomen. They may be next to or within the nipple and follow along the mammary chain and have appearance of firm and nodular forms. The size of the tumors varies and the skin over the mass may ulcerate and bleed and the affected areas may feel warm to touch and become painful. Mammary tumors appeared as either irregular or multiple nodules along the abdomen of the dog during physical examination. It is important to determine the type of tumor and whether it is benign or malignant.

A common procedure is the aspiration of a sample directly from the tumor by using fine needle aspiration and aspirate is microscopically investigated.

In some cases, results from (FNA) may not be entirely clear and a biopsy or remove of the entire tumor may be necessary obtained for histopathology. In case of suspected metastasis, blood analysis, urine analysis, x-ray of the lungs and possibly an abdominal ultrasound are required. The lymph nodes associated with the mammary glands may be sampled by FNA even if they seem normal.

Tumor types that are highly malignant showed average short survival time usually between 9-12 months. In case of inflammatory mammary gland tumors showing ulceration, edema and erythema, the tumors are characterized by rapid growing and the survival time for these patients is one to two months. Surgery is not recommended for patients with this tumor types.

Treatment of pet animals' mammary tumors only achievable by surgery. For dogs with individual mammary tumors surgery is the best treatment. For dogs with multiple tumors of one or both mammary chains, all the mammary glands may be removed. If surgery is needed to remove both sets of mammary glands from an animal is often done in two surgical procedures 2-3 weeks apart.

The local lymph node should be removed in cats, if possible, to assess for

evidence of spread of the cancer. Although surgery is the only tool used in treatment of pet animal, yet it is not recommended for dogs with inflammatory mammary carcinoma because it does not improve survival rate.

Moreover, surgery monotherapy may induce adverse effect in patients such as locoregional recurrence or metastatic tumor developed in distal tissues. Because occult cancer cells may remain in wound margins or in the bed of mastectomized tumor. In addition, after development of mammary tumors, some cells are usually detached from primary tumor and enter the circulation and defined circulatory tumor cells, and some CTC travel from circulation to reach the susceptible host tissues and persist dormant for years and defined as disseminated tumor cells (DTCs). DTCs persist in distant tissue dormant under equilibrium of immune response in tissues and the growth of the DTCs in new host tissues. In case of break this equilibrium equation under unknown reasons, DTCs initiate proliferation and established protumorigenic tumor microenvironment that enhance the development of macro-metastasis or tumor metastasis. For these reasons surgery alone can not prevent tumor recurrence or tumor metastasis. Unfortunately, an effective treatment has not been discovered. Radiations therapy may provide some benefit for dogs with inflammatory carcinomas in addition to chemotherapy, but prognosis remains poor as of now there is no proven efficacy of any chemotherapeutic protocol of the treatment of malignant mammary tumors in the dog. Certain therapeutic drugs are used for treatment, that may delay recurrence or metastasis, but their efficacy is unknown. For these reasons an urgently demand to design novel modalities to account for breast cancer treatment.

In recent years, biotechnology can be used to improve solving scientific problems in different aspects of life. It is considered as one of the most promising areas for nanobiotechnology in the antitumoral therapy. In particular, laser hyperthermia is a prospective method in oncology; however, low selectively of Laser heating for tissue destruction may cause significant damage of surrounding healthy tissues. It has been shown that gold nanorods (GNRs) are suitable for photothermal therapy due to its easy tuning of their plasmonic resonance to wavelength.

Experiments in vitro and in vivo have demonstrated high efficiency of gold nanorods in plasmonic photothermal therapy (PPTT). However, problems have been arising, in particular the selection of optimal doses for GNRs administration and selection of an optimal administration technology to ensure that the nanoparticles penetrate tumors to sufficient depth. After solving the technical problems under experimental conditions, the further challenge was investigation of

PPTT in treatment of naturally diseased patients with breast cancer because the behavior of PPTT in mice cannot be depended upon in treatment of clinical patients diseased with breast cancer.

Depending upon recommendations of WHO and many published investigations, pet animals (dogs and cats) are ideal models for experimentation of breast cancer therapies in human. Elsayed group was the first who investigated the efficacy of PPTT in treatment of breast cancer in pet animals.

Tuning of GNRs and laser irradiation was developed the developed technique induced complete ablation of small malignant mammary tumor without in situ recurrence or distance metastasis (Ali et al, 2016).

In larger (>10 cm³) highly malignant congested, inflamed and ulcerated tumors, PPTT failed to reduce complete ablation of large tumors. The reason is the uneven distribution of intra-tumoral administration of GNRs in the tumor due to presence of many obstacles that impair even distribution of GNRs in tumors such as presence of interstitial fluid pressure (IFP), aberrant compact structure of extracellular matrix and chronic inflammatory products. To solve this problem, Elsayed group applied PPTT in combination with surgery (mastectomy) and used PPTT as adjuvant therapy. All patients revealed complete recovery after 2 weeks post operation without in situ recurrence or distance metastasis. Unfortunately, PPTT could not combat distance metastasis if the patients were harboring distance metastasis in association with malignant large

tumors (Ali et al, 2017). This indicated that distance metastasis (lung or pulmonary metastasis) demand a new therapeutic approach concerning solving two problems and as the ideal technique to direct GNRs to the site of the tumor and secondly the ideal method to introduce laser irradiation to the lung metastasis to induce local selective hyperthermia.

It can be concluded that PPTT monotherapy or in combination with mastectomy is highly efficient in treatment of breast cancer in pet animals negative for x-ray distal metastasis (lung metastasis).

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