PHOTODYNAMIC ERADICATION OF NATURALLY OCCURRING TUMORS IN VETERINARY PRACTICE

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Summary. Photodynamic therapy as new and promising cancer treatment was applied to cure spontaneous tumors. In the first phase experimental mice bearing hepatoma tumors were treated by photodynamic therapy. Promising results obtained inspired us to continue the studies. A total of 8 dogs with tumors of different localization (rectum, leg, eyelid, skin, ear, mammary gland) were included in the study.

Photosensitizer was administrated i.v. 10 mg/kg body weight. After 48 hours irradiation with visible light was performed (630 nm, 90 mW/cm^2 25 min). Following treatment the tumors were evaluated by detection of tumor necrosis. The results indicate that in all cases examined, regardless of the histological type of tumor, localization and age of a dog, deep necrosis and tumor regression were observed.

Keywords: photodynamic theory, tumor, treatment.

FOTODINAMINIS SPONTANINIŲ NAVIKŲ GYDYMAS VETERINARIJOJE

Santrauka. Fotodinaminė terapija – naujas ir perspektyvus vėžio gydymo metodas, pradėtas taikyti klinikoje. Šio darbo tikslas – pritaikyti šį metodą spontaniniams gyvuliukų navikams gydyti. Pirmame etape eksperimentai buvo atliekami su pelių hepatomos A-22 navikais. Gauta stipri naviko augimo inhibicija ir ženklus gyvuliuko gyvenimo trukmės pailgėjimas. Antrajame etape buvo gydyti 8 šuniukai su spontaniniais įvairios lokalizacijos navikais. Sensibilizatorius buvo leidžiamas į veną (10mg/kg), po 48 val. navikas apspinduliuojamas matoma šviesa (630 nm, 90 mW/cm^2, 25min.) Gydymo poveikis buvo vertinamas pagal naviko nekrozę. Gauti rezultatai parodė, kad, nepriklausomai nuo naviko histogenezės, lokalizacijos ir šuniuko amžiaus, gili nekrozė ir smarkus naviko mažėjimas pastebėti visais atvejais.

Raktažodžiai: fotodinaminė teorija, navikai, gydymas.

Introduction. Since 1970 photodynamic therapy (PDT) has been considered as a potential method for skin, esophagus, lung, bladder, brain tumor eradication and was approved in a several countries all over the world: Canada, Japan, France, Germany, the Netherlands, the United States.

Ten years ago scientists of Vilnius university started to investigate the mechanisms of the photodynamic action with intension to integrate this new and promising cancer treatment modality in clinics (Fig. 1a). Now we have first successful results of this oncotherapy. Due to the existing facts, that dogs and cats especially at elder years very often are suffering from cancer, it was of importance to apply this new oncotherapy in veterinary as selective, effective, easy to perform, without hard side effects. (Fig. 1b).

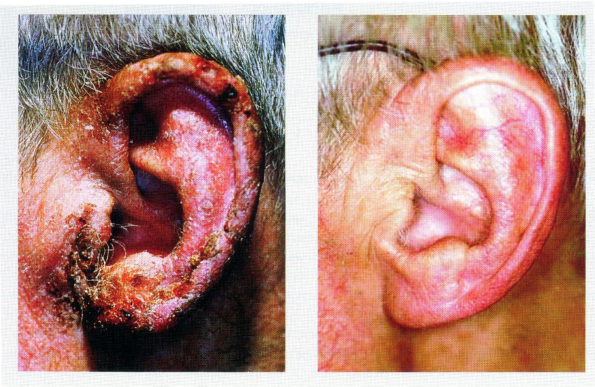


Fig.. 1a. **Patient with actinic keratosis before and after treatment with Metvix PDT.**

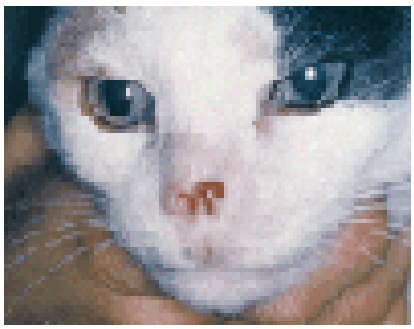
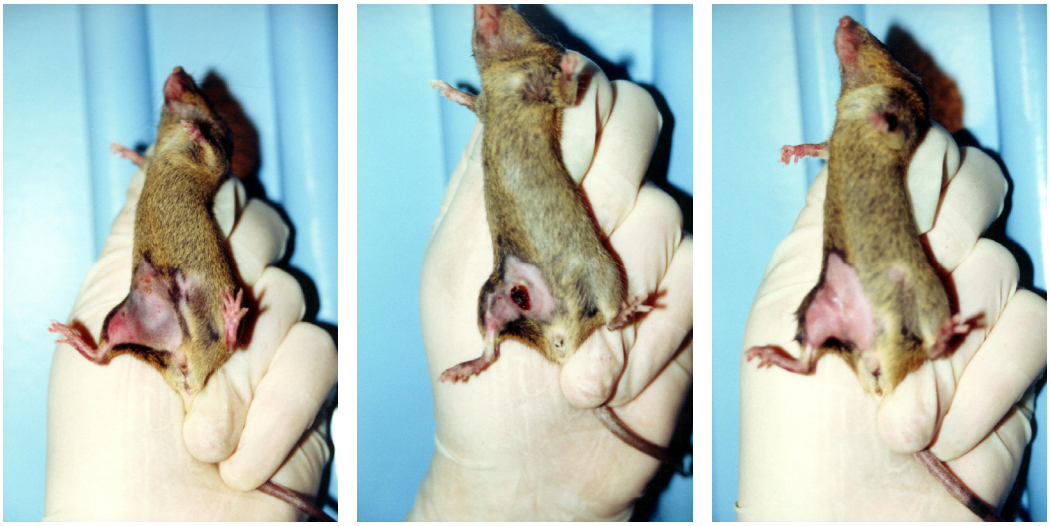


Fig. 1b. **Cat with malignancy**

Materials and Methods. Experimental mice bearing hepatoma A22 tumors were used firstly for the experiments. Afterwards studies on dogs with tumors of different histogenesis were continued (astrocitoma, squamous cell carcinoma, sarcoma, hemangiosarcoma, bazaliosarcoma, liposarcoma). Animals were anaestized with aminazine (1-2 mg/kg body weight) or narcoxyl (0,12 ml/mkg body weight). The drug (photosensitizer hematoporphyrin dimethyl ether) was administrated i.v. 10 mg/kg body weight. After 48 hours irradiation with lamp, producing visible light (λ=630 nm, power intensity 90 mW/cm^2, t=25 min) was performed. Tumor necrosis was the main indicator of successful treatment. Mice bearing hepatoma tumors were observed during 3-4 months after treatment.

Results and discussion. Firstly we would like to describe the results which were obtained with experimental mice bearing hepatoma A22 tumors. Fig. 2 clearly indicates that hepatoma tumor following 24 hours after photodynamic treatment is significantly destructed.

Moreover, total tumor remission was observed a week after treatment. Looking deeper at the mechanism of tumor destruction, histological analysis was performed. Data, presented in Fig. 3 reveal, that after photodynamic treatment tumor underwent necrosis with deep damage of tumor vasculature as well as tumor cells.



before 24 hours after week after

Fig. 2a. Mice bearing hepatoma A22 before photodynamic treatment and after (20 mg/kg HPde, i.p. injected, 3 hours incubation)

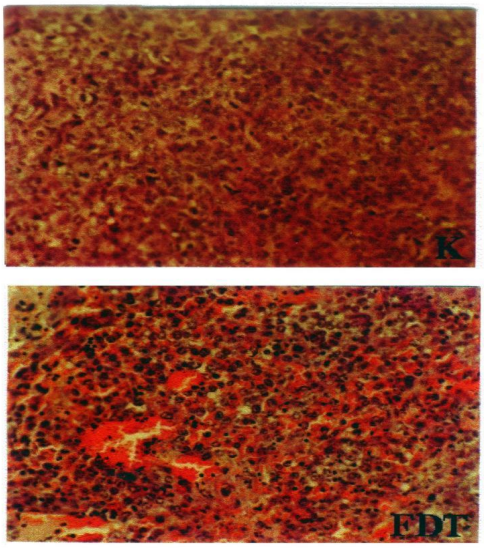


Fig. 2b. **MH-22A hepatoma in A – control, B – after HPde photodynamic treatment**

One may simply consider that the main evaluation of effective cure is animal surviving time. Thus, the next experiment was designed to determine the survival of mice after photodynamic treatment. Data, presented in Fig. 3 reveal, that not treated mice bearing tumors have died very fast. On the contrary, the lifespan of mice from the treated group prolonged 75 % and 25 % of them have been totally cured from cancer.

On these bases it appears of particular interest to determine, whether spontaneous tumors of dogs might be treated in the same manner. Eight dogs with naturally occuring carcinomas or sarcomas of different age (2.5 – 11 years) were treated with photodynamic therapy. In all cases the picture was very similar: hosts reported, that after treatment the tumors reduced in volume or disappeared at all (Table 1).

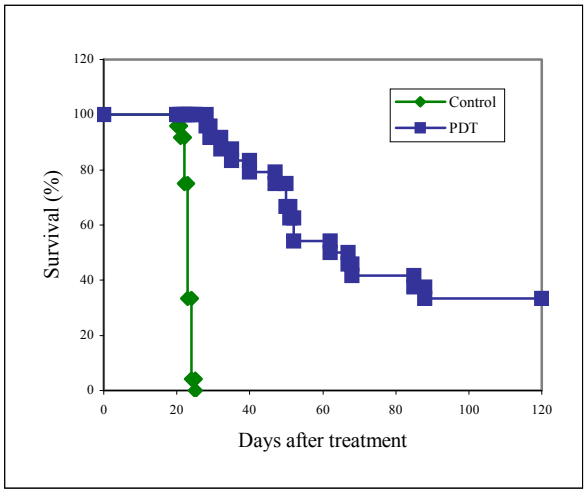


Fig. 3. **Survival of mice, bearing EAT: ¨ - control group; ■ – photodynamic treatment (PDT) treated group (40 mg/kg hypericin, i.p. injected, 3 hours incubated)**

It is important to note, that the results described are in line and close agreement with those published by other investigators. For instance, McCaw (2000) obtained good results treating canine oral squamous cell carcinomas with photodynamic therapy. Eight from eleven dogs were considered cured with no tumor recurrence for at least 17 months after treatment. Moreover, local treatment of oral squamous cell carcinomas with photodynamic treatment appears to give results similar to those obtained with surgical removal of large portions of the mandible or maxilla. Jacobs (2000) applied photodynamic therapy to

treat canine inntrathoracic esophageal squamous cell carcinoma, other investigators (Gloi et al., 2003) attempted to determine whether other type photosensitizers (*tin ethyl etiopurpurin, aluminum chlorophthalocyanine*) are effective to treat spontaneous tumors by photodynamic therapy. In all cases the cosmetic results with photodynamic treatment were superior to those of radical surgical removal.

Table 1. **Photodynamic treatment of naturally occuring canine tumors**

Age, weight	Histological type of tumor
11 years, 30 kg weight	astrocitoma (annal)
11 years, 10 kg weight	spnamous cell carcinoma (annal)
9 years, 25 kg weight	sarcoma (annal)
8 years, 22 kg weight	fibrolipoma (annal)
9 years, 30 kg weight	liposarcoma (eyebid)
4 years, 30 kg weight	hemangiosarcoma (leg)
2 years, 20 kg weight	bazoliosarcoma (leg)
4 years, 45kg weight	squamous cell carcinoma (skin)

In conclusion, data obtained support the idea, that photodynamic therapy has a potential for the non-invasive treatment of naturally occuring tumors of different histogenesis and might be successfully applied in veterinary.

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