Systemic Taxotere Chemotherapy for Metastatic Tumor Pleurisy in Cats with Spontaneous Breast Cancer

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 150, No. 11, pp. 574-576, November, 2010
Original article submitted August 9, 2009

Systemic and intrapleural chemotherapy for metastatic tumor pleurisy was carried out in cats with breast carcinoma. The animals (n=18) were divided into 2 groups. Cats of the systemic chemotherapy group received 3-6 courses of taxotere (30 mg/m^2; n=7) or 3 courses of taxotere (20 mg/m^2) in combination with doxorubicin (20 mg/m^2 at 21-day intervals (n=5) during the adjuvant period of therapy for metastatic tumor pleurisy. Objective effect was attained in 10 (84.6%) cats: partial remission in 3 (25%) and complete remission in 7 (58.3%, p<0.05) cats. Metastatic pleurisy progressed in 2 (16.7%) cats. The median time to progression reached 1.79 months, median lifespan 2.8 months. The animals of intrapleural chemotherapy group (n=6) received 1-4 courses of cyclophosphamide (250 mg/m^2) at 1-week interval during the adjuvant period without therapy for malignant pleurisy. Malignant pleurisy progressed in all cats. The median time to progression was equal to median lifespan (0.6 months). The therapy for malignant pleurisy in cats with breast cancer is regarded as the second-line chemotherapy with taxotere preferable as a monotherapy or in combination with doxorubicin.

Key Words: *metastatic tumorous pleurisy; spontaneous breast carcinoma in cats; systemic and intrapleural chemotherapy*

Involvement of the pleura and formation of malignant exudate (tumor pleurisy; TP) is the most hazardous manifestation of metastatic breast carcinoma (BC) in 70-80% cats [5]. TP develops during advanced stages of the disease in almost all cats and determines extremely unfavorable prognosis with drastic reduction of the lifespan to just several weeks [10,11]. Clinical manifestations of TP in cats with BC are similar to those in humans and are associated with the development of respiratory failure augmenting in proportion to decrease of vital capacity of the lungs [1]. The main symptoms of TP are dyspnea and cough, the cause of death is cardiopulmonary failure because of compression of the lungs and heart by the exudate. Conservative treatment of patients with metastatic TP consists in successive systemic and intrapleural therapy with effective antitumor cytostatics, including cyclophosphamide, doxorubicin, taxotere, *etc.* [1-4,6-8]. This leads to reduction or arrest of pleural exudation and appreciable prolongation of patient's lifespan. In veterinary, TP in cats is treated mainly by intrapleural injections of cyclophosphamide; the efficiency of systemic taxotere therapy is little studied [9].

We evaluated the prospects of systemic taxotere chemotherapy for metastatic TP in cats with BC.

MATERIALS AND METHODS

The study was carried out at Department of Experimental Therapy, Institute of Clinical Oncology, N. N. Blokhin Cancer Research Center, on 18 cats with BC complicated by metastatic TP developing during the postoperative period. The mean age of cats was 13 (8-15) years, 11 cats were sterilized. TP was detected by X-ray examination and verified by cytological findings. A case history was charted for each animal for

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0007-4888/11/1505-0642

examinations and therapy, after which 2 groups were formed.

Group 1 animals (n=6) received intrapleural chemotherapy (no specific therapy during the postoperative period). Therapy for TP consisted in injections of cyclophosphamide in a single dose of 250 mg/m^2, diluted in saline to a volume of 5.0 ml (1-4 cycles at 1-week intervals).

Group 2 animals (n=12) received systemic chemotherapy (no chemotherapy during the postoperative period or taxotere or doxorubicin chemotherapy). Cats receiving no chemotherapy or treated with doxorubicin (n=7) received 3-6 cycles of systemic taxotere monotherapy. Cats receiving taxotere during the postoperative period (n=5) received 3 cycles of systemic combined taxotere+doxorubicin chemotherapy. The interval between the cycles was 21 days. Taxotere (monotherapy) in a single dose of 30 mg/m^2 in 50 ml saline was infused during 30 min, doxorubicin was injected similarly. Taxotere and doxorubicin combination was injected in a single dose of 20 mg/m^2.

Before the therapy, the pleural exudate was evacuated in all animals and premedication was carried out with 15 mg prednisolone and 0.5 ml 1% suprastin. Repeated thoracocentesis was carried out in case of repeated accumulation of pleural exudate.

The efficiency of TP treatment was evaluated by the standard WHO criteria:

- objective effect: delay or arrest of pleural exudation;
- partial remission: pleural exudation delay;
- complete remission: pleural exudation arrest;
- progress: continuing accumulation of pleural exudate;
- median time to progression (MTP);
- median lifespan (MLS).

The efficiency was evaluated by the data of clinical and X-ray examinations. Time characteristics of the treatment efficiency were statistically processed using computer software and by plotting Kaplan–Meyer curves. The differences were considered significant at p<0.05.

RESULTS

No objective effect was seen in 6 cats of the intrapleural chemotherapy group. Pleural exudate continued to accumulate in 100% cases. The MTP was equal to MLS and was 0.6 months; only 20% cats survived during 1 month, and none survived as long as 1.5 months.

Of 12 animals receiving systemic taxotere chemotherapy, objective effect was attained in 10 (84.6%) animals, of these partial remission in 25% (3 cats) and complete in 58.3% (7 cats; p<0.05). The disease progressed in 16.7% (2 cats) animals (Fig. 1). The time parameters of treatment efficiency were as follows: MTP 1.79 months, 47% cats survived for 3 months, 23.9% for 6 months; MLS 2.8 months, 56.9% cats surviving for 3 months, 41.9% for 6 months, and 21% for 11 months (Table 1).

A 100% objective effect was attained in the group of 7 cats receiving taxotere monotherapy, of these, complete remission was attained in 71.4% (5 cats) and partial in 28.6% (2 cats); no accumulation of pleural exudate was noted. In the taxotere+doxorubicin group (5 cats) objective effect was 60%, of these, complete remission in 40% (2 cats) and partial in 20% (1 cat); exudation progressed in 40% (2 cats).

Analysis of the results indicates that systemic taxotere chemotherapy in a single dose of 20-30 mg/m^2 or taxotere in combination with doxorubicin (20 mg/m^2) significantly prolonged MTP (3-fold; p<0.00017) and MLS (4.6 times; p<0.0004) in comparison with ineffective intrapleural cyclophosphamide chemotherapy.

Hence, taxotere monotherapy or taxotere+doxorubicin therapy is effective in metastatic TP in cats

TABLE 1. Delayed Results of Treatment for Metastatic TP in Cats with BC

Month of observation	Animals surviving a certain period of observation, %			
	systemic chemotherapy (n=12)		intrapleural chemotherapy (n=6)	
	MTP	MLS	MTP	MLS
1	100	100	0	20.0±17.9
3	47±15	57±15	0	0
4	36±15	42±17	0	0
6	24±14	42±17	0	0
12	0	21±17	0	0

after surgery for BC. This therapy has brought about an objective effect in 84.6% cases and arrested accumulation of pleural exudate in almost 60% cats. Interestingly that high antitumor effect was attained in cases without taxotere therapy during the adjuvant period or taxotere+doxorubicin combination for TP treatment. This result can be attributed to development of resistance to taxotere in the metastatic cells causing TP. It seems that TP therapy in cats with BC should be regarded as the second line therapy; drugs used for neonadjuvant therapy should not be used in the monotherapy mode. The absence of available relevant information precludes more detailed discussion.

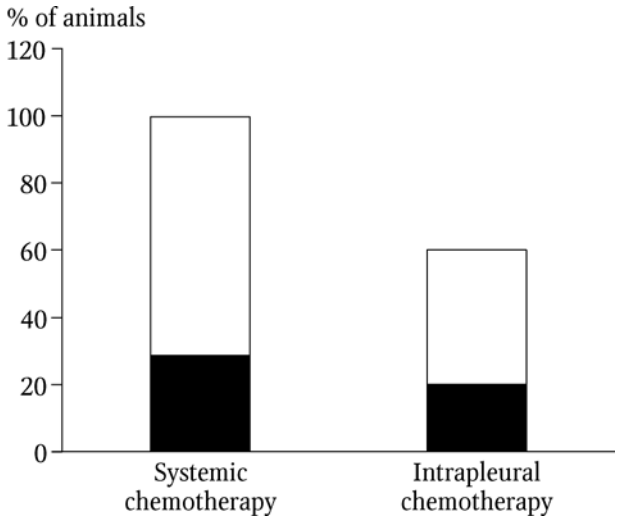

Fig. 1. Efficiency of TP treatment in cats with BC receiving different chemotherapies (systemic taxotere or intrapleural cyclophosphamide). Light sections: pleural exudation arrested; dark section: accumulation of exudate reduced.

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