Outcome of first-rescue cyclophosphamide treatment for relapse small cell gastrointestinal lymphoma in cats

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BACKGROUND

- Lymphoma is the most common tumor type found in the intestines of cats.
- The small cell variant of gastrointestinal (GI) lymphoma in cats carries a good prognosis.
- First line treatment with chlorambucil and steroids results in response rates of > 90% and survival times of ≥ 2 years.
- Standard rescue protocols have not been established for relapse feline small cell GI lymphoma.
- Rescue drugs typically include other alkylating agents, although response data are limited.

OBJECTIVES

- To determine the progression free survival (PFS) and overall survival time (OST) of cats with relapse small cell GI lymphoma treated with first-rescue cyclophosphamide/steroids after failing chlorambucil/steroids
- To evaluate potential prognostic factors associated with outcome

MATERIAL AND METHODS

- Multi-institutional retrospective case series
- Inclusion criteria
  - Cats with small cell GI lymphoma confirmed histologically or via PARR/flow cytometry
  - Cats treated with cyclophosphamide/steroids after failure from first-line treatment with chlorambucil/steroids
  - Cats with no concurrent cancers nor prior chemotherapies
- Response to therapy was based on clinical signs (CS).
  - Complete response (CR): complete resolution of CS (VCOG grade 0) ≥ 30 days
  - Partial response (PR): improvement but not complete resolution of CS (VCOG grade 1) ≥ 30 days
  - Progressive disease (PD): worsening of CS (VCOG grade > 1)
  - Stable disease (SD): neither improvement nor progression of clinical signs
  - Responses lasting < 30 days were considered either SD or PD, depending on severity of CS compared to pre-cyclophosphamide treatment
- Outcome definitions
  - PFS: days between initiation of cyclophosphamide and disease progression or death
  - OST: days between initial diagnosis and death
- Statistical analysis
  - Kaplan-Meier product limit estimates to compare survival times among cats grouped by categorical variables of interest
  - Cox proportional hazards regression analysis to assess associations between all variables and outcome in univariate analyses

RESULTS

- 20 cats met the inclusion criteria.
- Demographic data
  - Gender: 14 castrated male and 6 spayed female
  - Median age: 14.8 years old (range 6.2-19.8)
  - Median weight: 4.04 kg (range 2.8-5.1)
- CS
  - Weight loss (n=15)
  - Vomiting (n=10)
  - Diarrhea (n=8)
  - Anorexia (n=7)
  - Lethargy (n=5)
- Median duration of CS: 100 days (range 3-1095).
- Cyclophosphamide/steroid treatment
  - Median dose of cyclophosphamide: 206.9 mg/m² (range 161.3-281.8 mg/m²) every 2 weeks
  - Median number of cyclophosphamide treatments: 13 (range 3-54)
- Response
  - CR: 18/20 (90%)
  - SD: 1/20 (5%)
  - PD: 1/20 (5%)
- 17 cats discontinued therapy due to progression of CS.
- Median PFS: 215 days (95% CI 102-328, Fig 1)
- Median OST: 1065 days (95% CI 974-1156, Fig 2)

### Table 1. Univariate cox proportional hazard regression of prognostic factors with statistically significant impact (P < 0.05) on OST

<table>
<thead>
<tr>
<th>Predictive factors</th>
<th>P value</th>
<th>HR</th>
<th>95% CI Lower</th>
<th>95% CI Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of clinical signs</td>
<td>0.033</td>
<td>1.003</td>
<td>1</td>
<td>1.006</td>
</tr>
<tr>
<td>Duration of response to chlorambucil treatment</td>
<td>0.012</td>
<td>0.995</td>
<td>0.992</td>
<td>0.999</td>
</tr>
</tbody>
</table>

### Table 2. Univariate cox proportional hazard regression of prognostic factors with statistically significant impact (P < 0.05) on PFS

<table>
<thead>
<tr>
<th>Predictive factors</th>
<th>P value</th>
<th>HR</th>
<th>95% CI Lower</th>
<th>95% CI Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR vs Non-CR</td>
<td>0.024</td>
<td>0.139</td>
<td>0.023</td>
<td>0.768</td>
</tr>
</tbody>
</table>

CONCLUSION

- Cyclophosphamide was well-tolerated.
- Treatment with cyclophosphamide for relapse small cell GI lymphoma in cats resulted in moderate response duration with a high complete response rate.
- Overall prognosis of feline small cell GI lymphoma is favorable with chemotherapy.
- A prospective randomized study is necessary to determine the superiority of cyclophosphamide over other rescue therapies.

REFERENCES