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Pine processionary caterpillar *Thaumetopoea pityocampa* envenomation in 109 dogs: A retrospective study

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ABSTRACT

Contact with the caterpillars of the pine processionary moth (CPPM) *Thaumetopoea pityocampa* induces severe local allergic reactions. The purpose of this large-scale retrospective cohort-study was to describe the clinical manifestations and related risk factors of CPPM exposure. This cohort-study included 109 dogs between the years of 2000 and 2016. Tongue lesions ranging from oedema to severe necrosis were observed in 94/109 dogs (86%). The following systemic signs were observed in 60/109 dogs (55%): vomiting (52/109, 48%), dyspnoea (6/109, 5%), hypovolemia (4/109, 4%) and diarrhoea (2/109, 2%). Based on the time elapsed from CPPM contact to the first oral flushing, three groups were defined: <2 h (group 1, 37/105, 35%), 2 h–6 h (group 2, 39/105, 37%) and >6 h (group 3, 29/105, 28%). Tongue necrosis (TN) at admission was significantly more common in the dogs in group 3 than those in groups 1 and 2 (45% vs. 5% and 5% respectively, $p = 0.0002$). In addition, the development of TN during hospitalisation was significantly more common in the dogs in group 3 (65%) than in those in the other groups (21% in group 1, $p = 0.02$) and 31% in group 2, $p = 0.001$). The dogs in group 3 presented a 14.63-fold higher risk of TN at admission and a 3.78-fold higher risk of developing necrosis during hospitalisation compared with the other groups. The survival rate after exposure was 97%. Long-term follow-up data were available for 69/109 dogs (63%). Twenty-three dogs (37%) had persistent, definitive TN without major consequences on quality of life. Elapsed time between contact and first oral flushing appears to be a key determinant for the progression of necrotic lesions, and the best results were observed when flushing occurred within 6 h of contact. The prognosis of CPPM envenomation is excellent, with a short hospitalisation duration.

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1. Introduction

The caterpillar of the pine processionary moth (CPPM) *Thaumetopoea pityocampa* represents a public health hazard because contact with this insect can induce severe allergic reactions in humans and animals (Niza et al., 2012). These insects are mostly found in rural and urban areas near the Mediterranean Basin and the South Atlantic coast (Kaszak et al., 2015). The natural distribution of these caterpillars has recently expanded in latitude and longitude because of climate change and global warming (Roques, 2015). CPPM toxicity is localised to poisonous hairs (i.e., setae) (Fig. 1) that induce mechanical irritation and release at least seven irritant allergens, of which thaumetopoein is the most important (Rodriguez-Mahillo et al., 2012).

Compared with the literature on human medicine, the veterinary literature contains few studies on lepidopterism (Bruchim et al., 2005; Niza et al., 2012; Costa et al., 2016). CPPM toxicity causes significant morbidity in both humans and animals, and contact with the irritating hairs can provoke oral, skin and eye lesions that are usually benign (Kaszak et al., 2015). However, systemic reactions, such as hypertension, vomiting and allergic reactions, including anaphylactic shock, are occasionally induced (Kozer et al., 1999; Vega et al., 1997). In dogs, the most recent

Abbreviations: CPPM, Caterpillars of the pine processionary moth; TN, Tongue necrosis.

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Fig. 1. Caterpillars of the pine processionary moth *Thaumetopoea pityocampa* and visualisation of their setae.

available CPPM study, which included forty-one patients, describes main clinical signs as glossitis, ptyalism, tongue lesions (ulcers, wheals, and focal superficial necrosis), hyperthermia and vomiting (Niza et al., 2012). Ocular lesions, such as keratitis with corneal cellular infiltrates and anterior uveitis, were also described (Costa et al., 2016). Severe lesions leading to tongue necrosis (TN) and sloughing of one portion of the tongue are also observed; however, these lesions are rarely extensive and animals are usually able to eat and drink adequately (Bruchim et al., 2005).

The aims of this study were to describe the clinical manifestations of exposure to *Thaumetopoea pityocampa* caterpillars in a large cohort of dogs and determine the prognostic factors for TN, length of hospitalisation and outcomes of envenomation.

2. Materials and methods

Dogs admitted to the intensive care unit of a veterinary hospital (*SIAMU*, VetAgro Sup, Campus Vétérinaire de Lyon, France) between 2000 and 2016 were retrospectively enrolled. A computer-based search of the university database was conducted using the terms “pine processionary caterpillar envenomation”, “envenomation”, “pine processionary caterpillar intoxication”, “pine processionary caterpillar”, “erucism” and “glossitis”. All medical records that reported any contact with a CPPM and included clinical signs and history consistent with lepidopterism were selected. Dogs were excluded if the clinical signs were not consistent with caterpillar envenomation or if medical records were incomplete. Recorded data included the signalment, month of presentation, time from CPPM contact to presentation, time from CPPM contact to first oral flushing, physical examination with a description of local lesions and the length of hospitalisation, laboratory results, systemic complications, therapeutic measures, outcomes and the presence of permanent injuries.

Based on the time elapsed from CPPM contact to the first oral flushing, three groups were defined: less than 2 h (group 1), 2–6 h (group 2) and more than 6 h (group 3). Dogs in which oral flushing was not performed were included in group 3. Long-term outcomes were assessed based on interviews of the owners at the time of study enrolment. Owners were asked the following questions: 1. Whether necrotic lesions or changes in tongue colour remained or appeared after discharge, 2. Whether the consequences of CPPM envenomation led to another veterinarian consultation, 3. Whether the dog's appetite was present despite tongue injuries, and 4. Whether their animal had sequelae or disabilities from this event.

3. Statistics

Descriptive statistics were used for the categorical variables. The D'Agostino-Pearson omnibus test for normality revealed that almost all variables were non-parametric. For clarity, all continuous variables were presented as median values (interquartile range (IQR); Q1–Q3). Differences between variables were assessed by comparing the distributions of ranks with the Mann-Whitney *U* test. Because of the quantity of data to assess, a univariate statistical analysis was run in two steps. Correlations were assessed using the non-parametric Spearman's rank correlation test. Differences between groups for the selected variables were tested with the Mann-Whitney *U* and Fisher's exact tests. Odds ratios (ORs) and the associated 95% confidence intervals (CIs) were calculated. Receiver-operating characteristic (ROC) curves were used to evaluate the predictive capacity of continuous variables. The results of the ROC curve analysis were presented in terms of the increased risk above the cut-off value (sensitivity, specificity). A multiple linear regression analysis was used to determine the relative influence of significant factors (time from CPPM contact to presentation, time from CPPM contact to first oral flushing, length of hospitalisation, temperature and description of lesions) on the progression of lesions to necrosis or the composite outcome of progression to necrosis or death. The significance level was set at $P_{in} < 0.05$ for inclusion of variables in the model and at $P_{out} > 0.20$ for exclusion. A two-sided p value < 0.05 was considered to indicate statistical significance. All statistical analyses were performed and graphs were generated using the commercial software SPSS (version 24; SPSS, Chicago, IL, USA).[1]

4. Results

4.1. Population characteristics

One hundred and eleven medical records in our data base met the inclusion criteria of the study between 2000 and 2016. Two dogs were excluded because of a final diagnosis inconsistent with lepidopterism, leaving a total of 109 dogs. Forty-two percent were male, 58% were female, and the median age was 12.5 months [IQR; 8-48]. Various breeds were represented. The most represented breeds were Labrador Retriever (7%), Golden Retriever (6%), Cocker Spaniel (5%), and German Shepherd (4%).

The dogs were admitted between January to September, with 99 dogs (90%) admitted between March and May (Fig. 2).

4.2. Hospitalisation data

The median time between exposure and presentation to our facility was 3 h (IQR; 1-12). The median length of hospitalisation was 24 h (IQR; 1-24), and significant differences were not observed in this value between dogs that presented at <6 or >6 h from exposure ($p = 0.07$).

The overall survival rate was 97% (106/109). Of the 3 dogs that did not survive, one died because of severe pharyngeal oedema, which led to an acute obstruction of the upper airways. Another dog died from acute respiratory distress 24 h after hospitalisation without evidence of upper airway inflammation or oedema during intubation. The cause of death remained unknown as a necropsy was not performed. According to the owners' choice, euthanasia was performed on the third dog due to a worsening of its clinical state.

[1] SPSS version 24; SPSS, Chicago, IL, USA. Graphpad Prism version 7, Graphpad Software, Inc. La Jolla, CA.

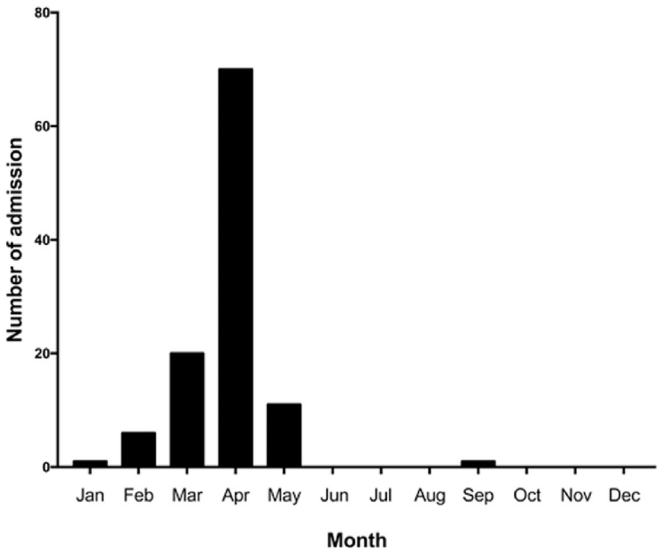

Fig. 2. Distribution of the months of presentation for the 109 dogs.

Data on the dogs' "appetite" during hospitalisation were available for 60 dogs. Anorexia was more frequently documented in dogs with TN than in those without TN (7/30, 23% vs. 2/26, 8%, respectively, $p = 0.04$).

4.3. Clinical signs

Tongue lesions were observed in 94 dogs (86%; Figs. 3 and 4). Descriptions of the lesions are summarised in Table 1.

At admission, ptyalism was present in 77 dogs (71%), and it was associated with the presence of tongue lesions (OR = 4.63, 95% CI: 1.45–15.08). The dogs in which changes in tongue colour were observed at admission had significantly more necrosis (62%) than those that did not have colour changes (32%; $p = 0.01$; OR = 4.24, 95% CI: 1.34–11.95).

Systemic signs were observed in 60 dogs (55%), and are summarised in Table 1. Rectal temperature was available for 85 dogs (78%). The median rectal temperature was 39.10 °C (IQR; 38.7–39.4 °C). The ROC analysis revealed that for each 1 °C increase above 39.15 °C in admission temperature, the risk of having tongue lesions increased by 1.8-fold (Sensitivity: 91.7%; Specificity: 49.3%).

Fig. 3. Ulceration and oedema of the tongue at admission in a dog one hour after CPPM exposure.

Fig. 4. Tongue necrosis at admission in a dog 16 h after CPPM exposure.

4.4. Laboratory abnormalities

A complete blood count was performed in 28 dogs. Haematological abnormalities were present in 4 dogs (14%) and included anaemia (2/28, 7%), leucopoenia (1/28, 3%) and leucocytosis (1/28, 3%). A biochemical panel was performed in 83 dogs, of which 2 (2%) were found to have azotaemia.

4.5. Treatment

The first-line medical treatment in 97 dogs (90%) consisted of flushing the mouth with a solution of sodium bicarbonate[2] diluted in isotonic sterile saline (1:1 ratio). Six dogs (5.5%) received flushing with a solution of isotonic saline only. In all cases, the eyes were irrigated with an eye cleaning solution.[3]

The time elapsed between CPPM contact and first oral flushing was available for 105 dogs (96%) (Table 1). Four dogs in group 3 (14%) did not receive any oral flushing, and the inclusion or exclusion of those dogs did not change any of the results. Dogs in group 3 had significantly more tongue lesion, more TN at admission (Fig. 5) and developed significantly more TN during hospitalisation than dogs from group 1, or dogs from group 2 (Table 1). Compared with combined groups 1 and 2 (76 dogs), dogs in group 3 had significantly more TN at admission (4/76, 5% and 13/29, 45% respectively; $p < 0.001$) and developed TN at a significantly greater rate during hospitalisation (23/76, 33% and 17/29, 59% respectively; $p < 0.001$).

For the dogs in group 3, the OR for TN at admission was 14.63

[2] Sodium bicarbonate Lavoisier® 1.4%, Chaix et Du Marais Laboratories, 7 rue Pasquier, 75008 Paris - FRANCE.

[3] Ocryl eye cleaning sterile solution, TVM, 57 rue des Bardines, 63370 Lempdes - FRANCE.

Table 1
Clinical signs for the 109 dogs and in groups 1, 2 and 3 (105/109). When not mentioned, clinical signs are at admission. p_1: p-value between group 1 and group 2, p_2: p-value between group 2 and group 3, p_3: p-value between group 1 and group 3. *Number of dogs for which data were available is specified for each group.

Clinical signs	Total n = 109 (%)	Group 1 n = 37 (%)	Group 2 n = 39 (%)	Group 3 n = 29 (%)	p_1	p_2	p_3
Tongue lesions	94 (86%)	29 (78%)	34 (87%)	27 (93%)	*0.01*	*0.69*	*0.003*
Oedema	72 (66%)	25 (68%)	28 (72%)	15 (51%)	*0.80*	*0.12*	*0.21*
Ulcerations	22 (20%)	5 (14%)	8 (21%)	9 (31%)	*0.54*	*0.39*	*0.12*
Vesicular lesions	14 (13%)	4 (11%)	7 (18%)	1 (3%)	*0.51*	*0.12*	*0.38*
Change in colour	21 (19%)	7 (19%)	8 (21%)	5 (17%)	*>0.90*	*>0.90*	*>0.90*
Necrosis at admission	17 (16%)	2 (5%)	2 (5%)	13 (45%)	*>0.90*	***0.0002***	***0.0002***
Necrosis during hospitalisation*	41/99 (41%)	7/33 (21%)	10/32 (31%)	17/26 (65%)	*0.40*	***0.02***	***0.001***
Other (*Labial and gingival oedema, ulcerations, facial oedema or cutaneous erythema*)	41 (38%)	15 (41%)	16 (41%)	9 (31%)	*>0.90*	*0.45*	*0.45*
Ocular lesions (*Blepharospasm, conjunctivitis, corneal oedema or ulcerations*)	9 (8%)	3 (8%)	5 (13%)	1 (3%)	*0.72*	*0.22*	*0.62*
Systemic signs	60 (55%)	22 (68%)	19 (49%)	16 (55%)	*0.36*	*0.63*	*0.80*
Vomiting	52 (48%)	20 (54%)	17 (44%)	14 (48%)	*0.49*	*0.80*	*0.80*
Dyspnoea	6 (5%)	3 (8%)	1 (3%)	2 (7%)	*0.35*	*0.57*	*>0.90*
Hypovolemia	4 (4%)	1 (3%)	2 (5%)	1 (3%)	*>0.90*	*>0.90*	*>0.90*
Diarrhoea	2 (2%)	0 (0%)	1 (3%)	1 (3%)	*>0.90*	*>0.90*	*0.44*

Bold are p-value < 0.05.

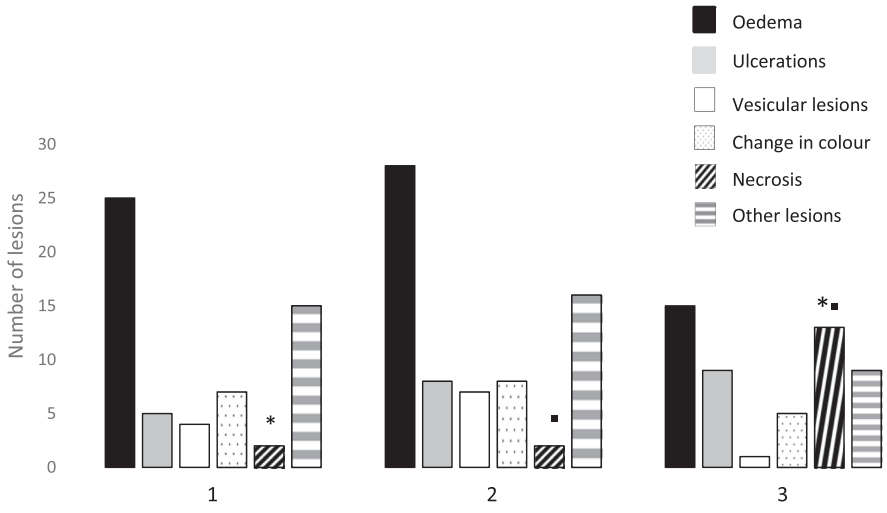

Fig. 5. Distribution of tongue lesions in groups 1, 2, and 3 at admission. *$p < 0.05$ between groups 1 and 3, ■ $p < 0.05$ between groups 2 and 3.

(95% CI: 4.38–43.78), and the OR for developing TN during hospitalisation was 3.78 (95% CI: 1.39–9.31).

All dogs received intravenous fluid therapy during hospitalisation. One hundred one dogs (93%) were treated with intravenous steroids (dexamethasone: 88/102 (86%); (methyl) prednisolone: 13/102 (13%)); 2 dogs (2%) were treated with antihistaminic drugs; 65 dogs (58%) were intravenously administered broad spectrum antibiotics; and 48 dogs (44%) received heparin therapy. Based on the pain scores, various types of opiates were used in 64 patients (58%). None of these treatments were correlated with the different types of tongue lesions or the length of hospitalisation.

4.6. Long-term outcomes

The response rate for the survey was 56% (62/109). The follow-up period varied from 3 months to 16 years. Two dogs (3%) presented to their regular veterinarian for a follow-up consultation related to the CPPM contact. Twenty-three dogs (37%) had persistent definitive TN that led to partial loss of their tongue. Of these 23 dogs, 16 (70%) were able to eat and drink without difficulties after discharge. The other 7 dogs required assisted nutrition (e.g., mixed food, food given by hand) for a short period.

4.7. Multivariate analysis results

The time between exposure and oral flushing, the temperature at admission, and changes in tongue colour during hospitalisation were correlated with the progression to necrosis or death (McFadden's $R^2 = 0.71$, $p < 0.01$ for all parameters).

5. Discussion

The present study is the first study to show that the time between exposure and oral flushing is a significant factor in the development of TN. A recent report (Niza et al., 2012) suggested that dogs presenting 2 h after CPPM contact developed necrosis and spent a longer time in the hospital (Niza et al., 2012). Compared with the findings of Niza et al. (2012), our findings indicated that an interval of two hours between CPPM contact and presentation is not statistically relevant. Moreover, our results suggest that a delay in oral flushing after CPPM contact by more than 6 h increases the risk of TN at admission by 14-fold and the risk of developing necrosis during hospitalisation by 3.7-fold. Therefore, irrigation of the mouth, eyes or any other portion of the skin that may have been in contact with poisonous hairs is key to removing the setae, diluting or deactivating the toxins and reducing local inflammation, and this

flushing should be done within the first 6 h after exposure.

Pine processionary moth envenomation affects humans and animals, and across species, the young are particularly vulnerable because of their natural curiosity and playfulness (Kozer et al., 1999; Niza et al., 2012). This epidemiological characteristic was observed in our study. The highest risks of contamination occurred from the end of winter to spring when mature larvae form processions on the ground to search for food and pupation sites in the soil. As previously described (Bruchim et al., 2005; Niza et al., 2012), CPPM exposure in dogs primarily occurs between March and April. However, our study showed that the months of presentation from ranged January to September. The temperate climate of France, where the present study was conducted, and the presence of different species of processionary moths in our area could explain the expanded time frame of presentation (Roques, 2015; Bernigaud et al., 2017). In our region, *Thaumetopoea pityocampa* (Fig. 1) is the main species of processionary moth and forms processions from November to March. However, *Thaumetopoea processionea* is also present in this area and forms processions from May to July (Bernigaud et al., 2017).

The clinical signs of CPPM envenomation result from mechanical irritation induced by contact with the setae and the subsequent release of thaumetopoein, which leads to a histamine-mediated hypersensitivity reaction (Rodriguez-Mahillo et al., 2012). In our study, the most frequent clinical signs were acute lingual and gingival oedema, ulceration, and vesicular lesions. Such lesions should be suspected in animals showing excessive ptyalism at admission because this sign was strongly correlated with the presence of tongue injuries (OR: 4.63). Thus, special precautions are strongly recommended (i.e. wearing gloves) when exploring the cause of ptyalism in dogs. As shown in Fig. 5, TN was significantly more frequent in group 3, and tongue oedema, even in non-significant cases, was more frequent in groups 1 and 2 at admission. Thus, this study confirms the predictable evolution of tongue lesion, starting with tongue oedema and evolving within hours to TN in more severe cases (Niza et al., 2012).

Tongue necrosis is one of the most frequent sequelae of CPPM contact, and it may present at admission or develop during hospitalisation. In our study, changes in tongue colour were identified as an early predictive marker for progression to necrosis. Another interesting finding from our study is that a rectal temperature above 39.15 °C is an indicator of further oral injuries. Hyperthermia could be explained by a systemic inflammatory reaction caused by thaumetopoein release from the setae (Rodriguez-Mahillo et al., 2012), and it is associated with more severe tongue lesions.

Consistent with the results of previous studies (Costa et al., 2016; Niza et al., 2012), ocular lesions were rare in our study. Despite the low prevalence of such lesions, a complete ophthalmic examination should be performed at admission and repeated during hospitalisation.

Our study confirms that most of the signs associated with lepidopterism are local, although systemic signs could appear, such as vomiting, dyspnoea or hypovolemia (Kozer et al., 1999; Kaszak et al., 2015). When present, these abnormalities may be early indicators of a systemic inflammatory response syndrome that requires close monitoring. Biochemical and haematological disturbances were rare in our study, which is consistent with the literature, and should be assessed on a case-by-case basis (Bruchim et al., 2005; Niza et al., 2012).

The first step of the management of animals exposed to a CPPM consists of intense and extended flushing of every body part that may have come in contact with the poisonous setae. Our study confirms the importance of oral flushing within 6 h. The second step is performed to prevent inflammatory reactions via the administration of short-acting steroids. Antihistaminic drugs were infrequently administered in our study but can be useful to reduce thaumetopoein-induced mast-cell degranulation (Kaszak et al., 2015). In the present study, 93% of the dogs were treated with steroids, therefore, its effectiveness to treat TN cannot be evaluated. This study presented certain limitations. The first is inherent to its retrospective nature, and the second is related to the long study period considering that modifications to therapeutic practices may have occurred over the years (i.e., the use of heparin and antibiotics). However, the removal of caterpillar hairs via intensive flushing (regardless of the fluid used) has been consistently implemented and appears to be the cornerstone of treatment.

In conclusion, this is the first report of such a large cohort of dogs to describe the results of contact with CPPMs, along with the prognostic factors and long-term prognoses. The time between contact and first oral flushing appears to be key in determining the progression of necrotic lesions, and our study suggests that the optimal timeframe is less than 6 h. Changes in tongue colour also seem to be a reliable clinical marker for the in-hospital development of TN. The overall prognosis is excellent, the length of hospitalisation is typically short, and patients are not prone to long-term sequelae. To our knowledge, this study is the first to report the outcomes of patients several months after hospitalisation.

Conflicts of interest

None.

Ethical statement

1) This material has not been published in whole or in part elsewhere;

2) The manuscript is not currently being considered for publication in another journal;

3) All authors have been personally and actively involved in substantive work leading to the manuscript, and will hold themselves jointly and individually responsible for its content.

Transparency document

Transparency document related to this article can be found online at http://dx.doi.org/10.1016/j.toxicon.2017.03.014.

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