

フレキシブル・アリゲーター鉗子による肺動脈内犬糸状虫摘出後の臨床効果

誌名	Japanese journal of veterinary science
ISSN	00215295
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巻/号	50巻3号
掲載ページ	p. 723-730
発行年月	1988年6月

Clinical Effects after Heartworm Removal from Pulmonary Arteries using Flexible Alligator Forceps in Dogs with Common *Dirofilariasis*

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(Received 6 November 1987/Accepted 18 February 1988)

ABSTRACT. Changes in clinical features after heartworm removal from the pulmonary arteries using flexible alligator forceps were examined in 36 dogs with common *dirofilariasis*. No dogs died owing to the removal manipulations. The removal efficiency was 90% in 18 dogs autopsied. In the mild cases (23 dogs), the signs such as coughing, anemia and so on were relieved or disappeared rapidly after removal. Serious cases were divided into ascites (9 dogs) and hemoptysis (4 dogs) cases. Their prominent signs before removal were less activity, anorexia, dyspnea and anemia in almost all cases, and subcutaneous edema, hydrothorax, icterus and hypothermia were seen in some ascites cases. The general condition improved considerably and the main symptoms were relieved or disappeared within 4 weeks after removal in most cases. The post-removal progress was good in all cases with hemoptysis and in 7 of 9 cases with ascites. However, 2 cases with ascites died of severe heart valvular disease or renal failure 3.5 or 4 months after removal. Anemia, leukocytosis and hypoalbuminemia were alleviated after removal in some mild and serious cases on laboratory tests. LDH and CK activities, which showed high levels before removal, decreased within 1 or 4 weeks after. These findings might suggest that injuries of the heart, lung and liver healed after the heartworm removal. However, the cases with insufficient compensation for severe lesions could not recover completely. These results showed that the heartworm removal using flexible alligator forceps was safe and excellent as a radical therapy for heartworm disease and could be recommended to apply for even serious cases.—**KEY WORDS:** canine *dirofilariasis*, flexible alligator forceps, heartworm removal.

Jpn. J. Vet. Sci. 50(3): 723-730, 1988

Canine *dirofilariasis* (heartworm disease) can be divided into common and special types in terms of the location of the heartworms and progress of clinical symptoms. In common type, heartworms inhabit only the pulmonary arteries, and symptoms are chronic. While in special type such as caval syndrome, the worms coil around the tricuspid chordae or paradoxical embolism in dogs with septal defect, the worms migrate from the pulmonary arteries to the tricuspid orifice or peripheral arteries. Symptom progress is acute and severe in terms of location and state of heartworms. The radical therapy for heartworm disease is the safe removal of adult heartworms. Hitherto, chemotherapy with adulticides or surgical removal of heartworms through thoraco-

tomy has been used for therapy in common *dirofilariasis*, but these methods were accompanied with high risk. In the chemotherapy, dogs died occasionally by toxicosis of the drugs, or by embolisms in the pulmonary arteries with dead adult heartworms [2, 3, 4, 8, 13]. Thoracotomy has large operative attacks for animals and sometimes causes the death of dogs [1, 5, 14, 15]. Therefore, thoracotomy and chemotherapy have not been recommended for serious cases [11, 13].

Recently, the authors [7] developed a flexible alligator forceps to remove heartworms from the pulmonary arteries through the jugular vein without thoracotomy. This paper presents the clinical effects after heartworm removal from the pulmonary

arteries in dogs with common dirofilariasis using the flexible alligator forceps.

MATERIALS AND METHODS

Thirty-six dogs of various sizes, ages and breeds were used in this study. These included the dogs from the local dog pounds (experimental dogs) and patients of the Veterinary Hospital of Gifu University (patient dogs). The clinical histories were obtained from the owners of patient dogs, but not in the experimental dogs. Dogs were divided into mild cases (23 dogs; 17 experimental and 6 patient dogs) and serious cases (13 dogs; 1 experimental and 12 patient dogs) by their clinical signs before the removal. Cases with ascites and hemoptysis were grouped into the serious category, and serious cases were sub-divided into hemoptysis cases (4 dogs) and ascites cases (9 dogs). Removal manipulation was performed under light general anesthesia. The dogs were premedicated with atropin sulfate (0.05 mg/kg) and xylazine (1.0–2.0 mg/kg) or with diazepam (0.25–0.5 mg/kg), then anesthetized by ketamine hydrochloride (2.0–10.0 mg/kg) intramuscularly, respectively. The procedure of heartworm removal was the same as in our previous report [7].

Only antibiotics were administered to dogs in mild cases for 3 days after removal. Antibiotics, diuretics, cardionics, hemostatics and/or glucocorticoids were used for serious cases according to the clinical signs for 1 to 3 weeks after removal.

Clinical examinations were conducted before, 1 and 4 weeks after removal. Red and white blood cells (RBC and WBC) were counted with a Coulter Counter (Model ZF, Coulter Electronics, Inc., Florida), and hematocrit (Ht) was measured by microhematocrit method. Serum total protein (T.P) concentration was determined with a refractometer, and serum protein fractions were analysed by cellulose acetate elec-

trophoresis. Hemoglobin (Hb) concentration, serum glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), lactic dehydrogenase (LDH) and creatinine phosphokinase (CK) activities were measured with RaBA-Super System (Chugai Pharmaceutical Co., Ltd., Tokyo). LDH and CK isozymes were separated by agarose gel electrophoresis, and stained by the method of Kuroda [10] and the CK Isozyme Kit-N (Nippon Shoji Kaisha, Ltd., Osaka), respectively.

Experimental dogs were euthanatized by overdose anesthesia at the end of the experiment and examined for macroscopic lesion and the number of heartworms remaining in the heart and pulmonary arteries.

RESULTS

The mean number of heartworms removed in mild, hemoptysis and ascites cases were 49.8, 38.0 and 55.8, respectively, and removal efficiency was 90.2% in total (Table 1). Relatively low removal efficiency seemed to be observed in cases with remarkable enlargement of the pulmonary arteries or embolism with dead heartworms. Low removal efficiencies were also seen in cases harboring immature worms in the peripheral pulmonary arteries.

There were no dead dogs during removal manipulations in all mild and serious cases. Premature heart beats were seen during the manipulation of the forceps by monitoring with electrocardiography. It might be induced by the irritation of the forceps, but no other abnormal signs were seen. On macroscopy, thrombosis in the jugular vein was observed in some cases, but no other lesions owing to manipulation of the forceps were seen in the heart or pulmonary arteries in all cases.

The improvement of clinical signs after removal in mild cases were almost the same

Table 1. Number of heartworms removed from pulmonary arteries using flexible alligator forceps

Group	Dog			No. of removed heartworms	Removal efficiency (%)
	Number	Age (year)	Body weight (kg)		
Mild cases	23	4.6±2.2 ^{a)} (3-11) ^{b)}	10.1±3.2 (5.5-15.5)	49.8±44.6 (13-229)	89.9±6.9 ^{c)} (78-98)
Hemoptysis cases	4	3.7±1.0 (3-5)	11.8±3.1 (9-12)	38.0±23.4 (16-71)	NC ^{d)}
Ascites cases	9	5.6±2.0 (3-10)	13.4±9.1 (6-31)	55.8±43.5 (5-121)	95.7 ^{e)}
Total	36	4.8±2.1 (3-11)	11.1±.53 (5.5-31)	50.0±41.9 (5-229)	90.2±6.8 (78-98)

- a) Mean±standard deviation.
- b) Range.
- c) n=9.
- d) Not calculated.
- e) n=1.

Table 2. Clinical signs before and after heartworm removal in mild cases

Sign	Before removal (n=23)	1 week after (n=23)	4 weeks after (n=18)
Anemic color in visible membranes	14 ^{a)}	8	3
Harsh pulmonary vesicular sound	6	4	0
Coughing	6	1	0
Dyspnea	2	1	0
Accentuated second heart sound	9	2	1
Systolic heart murmur	4	3	2
Arrhythmia	11	8	6
No signs	2	5	9

- a) Number of dogs.

in every case. Slight to moderate anemia, sporadic coughing, harsh pulmonary vesicular sound, dyspnea, accentuated second heart sound or systolic murmur were observed in 21 of 23 cases before removal. These clinical signs were relieved or disappeared by 1 or 4 weeks after removal (Table 2). However, systolic murmur and arrhythmia remained in many cases even at

4 weeks after. Edematous or nodular thickening of the tricuspid and mitral valvular leaflets was observed on macroscopy in the cases with systolic murmur.

Although mean Ht values did not change significantly after removal in mild cases (Table 3), low Ht values (22 to 29%) in 4 of 5 cases before removal increased to 30 to 38% after removal. Changes in Hb concentrations and RBC counts were almost parallel with Ht values. Total WBC counts significantly decreased with decreases in neutrophils and eosinophils at 4 weeks after removal. Mean T.P concentrations did not change throughout the experiment, but mean A/G ratio decreased at 1 week after. These changes were due to a temporal decrease of albumin and increase of α_2 -globulin. Mean GPT activity elevated slightly 1 week after. Mean LDH and CK activities, as well as mean BUN values, did not change significantly at 1 and 4 weeks after. However, high LDH activities (181 to 306 IU/l) in 8 of 17 cases before removal fell to 61 to 149 IU/l in 7 of 8 cases at 1 or 4 weeks after. High CK activities (53 to 124

Table 3. Changes in hematological and biochemical data before and after heartworm removal in mild cases

Item	Before removal		1 week after		4 weeks after	
	n	Mean±SD	n	Mean±SD	n	Mean±SD
HT (%)	23	34±7 (22-44) ^{a)}	23	33±6 (23-44)	17	35±6 (24-44)
WBC ($\times 10^2/\mu$ l)	20	172±62 (99-406)	20	172±61 (67-319)	16	123±44 ^{a,b)} (66-220)
T.P (g/dl)	23	7.0±1.0 (5.0-9.0)	23	7.0±0.9 (5.0-8.6)	18	6.7±0.9 (4.8-8.2)
Albumin (g/dl)	23	2.8±0.4 (2.2-4.0)	23	2.6±0.4* (1.8-3.3)	18	2.7±0.4 (1.9-3.2)
A/G ratio	23	0.7±0.3 (0.5-1.7)	23	0.6±0.1* (0.4-0.9)	18	0.7±0.1 (0.4-1.0)
GPT (IU/l)	23	51±46 (18-238)	23	64±56* (19-262)	17	45±29 (20-137)
LDH (IU/l)	17	183±58 (94-306)	17	144±76 (56-323)	15	152±84 (28-303)
CK (IU/l)	17	38±32 (5-124)	17	25±16 (11-67)	15	29±23 (1-80)
BUN (mg/l)	23	17±6 (7-27)	23	17±6 (10-27)	18	18±7 (9-37)

a) Range.

b) Significantly different from those before removal at $p < 0.05$.

IU/l) in 5 of 17 cases before removal also fell to 13 to 41 IU/l at 1 week after.

The changes in clinical findings of serious cases varied in each case. In cases with hemoptysis, one case discharged a large amount of blood with coughing several times for 3 days before removal, and showed less activity and anorexia. In this case, vigor, appetite and other signs recovered gradually, and a small amount of hemoptysis was seen only on time 3 weeks after removal. In the other 3 cases, slight hemoptysis were seen with coughing several times before removal, but the general condition was relatively good. In these cases, coughing, hemoptysis and the other signs recovered rapidly after removal (Table 4).

In the cases with ascites, less activity and anorexia had been observed since 1 to 3 months before removal. Three of 9 cases with ascites were given medical therapies, but the signs were worse at the 1st admis-

sion. Six cases with ascites showed marked emaciation, difficulty in standing, dyspnea and other severe signs. Two of them were in hypothermia (36.8 and 37.0°C) with marked prostration. Removal of fluid from abdominal or thoracic cavities was performed before the removal in 5 cases with severe ascites or in one case with hydrothorax. No dogs died during or immediately after removal manipulation in all such serious cases, and relief of their general condition was relatively rapid. Ascites disappeared within 1 to 3 weeks in 7 of 9 cases. Other signs noticed before the removal also improved within 4 weeks after in almost all cases, but systolic murmur was not relieved in 3 or 4 cases.

In cases with hemoptysis, the mean values of hematological and biochemical data except LDH activity did not change significantly after removal (Table 5). However, low Ht values (23 to 27%) before removal

Table 4. Clinical signs before and after heartworm removal in serious cases

Sign	Hemoptysis case (n=4)			Ascites case (n=9)		
	Before removal	1 week after	4 weeks after	Before removal	1 week after	4 weeks after
Anemic color in visible membranes	3 ^{a)}	0	0	8	8	6
Harsh pulmonary vesicular sound	4	1	0	7	4	2
Coughing	4	1	1	3	0	0
Dyspnea	3	0	0	8	2	0
Accentuated second heart sound	3	0	1	9	6	4
Systolic heart murmur	0	0	0	4	3	3
Arrhythmia	2	2	1	6	4	4
Edema in subcutis	0	0	0	2	1	0
Icterus	0	0	0	3	3	0
Loss of vigor	2	0	0	9	5	1
Ascites	0	0	0	9	6	2
Hemoptysis	4	1 ^{b)}	0	0	0	0

a) Number of dogs.

b) Slight hemoptysis occurred at 3 weeks after removal.

increased in 2 cases, high WBC count ($400 \times 10^2/\mu\text{l}$) and high CK activity (240 IU/l) decreased in 1 case after removal, respectively.

In cases with ascites, the mean Ht value increased significantly at 1 and 4 weeks after removal. The mean WBC count did not change after removal, and high WBC counts (144 to $451 \times 10^2/\mu\text{l}$) in 5 of 9 cases before removal decreased at 4 weeks after. Mean T.P and albumin concentrations were considerably low before removal, and these concentrations tended to increase after removal. In globulin fractions, α_2 -globulin concentrations increased in 3 of 9 cases at 1 week after and β - and γ -globulin concentrations decreased in 2 cases at 4 weeks after. Mean A/G ratio did not change after removal. Mean GPT activity was slightly high throughout the experiment. This was owing

to high levels (317–685 IU/l) in a case throughout the experiment and to temporal increase of the activity in a case at 1 and 4 weeks after removal, but those in the other cases were nearly within the normal range or slightly decreased after removal. Mean LDH activity fell at 4 weeks after removal. On analysis of LDH isozyme in 2 cases, decreases of LDH activities were mainly due to the decrease of LDH₃- and LDH₅-isozymes. Mean CK activity tended to decrease after removal. In 4 cases with high CK level before removal, the enlarged heart reduced in size 1 week after on radiography and echocardiography. On analysis of CK isozyme in 3 cases, the decreases of CK activities were due to a large decrease in the amount of MM-isozyme and a small amount of BB-isozyme. Moderately high BUN values in 2 cases before removal did not

Table 5. Changes in hematological and biochemical data before and after heartworm removal in serious cases

Item	Hemoptysis cases (n=4)			Ascites cases (n=19)		
	Before removal	1 week after	4 weeks after	Before removal	1 week after	4 weeks after
Ht (%)	30±7 ^{a)} (23-39) ^{b)}	32±5 (28-39)	33±4 (29-37)	25±8 (12-38)	30±7 ^{*c)} (18-38)	30±6 [*] (23-38)
WBC (×10 ³ /μl)	209±129 (116-400)	218±77 (107-270)	138±21 (118-166)	238±94 (144-451)	253±143 (79-487)	189±95 (94-419)
T.P (g/dl)	7.7±0.9 (7.0-8.8)	7.4±0.6 (7.0-8.2)	7.4±0.7 (6.8-8.4)	6.0±1.3 (4.4-8.8)	6.8±0.9 [*] (5.9-8.9)	6.6±1.5 (4.8-9.2)
Albumin (g/dl)	3.2±0.2 (3-3.4)	3.0±0.2 (3.1-2.7)	2.9±0.6 (2.0-3.3)	1.7±1.0 (0.5-3.2)	2.0±0.9 ^{**d)} (0.8-3.6)	2.2±0.9 ^{**} (1.0-3.4)
A/G ratio	0.7±0.2 (0.5-1.0)	0.7±0.2 (0.5-0.8)	0.6±0.2 (0.4-0.8)	0.4±0.2 (0.1-0.9)	0.4±0.2 (0.1-0.8)	0.5±0.2 (0.3-0.9)
GPT (IU/l)	64±18 (43-80)	78±48 (37-129)	56±45 (30-123)	68±94 (17-317)	103±135 (18-370)	118±213 (12-685)
LDH (IU/l)	232±65 (144-303)	141±50.3 (93-212)	101±35 ^{**} (62-135)	255±152 ^{e)} (100-513)	99±119 ^{e)} (63-415)	153±60 ^{e)*} (965-288)
CK (IU/l)	80±106 (22-240)	23±11 (8-36)	24±7 (17-31)	104±120 ^{e)} (14-372)	80±110 ^{e)} (11-345)	26±17 ^{e)} (5-60)
BUN (mg/l)	17±9 (9-30)	16±5 (10-21)	11±3 (9-15)	25±18 (7-59)	58±95 (13-309)	27±18 (2-56)

a) Mean±standard deviation.

b) Range.

c) Significantly different from those before removal at p<0.05.

d) Significantly different from those before removal at p<0.01.

e) n=8.

change after removal.

Post-removal progress was good in all cases with hemoptysis at 4 to 17 months after removal. In cases with ascites, 7 of 9 cases also showed good progress at 6 to 26 months after. In 2 cases with ascites, slight or severe ascites and anemia remained at 2 and 4 months, but they gradually disappeared after that. In the other 2 cases with ascites, one case relapsed into ascites after 3 months and died at 3.5 months. On macroscopy, this dog displayed severe hypertrophy and sclerosis of the tricuspid valvular leaflets and chords. In another case, vigor and appetite recovered rather well at 4 weeks, but oliguria and high BUN value remained, and the general condition became worse at 3 months, and the dog died at 4 months.

DISCUSSION

The efficiencies of heartworm removal in dogs with common dirofilariasis using a flexible alligator forceps was over 90% both in the present and previous studies [7]. Heartworm echoes were noticed only in the pulmonary arteries by two-dimensional echocardiography, and heartworms were removed only from the pulmonary arteries, but not from the ventricle in both studies. These facts corroborated the supposition that the normal habitat of heartworms is the pulmonary arteries [15]. The efficiency of heartworm removal was almost the same as that by thoracotomy [1, 5, 14, 15]. In thoracotomy, some dogs died during or immediately after surgery, and survival rates were 57 to 90% [1, 5, 14, 15]. There are no detailed descriptions of clinical fea-

tures following heartworm removal by thoracotomy, but the plural adhesion is observed at a high rate [14]. Therefore, thoracotomy might not be applied in serious cases. On the other hand, the heartworm removal using flexible alligator forceps could be applied safely even in severe serious cases with ascites and hypothermia, without surgical attacks and sequelae, and with good post-removal progress. Therefore, this method was by far greater than in thoracotomy or chemotherapy.

Clinical signs in heartworm disease were decrease of exercise tolerance, dyspnea, coughing, anemia, ascites, hemoptysis, cachexia and so on. These signs were mainly induced by right side congestive heart failure due to increased right ventricular afterload which was elicited by parasitism of adult heartworms and by lesions of the pulmonary arteries [11, 13]. The main clinical signs improved or disappeared without special medication after removal in mild cases, and did not recur after discontinuing the medication in many serious cases. These findings suggest that congestive heart failure or inflammation of the pulmonary arteries are relieved by heartworm removal. Actually, hemodynamic parameters were markedly improved after removal [demonstrated in a separate paper]. However, the findings such as arrhythmia, systolic murmur and renal failure which were not correlated directly with parasitism of adult heartworms were not relieved after the removal. Hemoptysis develops when the pulmonary vessels are ruptured by lesions or irritation of live or dead worms [13]. Hemoptysis disappeared completely after heartworm removal in 3 of 4 cases, but relapsed after 3 weeks in one case. These findings suggest that irritation by live heartworms is mostly eliminated by heartworm removal, but that reduction of lesions in pulmonary arteries requires a long time. Thus, the case with a severe lesion occasionally relapsed into

hemoptysis by a slight irritation of a few heartworms remaining or other causes.

It has been considered that anemia in chronic heartworm disease develops by heartworm-induced trauma [13] or that intravascular hemolysis depending on increase of the mechanical fragility of erythrocytes resulted from the liver dysfunction or abnormal blood stream associated with heartworms and lesions in pulmonary arteries [6, 10]. The improvement of anemia might depend on excluding the above causes after heartworm removal. Leukocytosis in dogs with heartworms frequently occurred, and it was considered that leukocytosis was accompanied by inflammation owing to congestive heart failure and pneumonia [13]. WBC count decreased 4 weeks after the removal in mild and serious cases. This finding might reflect a recovery from congestive heart failure or inflammation of the lung. The increased WBC count and α_2 -globulin at 1 week after the removal might be associated with the inflammation due to the surgery. The increased serum albumin concentration after the removal in the cases with ascites suggested the decreased leak of albumin into ascites resulted from recovery of congestion and dysfunction in the liver. Other findings such as decreases of β - and γ -globulins, a decrease of LDH₅-isozyme and disappearance of icterus also suggested improved liver function or healed injury. The increase of GPT activity 1 week after contradicted the above findings. This finding might be influenced by the surgery, but the true cause was unknown in this study. CK activity decreased remarkably 1 week after in some of the mild and serious cases. The decrease of CK activity was due to a large decrease in the amount of MM-isozymes and a small amount of BB-isozyme. A large amount of MM-isozyme was contained in the skeletal muscle and myocardium, a large amount of BB-isozyme in the brain and a small amount of BB-isozyme in the lung and

blood vessels in dogs [9]. The decrease of CK activity suggested recoveries from injuries of the myocardium, lung or blood vessels after removal.

From these results, it was considered that the removal of heartworms from the pulmonary arteries with the flexible alligator forceps was safe and efficacious as a radical therapy for dogs with mild and serious heartworm disease.

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要 約

フレキシブル・アリゲーター鉗子による肺動脈内犬糸状虫摘出後の臨床効果：石原勝也・佐々木栄英・北川均・葉山みどり（岐阜大学農学部家畜内科学講座）——一般病型の犬糸状虫症36例について、フレキシブル・アリゲーター鉗子を用いて肺動脈から犬糸状虫を摘出し、臨床効果を検討した。摘出操作による死亡例はなく、最終的に剖検した18例の平均摘出率は約90%であった。軽症例（23例）では、摘出後速やかに発咳、貧血などの症状が消失した。重症例（13例）は腹水例（9例）および咯血例（4例）より成り、いずれの症例にも元気、食欲の消失、発咳、呼吸困難および貧血などがあり、腹水例では皮下浮腫、胸水、黄疸あるいは低体温なども散見された。犬糸状虫摘出後、全例とも一般状態は4週後までにかなり回復し、多くの症状も4週後までに消失した。その後の経過は、咯血例では全例、腹水例では9例中7例が良好であったが、腹水例2例は重度の弁膜症あるいは腎不全により3.5ヵ月と4ヵ月後に死亡した。血液生化学的所見では、多くの軽症例および重症例で貧血、白血球增多症、低アルブミン血症などが摘出後1週または4週までに回復し、また、LDH及びCK活性値上昇例では、摘出後1週ないし4週までに著しく低下した。この鉗子による虫体摘出法は、犬糸状虫症の重症例にも適用できる原因療法として推奨できる。