Clinical Studies on *Dirofilarial* Hemoglobinuria: Central Venous Pressure Before and After Heartworm Removal

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ABSTRACT. Central venous pressure (CVP) was measured before and immediately after surgical heartworm removal from the jugular vein in 22 dogs with *dirofilarial* hemoglobinuria (caval syndrome). In 19 cases which recovered by surgical removal, CVP was considerably high from 32 mmH₂O to 187 mmH₂O with a mean of 101.6 ± 35.1 (S.D.) mmH₂O before heartworm removal. CVP fell in all cases immediately after heartworm removal. The mean CVP after heartworm removal was 61.0 ± 42.9 mmH₂O. This level was significantly lower than that before heartworm removal ($p < 0.001$). After heartworm removal, systolic cardiac murmur and jugular pulse improved and hemoglobinemia and hemoglobinuria disappeared. Two of 3 cases, which died after heartworm removal, indicated a high CVP over 200 mmH₂O and showed the signs of severe circulatory failure (right heart failure). They also displayed terminal signs such as prostration and low body temperature. After heartworm removal, systolic murmur improved passably, but high CVP levels over 175 mmH₂O remained in both cases. Another case did not indicate a high CVP level (66 mmH₂O) before heartworm removal. Forty-seven heartworms were removed from this case. However, there was no recovery of the systolic murmur, and CVP fell only 5 mmH₂O. In this case, the knotting of a heartworm around the tricuspid chordae was confirmed by autopsy. It was considered that the existence of heartworm mass at the tricuspid valve orifice would be the cause of the high CVP level in this disease. And it was suggested that the tricuspid insufficiency by heartworm mass at the tricuspid valve orifice would be the direct cause of acute circulatory insufficiency that indicates the onset of *dirofilarial* hemoglobinuria together with many symptoms.—**KEY WORDS:** central venous pressure, *dirofilarial* hemoglobinuria, dog, heartworm removal.

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Central venous pressure (CVP) is the luminal pressure of the intrathoracic anterior or posterior venae cavae near the atrium, and it indicated the flow pressure of venous blood to the right atrium [4, 11]. CVP level is determined by a complex interaction of blood volume, cardiac pumping action and alterations in the vascular bed [1, 4, 10–12]. It has been important clinically to the guide for body fluid replacement and index of cardiac pumping ability [1, 7, 12].

In *dirofilarial* hemoglobinuria (caval syndrome), massive heartworms have always been found at the tricuspid valve orifice by autopsy [5, 6] and echocardiography [9]. Therefore, this disease always shows the

symptoms which indicate tricuspid insufficiency such as positive jugular pulse and systolic cardiac murmur. The dilatation of pulmonary arteries is also observed in radiograph [9]. There will be acting as the factors to elevate CVP. After surgical removal of heartworms, however, jugular pulse and cardiac murmur disappear, and general states are also dramatically improved. These findings suggest that CVP will change after heartworm removal. This study describes the CVP level before and after heartworm removal, and discusses the relationship between the CVP and heartworms at the tricuspid valve orifice in *dirofilarial* hemoglobinuria.

Table 1. Laboratory test results in dirofilarial hemoglobinuria cases

Item	n	Mean	S.D. ^{a)}
Ht (%)	20	21.2	7.7
Hb (g/dl)	14	7.4	3.1
RBC ($\times 10^4/\mu l$)	14	340	119
WBC ($\times 10^2/\mu l$)	14	210	104
GOT (IU/l) ^{b)}	15	245.3	219.4
GPT (IU/l)	15	163.7	169.7
LDH (IU/l)	15	1081	926
ALP (IU/l)	14	359.8	270.6
Total protein (g/dl)	14	7.6	1.3
Albumin (g/dl)	14	2.11	0.51
A/G ratio	14	0.40	0.14
Blood urea nitrogen (mg/dl)	15	47.8	43.9
Glucose (mg/dl)	13	95.8	20.7

a) Standard deviation.

b) International unit/liter.

MATERIALS AND METHODS

A total of 22 dogs from 3 to 10 years old (18 males, 4 females) were used. They were diagnosed as dirofilarial hemoglobinuria from their chief signs and laboratory test results. These dogs all displayed the signs of so-called "caval syndrome" such as hemoglobinuria, weakness, dyspnea, anemia, positive jugular pulse and systolic cardiac murmur, and some cases showed ascites and jaundice. Nineteen cases recovered and 3 cases died after surgical heartworm removal. Table 1 shows the laboratory test results of dirofilarial hemoglobinuria cases before removal.

Heartworm removal from the external jugular vein was carried out by modified Fujii's method [2]. The dog was restrained in the right lateral recumbency and anesthetized locally with procain hydrochloride. CVP was measured with a commercial kit (C.V.P. Set, Top Surgical Mfg. Co., Ltd., Tokyo). A catheter, filled with 3.8% sodium citrate solution and connected to the fluid manometer, was inserted from the external jugular vein to the anterior or posterior venae cavae. The catheter position was established under flu-

oroscopy. The 0-reference was the midpoint of thoracic thickness at the 3rd intercostal space. CVP was measured before and immediately after heartworm removal. Plasma hemoglobin concentration was measured by benzidine reaction, and other conventional tests were carried out by the standard procedures.

RESULTS

Table 2 shows the number of removed heartworms and CVP before and immediately after heartworm removal in the recovery group. The number of removed worms was from 17 to 78 with a mean of 44.4. Before removal, CVP of 19 cases ranged from 32 to 187 mmH₂O with a mean of 101.6 ± 35.1 (standard deviation) mmH₂O. CVP fell in all cases immediately after heartworm removal. CVP ranged from -10 mmH₂O to 130 mmH₂O with a mean of 61.0 ± 42.7 mmH₂O after heartworm removal. There was a significant difference between the level of CVP before and after heartworm removal ($p < 0.001$). The improvement of systolic cardiac murmur and jugular pulse were observed in all cases after heartworm removal.

Fig. 1 shows the plasma hemoglobin concentration before and 20 hr after heartworm removal. Before heartworm removal, plasma hemoglobin concentration revealed a high level with a mean of 242 ± 230 mg/dl. Plasma hemoglobin concentration already decreased 2 hr after heartworm removal. Twenty hr after heartworm removal, it decreased in all cases. The mean was 18 ± 31 mg/dl 20 hr after heartworm removal.

The clinical data of 3 dead cases are shown in Table 3. CVP was remarkably high (above 200 mmH₂O) in 2 cases (Nos. 279 and 530) before heartworm removal. Nos. 279 and 530 showed caval syndrome together with prostration, low body temperature and ascites. No. 530 also was semicomatose and jaundiced. Removed heartworms numbered 22 in

Table 2. Number of removed heartworms and central venous pressure before and immediately after heartworm removal in the recovery group

Dog No.	No. of removed worms	Central venous pressure (mmH ₂ O)		
		Before removal	After removal ^{a)}	Discrepancy
268	23	100	84	16
273	32	112	98	14
275	50	90	51	39
280	77	132	92	40
281	22	121	97	24
282	58	116	101	15
283	33	32	-5	37
284	63	46	17	29
285	49	96	26	70
286	78	106	54	52
533	38	111	50	61
540	33	56	-10	66
542	20	112	87	25
551	17	134	111	23
560	50	63	3	60
563	22	117	104	13
571	48	187	130	57
596	63	92	30	62
597	58	107	39	68
Mean	43.9	101.6	61.0	40.6
S.D. ^{b)}	19.2	35.1	42.9	20.6

a) Immediately after heartworm removal.

b) Standard deviation.

Fig. 1. Plasma hemoglobin concentrations before and 20 hr after heartworm removal.

No. 279, and 64 in No. 530. After heartworm removal, CVP fell from 216 mmH₂O to 200 mmH₂O in No. 279, and from 254 mmH₂O to 175 mmH₂O in No. 530. Even though cardiac murmur, jugular pulse and hemoglobinuria improved passably, and plasma hemoglobin concentration decreased in both cases, general states did not improve. No. 279 died 9 days after heartworm removal (no autopsy). No. 530 died 4 days after removal. On autopsy, there were dilatation of the right heart and pulmonary artery and pulmonary edema. One heartworm was located in the right atrium and 47 in the right ventricle and pulmonary artery. No heartworms were found at the tricuspid valve orifice.

No. 549 showed caval syndrome taken with prostration and severe jaundice (serum bilirubin 14.2 mg/dl). Forty-seven heartworms were removed surgically, but systolic cardiac

Table 3. Clinical data before and after heartworm removal in 3 dead cases

Item	Dog No.		
	279	530	549 ^{a)}
Sex	Female	Male	Male
Age (Year)	6	5	5
Body temperature (°C)	37.1	37.4	39.1
Heart rate (beat/min)	146	144	148
Chief sign	Caval syndrome ^{b)} , cough, ascites	Caval syndrome, subcutaneous edema, ascites jaundice, semi- comatose	Caval syndrome, jaundice
No. of removed heartworms	22	64	47
CVP (mmH ₂ O)			
Before removal	216	254	66
Immediately after removal	200	175	61
Plasma Hb (mg/dl)			
Before removal	281	205	83
20 hr after removal	11	41	47 ^{c)}
Ht (%) ^{d)}	14	18	23
Hb (g/dl)	ND ^{e)}	5.5	6.7
RBC ($\times 10^4/\mu l$)	ND	258	311
WBC ($\times 10^2/\mu l$)	ND	286	401
GOT (IU/l)	124	170	101
GPT (IU/l)	114	352	327
Blood urea nitrogen (mg/dl)	63.8	188.7	27.6
Bilirubin (mg/dl)	0.57	8.64	14.02

a) Dead heartworm was knotted around the tricuspid cordae in this case.

b) Hemoglobinemia, hemoglobinuria, prostration, dyspnea, anemia, jugular pulse and systolic cardiac murmur.

c) 5 hr after removal.

d) Hematological and biochemical data were those from before removal.

e) Not done.

murmur and jugular pulse evidenced no recovery. CVP fell only 5 mmH₂O from 66 mmH₂O. Plasma hemoglobin concentration decreased 5 hr after heartworm removal. This case died 15 hr after treatment. On autopsy, 12 alive heartworms were located in the right ventricle and pulmonary artery and 1 dead heartworm knotted around the tricuspid chordae. The dilatation of the right heart and liver congestion was severe.

There was a significant positive correlation between the number of removed worms and the CVP discrepancy before and after heartworm removal in 21 cases except No. 549 as shown in Fig. 2 ($r=0.51$, $p<0.025$).

DISCUSSION

The normal CVP level of dogs has been reported to range from 20 mmH₂O to 60 mmH₂O [3], -1 cmH₂O to 5 cmH₂O [7], 1.78 ± 1.24 mmH₂O [8] and from 0 cmH₂O to 5 cmH₂O [4]. It is difficult to compare our data with these values simply, because CVP was altered by the position of the dog, the height of 0-point, and the use of general anesthesia. However, taking these points into account, it is considered that CVP in dirofilarial hemoglobinuria can be regarded as considerably high. As mentioned above, massive heartworms exist at the tricuspid

Fig. 2. Correlation between the discrepancy of central venous pressure before and after heartworm removal and number of removed heartworms.

○ : Recovery case.

● : Dead case.

valve orifice [5, 6]. The signs which indicated tricuspid insufficiency were observed and the regurgitation of contrast medium at the tricuspid valve was also clearly observed by angiocardiology [9]. After heartworm removal, CVP fell significantly, and the findings which indicate tricuspid insufficiency improved. These findings indicate a direct relationship between the elevated CVP and massive heartworms at the tricuspid valve orifice. However, in some cases high CVP levels remained immediately after heartworm removal in the recovery group. In the cases which were also measured 20 hr after heartworm removal, CVP level was lower than that immediately after removal. These findings suggest that the cardiac function (right side cardiac output) and venous return (effective circulating blood volume and cardiovascular volume) do not show sufficient improvement immediately after heartworm removal.

It has been generally said that markedly high CVP (>200 mmH₂O) indicated the severe right heart failure and pulmonary edema [4]. In this study, 2 of 3 cases had a marked-

ly high CVP level, and displayed the signs of severe right heart failure. It was considered that the influence of right heart failure, pulmonary edema in addition to tricuspid insufficiency by heartworm mass for CVP were large in these cases. These cases also displayed the terminal signs such as prostration and low body temperature. Though it has to be investigated in more cases, the extremely high CVP levels may indicate a bad prognosis in dirofilarial hemoglobinuria. From the above mentioned findings, it was considered that CVP was one of the indices for the degree of tricuspid insufficiency and improvement of that in dirofilarial hemoglobinuria.

In No. 549, the number of removed worms was relatively large (47). After heartworm removal, however, CVP fell only 5 mmH₂O, and systolic cardiac murmur did not improve. These findings suggest the existence of tricuspid insufficiency different from that caused by massive heartworms at the tricuspid orifice. No. 549 had a knotted heartworm around the tricuspid chordae as revealed by autopsy. This case was complicated with dirofilarial hemoglobinuria and knotting of a heartworm around the tricuspid chordae at the same time. The case in which a heartworm was knotted around the tricuspid chordae revealed intravascular hemolysis and could be detected hemoglobin in urine. However, these were not so clear as in dirofilarial hemoglobinuria [9].

From these findings (fall of CVP, decrease of plasma hemoglobin concentration and improvement of clinical signs after heartworm removal), it was suggested that the tricuspid insufficiency by heartworm mass at the tricuspid valve orifice would be the direct cause of the circulatory disturbance that indicates the onset of dirofilarial hemoglobinuria (caval syndrome) together with many symptoms.

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要 約

犬糸虫性血色素尿症に関する研究。糸状虫摘出前後の中心静脈圧：北川 均・佐々木栄英・石原勝也（岐阜大学農学部家畜内科学教室）——犬糸状虫性血色素尿症（caval syndrome）22例について、糸状虫摘出手術直前と摘出直後に中心静脈圧（CVP）を測定した。摘出後回復した19例のCVPは、摘出前から高く 101.6 ± 35.1 (S.D.) mmH₂O であった。17～78匹の糸状虫を摘出した直後のCVPは全例で下降し、その平均値は摘出前より有意に低く 61.0 ± 42.7 mmH₂O となった ($P < 0.001$)。糸状虫摘出後、頸静脈拍動と収縮期心内雑音は改善され、血漿 hemoglobin 濃度は低下し、血色素尿も消失した。糸状虫摘出後死亡した3例中2例では、CVPは200 mmH₂O以上の高値を示し、激しい右心不全を示唆した。これらの例では虚脱や低体温等の末期症状が認められた。糸状虫摘出後、収縮期雑音の改善、血漿 hemoglobin 濃度の低下、血色素尿の消失が認められ、CVPも下降したが、その値は高く179 mmH₂O以上であった。他の1例では、摘出前のCVPの上昇は軽く66 mmH₂Oであった。この例では、47匹の糸状虫を摘出した後も、収縮期雑音は改善されず、CVPの下降も5 mmH₂Oにとどまり、剖検では糸状虫の三尖弁腱索でん絡が確認された。犬糸状虫性血色素尿症におけるCVP上昇の主因は、三尖弁口部位に束状に寄生する糸状虫であり、三尖弁機能不全に起因する循環不全がこの病態の発症原因であることが示唆された。