犬糸状虫性血色素尿症に関する研究,肺動脈から犬糸状虫の移動を誘発する右心系の血流動態の変化

誌名	Japanese journal of veterinary science
ISSN	00215295
著者	北川, 均 佐々木, 栄英 鋤柄, 卓夫
巻/号	49巻3号
掲載ページ	p. 485-489
発行年月	1987年6月

Clinical Studies on Canine Dirofilarial Hemoglobinuria: Changes in Right Heart Hemodynamics Inducing Heartworm Migration from Pulmonary Artery

Hitoshi KITAGAWA, Yoshihide SASAKI, Takuo SUKIGARA, and Katsuya ISHIHARA

Department of Veterinary Internal Medicine, Faculty of Agriculture, University of Gifu, 1–1 Yanagido, Gifu 501–11, Japan

(Received 22 Jaunary 1987/Accepted 6 March 1987)

ABSTRACT. In order to examine the changes in hemodynamics inducing heartworm migration from the pulmonary artery, the pressures of the right ventricle and pulmonary artery and right cardiac output were measured after administration of 1.5 mg/kg body weight of milbemycin D (Milbe) in 6 heartworm-infected dogs under general anesthesia. The heartworms migrated from the pulmonary artery to the tricuspid valve orifice and right atrium from 50 to 105 min after Milbe administration in 4 of the dogs. After Milbe administration, heart rate increased transiently, then subsequently decreased. Systolic right ventricular and mean pulmonary pressures did not show uniform changes in heartworm-migration cases. The right cardiac output decreased clearly before heartworm migration in all such cases. Stroke volume (right cardiac output/heart rate), cardiac index (right cardiac output/kg body weight) and stroke index (stroke volume/kg body weight) also decreased in heartworm-migration cases. The heartworm migration from the pulmonary artery towards the right atrium may be associated with the decreases of blood flow volume and velocity in the right heart.—KEY WORDS: cardiac output, dirofilarial hemoglobinuria, dog, heartworm migration, milbemycin D.

Jpn. J. Vet. Sci. 49(3): 485–489, 1987

Canine dirofilarial hemoglobinuria (caval syndrome) occurs by the migration of heartworms from the pulmonary artery to the tricuspid valve orifice and right atrium [7]. In this disease, the heartworms at the tricuspid valve orifice cause many disturbances such as acute circulatory insufficiency, intravascular hemolysis, liver and renal failures and others [4, 6, 7]. However, the cause of heartworm migration from the pulmonary artery towards the right atrium has not been clear. Some investigators suggested that parasitism of a critically large number of heartworms and pulmonary hypertension were the predisposing factors in the development of this disease [1, 2, 10]. Certainly, many dogs so affected harbored a large number of heartworms [1, 3–5]. However, all dogs did not harbor so many worms [4, 8], and parasitism of a critical number of heartworms cannot explain sufficiently the heartworm migration.

In the previous study, the authors reported the onset of canine dirofilarial hemoglobinuria induced administration of milbemycin D (Milbe), and suggested that decreases of cardiac output and blood flow velocity might cause the migration of heartworms from the pulmonary artery [8]. In the present study, in order to examine the changes in hemodynamics inducing heartworm migration, the pressures of he right ventricle and pulmonary artery and right cardiac output were measured before and after administration of Milbe. The data indicated that a decrease of cardiac output induced the heartworm migration from the pulmonary artery towards the right atrium.

MATERIALS AND METHODS

Six adult Japanese mongrel dogs, 3 to 10

Table 1. Experimental dogs

Group	Dog No.	Age (y)	Sex	Body weight (kg)	No. of heartworms	No. of worms/ kg body weight
Hearworm-migration	1036	3	Male	9.0	20	2.2
	1039	5	Male	6.0	20	3.3
	1148	10	Male	9.0	27	3.0
	1152	4	Male	10.0	45	4.5
Heartworm-non-migration	1081	4	Female	6.5	22	3.4
	1129	5	Female	13.5	53	3.9

years old of presumed age, and 6 to 13.5kg in body weight, were used. These dogs were heatworm (*Dirofilaria immitis*)-infected and circulating microfilaria positive. The number of heartworms in the right heart was 20 to 53, and the number of heartworms per kg body weight 2.2 to 4.5 (Table 1). The dogs were anesthetized with a drip infusion of 0.2 % ketamine-hydrochloride (Ketalar, Sankyo Co., Ltd., Tokyo). Two catheters were placed in the right ventricle and pulmonary artery via the jugular vein under fluoroscopy. Milbe (Sankyo Co., Ltd.) was administered intra-gastricly at a dose rate of 1.5 mg/kg body weight. Electrocardiograms and phonocardiograms were recorded with a Cardiojet (Nihon Kohden Corp., Tokyo). Blood pressure transducer (TP-101T, Nihon Kohden) and multipurpose polygraph (RM-85, Nihon Kohden) were used for measurement of right ventricular and pulmonary arterial pressures. For measurement of right cardiac output, a Swan-Ganz flow-directed pediatric thermodilution catheter (93–132–5F, Edwards Lad., Santa Ana, California, U.S.A.), a thermodilution amplifier and a cardiac output computer (AH-611V and EQ-611V, Nihon Kohden) were used. Stroke volume (Cardiac output/ heart rate), cardiac index (cardiac output/kg body weight) and stroke index (stroke volume/kg body weight) were calculated from each parameter. Two-dimensional echocardiography was done with a ultrasonic convex array scanner (EUB-40, Hitachi Medical Corp., Tokyo).

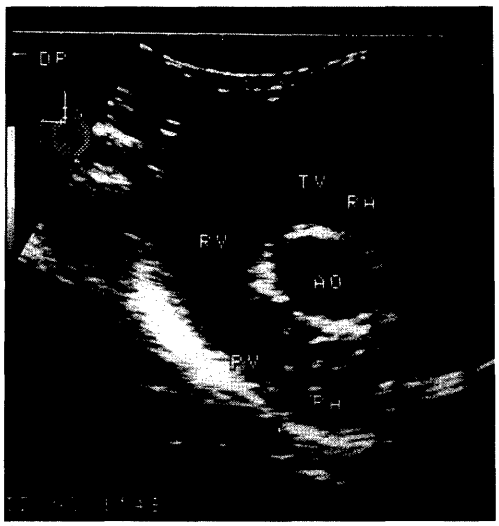

Fig. 1. Two-dimensional echocardiogram before milbemycin D administration. TV: Tricuspid valve, RA: Right atrium, RV: Right ventricle, AO: Aorta, PV: Pulmonary valve, PA: Pulmonary artery.

RESULTS

Before milbe administration, heartworms located only at the pulmonary arteries, and were not found at the right ventricle, tricuspid valve orifice and right atrium in all the cases on two-dimensional echocardiogram (Fig. 1). Heartworms migrated from the pulmonary artery to the tricuspid valve orifice and right atrium from 50 to 105 min after drug administration in 4 of the 6 cases. Two-dimensional echocardiogram immediately after heartworm migration is

shown in Fig. 2. The heartworm mass projecting from the right atrium to the right ventricle with the motion of the tricuspid valbe was the same as that in spontaneous cases. Ventricular premature heart beats appeared at the time of heartworm migration. A systolic cardiac murmur, the same as in spontaneous cases, was audible and coincided with the occurrence of heartworm echoes at the tricuspid valve orifice.

After administration of Milbe, the heart rate increased transiently in 5 of 6 cases, and decreased gradually. The heart rate was slightly higher in the heartworm-migration group immediately before heartworm migration (Table 2). Changes in systolic right ventricular pressure and mean pulmonary arterial pressure are shown in Figs. 3 and 4. Systolic right ventricular pressure and mean pulmonary arterial pressure rose strikingly in one case (No.1129) after Milbe administration, but heartworms did not migrate in this case. Another heartworm-non-migration case (No. 1081) showed the drifting changes in systolic right ventricular pressure and mean pulmonary arterial pressure. In 4 heartworm-migration cases, changes in systolic right ventricular pressure and mean pulmonary arterial pressure did not display the uniform changes; they elevated gradually and subsequently fell in one case (No. 1036), decreased slightly in one case (No.1037), and dropped but subsequently rose in two cases (Nos. 1148 and 1152).

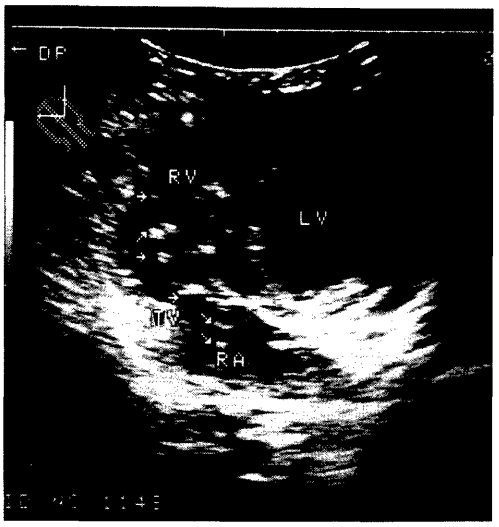

Fig. 2. Two-dimensional echocardiogram at the time of heartworm migration. RV: Right ventricle, LV: Left ventricle, TV: Tricuspid valve, RA: Right atrium, Arrow: Heartworm echo.

The changes in cardiac output are shown in Fig. 5. Cardiac output did not change in heartworm-non-migration cases. In all the heartworm-migration cases, however, cardiac output decreased clearly before heartworm migration. Cardiac output fell from 46.7 to 69.3% of the pre-administration

Table 2. Changes in indices of right heart function

Item	Group	Before administration			Before heartworm migration[a)]	
		n	Mean	SD	Mean	SD
Heart rate (beat/min)	Migration	4	118	16	133	26
	Non-migration	2	145	15	111	23
Stroke volume (ml/min/beat)	Migration	4	23.3	2.2	12.3	2.0
	Non-migration	2	28.3	7.9	31.1	10.6
Cardiac index (ml/min/kg)	Migration	4	331	54	194	39
	Non-migration	2	435	154	376	123
Stroke index (ml/min/beat/kg)	Migration	4	3.25	0.55	1.53	0.53
	Non-migration	2	3.01	0.70	2.85	0.82

a) 90 min after administration of milbemycin D in the non-migration group.

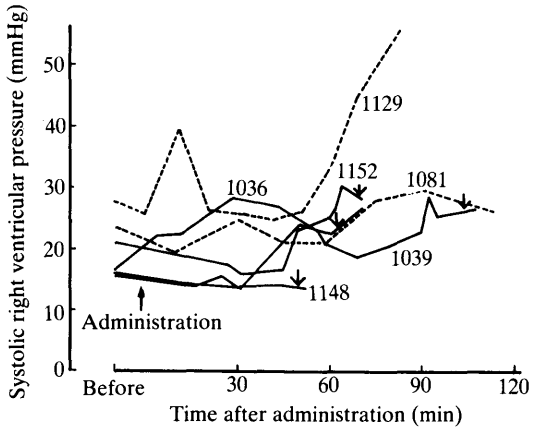

Fig. 3. Changes in systolic right ventricular pressure after milbemycin D administration. -- Heartworm-non-migration case. — Heartworm-migration case. ↓ Heartworm migration.

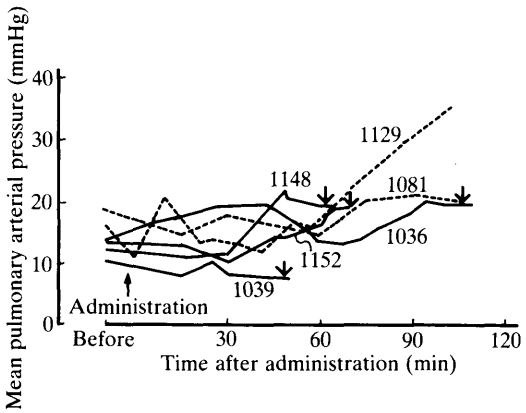

Fig. 4. Changes in mean pulmonary arterial pressure after milbemycin D administration. -- Heartworm-non-migration case. — Heartworm-migration case. ↓ Heartworm migration.

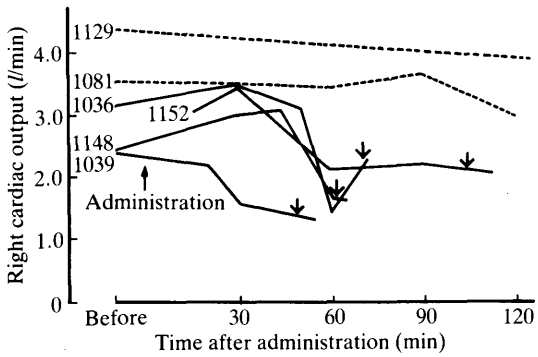

Fig. 5. Changes in right cardiac output after milbemycin D administration. -- Heartworm-non-migration case. — Heartworm-migration case. ↓ Heartworm migration.

level. Stroke volume, cardiac index and stroke index also decreased the same as cardiac output before any heartworm migration (Table 2).

DISCUSSION

Before any heartworm migration, cardiac output and stroke volume decreased clearly in the present study. These findings indicated the decreases of blood flow volume at the pulmonary artery where the heartworms existed. The heartworm migration from the pulmonary artery towards the right atrium may be associated with decreases of blood flow volume and velocity in the right heart. However, the significant increase of pulmonary arterial pressure did not induce heartworm migration in one case (No. 1129). Therefore, the pulmonary hypertension might not associate directly with the heartworm migration. However, pulmonary hypertension, which results from the parasitism of a large number of heartworms and lesions of the pulmonary artery and lung [9], may become one of the indirect causes of heartworm migration in spontaneous cases. Under this condition in heartworm disease, cardiac output may be decreased, so heartworm migration from the pulmonary artery may be induced. Other reasons for the decrease in cardiac output and heartworm migration may be the tonus of the vagus nerve (nerval depress of heart action), cardiac disfunctions following abnormality of the valves or heart muscles, or decrease of venous return in heartworm disease.

In dirofilarial hemoglobinuria induced by Milbe administration, the heartworms returned to the pulmonary artery from 21 to 117 hr after onset without treatment in all the cases [8]. The cardiac output may well recover by that time, and the recovery of

blood flow in the right ventricle and pulmonary artery may be followed by the return of heartworms to the pulmonary artery. In spontaneous cases, the heartworms cannot return to the pulmonary artery because of the duration of low blood flow in the right heart, the entanglement of heartworms themselves or other unknown reasons.

REFERENCES

1. Atwel, R. B., and Farmer, T. S. 1982. Clinical pathology of the 'caval syndrome' in canine dirofilariasis in Northern Australia. *J. Small Anim. Pract.* 23: 675–685.
2. Buoro, I. B. J., and Atwell, R. B.1984. Development of a model of caval syndrome in dogs infected with *Dirofilaria immitis.Aust. Vet. J.* 61: 267–268.
3. Fujii, I. 1975. A clinical study on the venae cavae embolism by heartworms of dogs. *Bull. Azabu Vet. Coll.* No. 30, 105–118 (in Japanese).
4. Ishihara, k., Kitagawa, H., Ojima, M., Yagata, Y., and Suganuma, Y. 1978. Clinicopathological studies on canine dirofilarial hemoglobinuria. *Jpn. J. Vet. Sci.* 40: 525–537.
5. Jackson, R. F., Lichtenberg, F., and Otto, G. F. 1962. Occurrence of adult heartworms in the venae cavae of dogs. *J. Am. Vet. Med. Assoc.* 141: 117–112.
6. Kitagawa, H., Sasaki, Y., and Ishihara, K. 1985. Clinical studies on dirofilarial hemoglobinuria: Central venous pressure before and after heartworm removal. *Jpn. J. Vet. Sci.* 47: 691–696.
7. Kitagawa, H., Sasaki, and Ishihara, K. 1986. Clinical studies on canine dirofilarial hemoglobinuria: Relationship between the presence of heartworm mass at the tricuspid valve orifice and plasma hemoglobin concentration. *Jpn. J. Vet. Sci.* 48: 99–103.
8. Kitagawa, H., Sasaki, Y., and Ishihara, K. 1986. Canine dirofilarial hemoglobinuria induced by milbemycin D administation. *Jpn. J. Vet. Sci.* 48: 517–522.
9. Rawlings, C. A. 1986. Heartworm Disease in Dogs and Cats. W. B. Saunders Co., Philadelphia.
10. Sawyer, T. K. and Weinstein, P. P. 1963. Experimentally induced canine dirofilariasis. *J. Am. Vet. Med. Assoc.* 143: 975–978.

要　約

犬糸状虫性血色素尿症に関する研究，肺動脈から犬糸状虫の移動を誘発する右心系の血流動態の変化：北川均・佐々木栄英・鋤柄卓夫・石原勝也（岐阜大学農学部家畜内科学講座）――肺動脈から犬糸状虫の移動をひきおこす血流動態の変化を検討する目的で，全身麻酔下の犬糸状虫寄生犬に milbemycin D (Milbe) を投与した後，右心室圧，肺動脈圧及び右心拍出量を測定した。Milbe 投与50～100分後，6 例中 4 例において，糸状虫は肺動脈から三尖弁口部及び右心房に移動した。Milbe 投与後，心拍数は一時的に増加したが，その後除々に減少した。糸状虫移動例では，収縮期右心室圧と平均肺動脈圧は一定の変化を示さなかったが，右心拍出量は糸状虫移動前に明瞭に減少した。1 回拍出量（右心拍出量/心拍数），心指数（右心拍出量/体重）及び拍出量指数（1 回拍出量/体重）も糸状虫移動例では減少した。肺動脈から右心房方向への糸状虫の移動には，右心系の血流量と血流速度の低下が関与するように推察された。