Sudden Cardiac Death in Calves with Experimental Heavy Infection of Strongyloides papillosus

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ABSTRACT. For obtaining the preliminary data on the pathogenesis of sudden death in calves naturally heavily infected with Strongyloides papillosus, we monitored 8 Holstein calves experimentally infected with the larvae on electrocardiographic and pneumographic changes. Six calves died suddenly on days 11 to 17 after infection. Sinus tachycardia had been recorded continuously since 1 to 6 days before death. Heart rates increased gradually until death. Since 1 or 2 days before death, various patterns of tachyarrhythmia and bradyarrhythmia had been observed among patterns of sinus tachycardia. Arrhythmias included serious ventricular premature beat, paroxysmal ventricular tachycardia, complete atrioventricular block and so on. The terminal pattern observed suddenly in all of the cases was ventricular arrhythmias consisting of serial ventricular tachycardia, flutter and fibrillation, which were followed by respiratory arrest. Abnormal pneumograms were not obtained before the terminal ventricular fibrillation. Two of 8 calves recovered from the infection, only one of which showed sinus arrest and the second degree of atrioventricular block transiently. We concluded that calves heavily infected with the larvae died due to sudden cardiac arrest.—KEY WORDS: calf, electrocardiogram, ruminant, Strongyloides papillosus, sudden death.

In recent years, a number of cases with sudden death have been reported in Japan in calves reared in the farm where sawdust is used as litter [8]. Calves often died in a few minutes of a violent fall without any premonitory signs. In necropsy, no significant lesion suggesting sudden death was observed, although a heavy infection with Strongyloides papillosus (S. papillosus) was found in all cases. The outbreaks of these fatal cases ceased after medication with thiabendazole or ivermectin. Thus, it was assumed that the sudden death was caused by heavy infection with S. papillosus.

Experimental S. papillosus infections of the domestic ruminant terminating in death were made in the 1950s [9, 11]. In these studies, however, sudden death or unexpected acute death was not shown as a clinical sign, except emaciation terminating in death. Recently, an evidence that sudden death could be experimentally induced by heavy infection of S. papillosus in calves was demonstrated by the present authors (submitted to Veterinary Parasitology). LD50 larval dose of S. papillosus infection was 32×105 per 100 kg of body weight. The larger the infection dose of larvae was, the shorter the interval between infection and death was.

A field observation on the sudden death of calves heavily infected with S. papillosus [3] indicated that their heart sounds could not be detected immediately after their falling down, when respiratory arrest not yet occurred. This observation suggests that the sudden death is of cardiac origin. In the present study, therefore, prolonged electrocardiographic (ECG) and pneumographic monitorings were carried out to substantiate this suggestion in calves experimentally heavily infected with S. papillosus.

MATERIALS AND METHODS

Animals used and methods of infection: Eight Holstein calves, 2 to 4 months of age, were employed (Table 1). The calves were housed two each at a time in a quiet recording room, which was lighted bright enough to allow continuous observation by television, and restrained loosely by a stanchion on a recording platform. Calves were fed twice a day at 9:00 and 17:00, and water was freely accessible. The method of percutaneous inoculation of S. papillosus larvae will be detailed elsewhere by our group of authors. The infective doses of S. papillosus larvae are listed in Table 1.

Methods of recording polygrams: Small disk type electrodes were anchored in the subcutaneous tissue 10 days before infection for recording ECG in the apex-base (A-B) lead. Respiration was monitored
by a breast-belt transducer (TR-701T, Nihon Kohden Co., Ltd., Tokyo). ECG and respiration were recorded on a polygraph (RM-80, Nihon Kohden Co., Ltd., Tokyo) placed outside the recording room. A full-day recording was started from at least 3 days before the infection and continued until the respiratory arrest. Heart and respiration rates were counted every 2 hours on polygrams for 30 seconds when the animals were resting, so their traces were stable and sinus rhythm was present.

RESULTS

Effects of infection with the smallest dose of larvae on ECG and respiration: Three calves, Nos. 219, 220 and 215, were infected with the smallest dose of larvae, 32×10^5/100 kg of body weight (Table 1). Two of them, Nos. 219 and 220, recovered from the infection and were killed on day 34 post-infection by the inhalation of carbon dioxide. Calf No. 219 showed no abnormal ECG and calf No. 220 showed transient sinus arrest (Fig. 1a) and the second degree of atrioventricular (AV) block on days 26 to 28, which were not associated with abnormal behavior and disappeared thereafter. Both calves showed no abnormal respiration and heart rates (Fig. 2), and their maximum heart rates were 67 and 65 beats/min respectively at rest.

One of the 3 calves, No. 215, died suddenly on day 17. Various changes in ECG and respiration observed in this calf were similar to those found in

Table 1. Effects of Strongyloides papillosus infection on calves

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Body weight</th>
<th>Larval dose</th>
<th>Abnormal ECG</th>
<th>Starting days of abnormal ECG</th>
<th>Sudden death (Euthanasia)</th>
</tr>
</thead>
<tbody>
<tr>
<td>219</td>
<td>♀</td>
<td>75</td>
<td>320</td>
<td>None</td>
<td>None</td>
<td>(34)</td>
</tr>
<tr>
<td>220</td>
<td>♂</td>
<td>76</td>
<td>320</td>
<td>Sinus arrest AV block</td>
<td>26-28 only</td>
<td>(34)</td>
</tr>
<tr>
<td>215</td>
<td>♀</td>
<td>80</td>
<td>320</td>
<td>Sinus tachycardia Sinoatrial exit block AV block Ventricular premature beat Paroxysmal ventricular tachycardia</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td>214</td>
<td>♂</td>
<td>86</td>
<td>1000</td>
<td>Sinus tachycardia AV block</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>211</td>
<td>♂</td>
<td>64</td>
<td>3200</td>
<td>Sinus tachycardia AV block</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
<td>212</td>
<td>♀</td>
<td>59</td>
<td>3200</td>
<td>Sinus tachycardia AV block Ventricular premature beat Paroxysmal ventricular tachycardia</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>207</td>
<td>♂</td>
<td>46</td>
<td>10000</td>
<td>Patterns similar to those of No. 212 and sinoatrial exit block</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>208</td>
<td>♀</td>
<td>48</td>
<td>32000</td>
<td>Patterns similar to those of No. 212</td>
<td>5</td>
<td>11</td>
</tr>
</tbody>
</table>

a) Holstein breed.
b) A-B lead. Sinus tachycardia was the first abnormal pattern, and ventricular fibrillation was the terminal pattern in all the sudden death cases.
c) Sudden ventricular fibrillation was followed by vigorous abdominal breathing, a queer cry and respiratory arrest.
Fig. 1. ECG changes in calves infected with $32 \times 10^4$ Strongyloides papillosus larvae/100 kg of body weight. Section a is of calf No. 220, recovered, 27 days after infection: Sinus arrest. Sections b to g are of calf No. 215, died suddenly. Section b (before infection): Normal pattern. Section c (22 hr before death): AV blocks—1st and 2nd degree and a ventricular premature beat (R on T). Section d (20 hr) and e (10 hr): AV blocks—1st and 2nd degree and paroxysmal ventricular tachycardia. Sinus tachycardia with prolonged PQ interval is also indicated in the right parts of these sections. Section d (17 hr): AV block—the second degree. Section g (10 hr): AV blocks—3rd degree.

the other cases with sudden death as noted below. ECG and respiration observed in cases with sudden death: Six calves, Nos. 215, 214, 211, 212, 207 and 208, died suddenly on days 11 to 17 (Table 1). The calves suddenly lowered their heads to the platform at recumbent position or fell down on the floor, simultaneously developing terminal ventricular fibrillation as noted below, and started to show agonizing abdominal breathing. Before these abnormal behaviors occurred suddenly, any clinical symptoms were not detected in all the calves tested excluding calves Nos. 207 and 208, in which anorex-
ia was seen a day before death.

Since 1 to 6 days before sudden death, sinus tachycardia had been recorded continuously (Table 1). Since 1 or 2 days before the terminal stage of infection, various types of arrhythmia had appeared among patterns of sinus tachycardia. The arrhythmias included sinus tachycardia (more than 80 beats/min [1]), sinoatrial exit block, all degrees of AV block, ventricular premature beat (R on T) and paroxysmal ventricular tachycardia (Table 1 and Fig. 1c-g). Transient ST depression was seen in calves Nos. 215 (Fig. 1g) and 212. Complete (the third degree) AV block was recorded only in calf No. 215 (Fig. 1g). Terminal patterns of ECG were serial ventricular tachycardia, flutter and fibrillation (Fig. 3c-f). The loss of cardiac pumping at ventricular fibrillation preceded respiratory arrest.

No significant change was seen in respiration rate, but cardiac tachycardia was detected up to the terminal ventricular fibrillation (Fig. 4). Maximum heart rates in the sudden death cases ranged from 110 to 130 beats/min at rest. Increased heart rate seen around day 3 after infection (Fig. 4) was not always detected in all the calves.

Changes of RR, QT and PQ intervals of ECG seen after infection: ECG parameters such as RR, QT and PQ intervals were measured in all the calves employed. After RR interval was abnormally shortened, QT interval changed similarly. On the contrary, PQ interval was prolonged (Fig. 5a) or maintained at a similar level to that measured before sinus tachycardia appeared (Fig. 5b). PQ interval was relatively prolonged in the latter case. Either absolute or relative prolongation of PQ interval was seen in all the calves which died suddenly.

**DISCUSSION**

Cardiac arrhythmias including tachy- and brady-arrhythmias could be demonstrated a few days before death in all the cases with sudden death. PQ interval was prolonged even in the pattern of sinus tachycardia. These clinical signs indicate that some factors relating to the sudden cardiac death may stimulate the sinus node and then damage the conduction route to the atroventricular node which induces the various patterns of AV block.

Terminal arrhythmias suddenly seen prior to the respiratory arrest consisted of serial ventricular tachycardia, flutter and fibrillation. Nishitateno [3]
reported that heart sounds could not be ausculted, even just after falling down, in the calves which had a heavy infection with *S. papillosus* and died suddenly in a farm. This observation was supported by the terminal occurrence of ventricular fibrillation suddenly observed in the present study.

Sudden death is known to occur in healthy-looking swine [10] and broiler chickens [4], and its significant clinical feature is acute cardiac arrest. No information about ECG in the sudden death has been available. Pathological examinations revealed heart damages in the cases of sudden death, and

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Fig. 3. ECG changes in calf No. 214 infected with 10⁶ *Strongyloides papillosus* larvae/100 kg. The animal died suddenly. Section a (before infection): Normal pattern. Section b (several minutes before death): Sinus tachycardia and an AV block—1st and 2nd degree. Section c (terminal polygram, slow record): Sinus tachycardia designated by d in this section, ventricular tachycardia (e), flutter and fibrillation (f). These patterns d, e, and f are also shown in sections d, e, and f, respectively. Section d: Sinus tachycardia. Section e: Onset of the terminal ventricular arrhythmias. Ventricular tachycardia. Section f: Ventricular flutter and fibrillation. Quiet respiration was changed, after the onset of ventricular fibrillation, to vigorous abdominal breathing. Respiration discontinued in a few minutes.
nutritional, hereditary or stressful feeding condition has been thought to be related to the death.

Heavy *Strongyloides stercoralis* infection caused respiratory failure, followed by cardiac arrest in humans [5]. Swine infected with *Strongyloides ransomi* died suddenly and many live larvae of this worm could be recovered from the myocardium [6]. Furthermore, heart sounds indicated partial AV block in the infected pigs, so migrating larvae might injure the AV conduction system. However, our unpublished data indicate that only 1 and 2 live larvae were found in each 10 g of tissue of the heart and brain, respectively, of all the calves employed in the present study and that no significant myocardial invasion by the filariform larvae was observed by

Fig. 4. Cardiac tachycardia seen in calf No. 211 infected with $32 \times 10^7$ *Strongyloides papillosus* larvae/100 kg. The calf died suddenly. No significant change was noted in respiration rate.

Fig. 5. Changes in RR, QT and PQ intervals in calves Nos. 214 (a) and 211 (b). With these animals, see also the legends for Figs. 3 and 4. Shortening of RR and QT intervals and absolute (a) and relative (b) prolongation of PQ interval are shown at right side of each chart. In normal cases, PQ interval as well as QT interval changes in parallel with RR interval.
histopathological examination.

Cardiac arrhythmia is considered as one of the major causes of sudden cardiac death in humans [2, 7]. However the mechanism for genesis of arrhythmia followed by sudden death is not clarified in those studies of humans. Similarly, the reason why the heavy infection of calves with *S. papillosus* causes cardiac arrhythmias terminating in death also remains unsolved. Pathological and clinical biochemical analyses on the calves employed in the present study have not yet revealed the reason. First of all, the primary factor causing the cardiac death should be clarified to be the migrating filariform larvae of adults in the intestine, or both. Subsequently, various possible causative factors such as cardiotropic (or -toxic) substances, worm products and cardiac nerve actions should be examined. Our working hypothesis is that the main causative agent involved might be a cardiotoxic substance absorbed from the intestine parasitized by adult *S. papillosus* worm and should be substantiated by future studies.

REFERENCES