Cardiac Lesions in Dairy Cows with Idiopathic Atrial Fibrillation

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ABSTRACT. Histopathological examination of the heart, particularly the right atrium including the sinoatrial (SA) node, was carried out in 9 Holstein dairy cows with idiopathic atrial fibrillation (AF; AF group) and 12 healthy cows of the same breed (control group) in order to establish the correlation between idiopathic AF and histopathological changes in the heart in dairy cows. None of the 9 cows had clinical evidence of other diseases, and they consisted of 5 cases of short-term AF which lasted a few days or weeks, and 4 cases of long-term AF which lasted more than 1 month. The pathological changes found in the present series included multifocal or fairly large areas of myocardial fibrosis in the right atrium (in all the 9 cows of the AF group and 2 of the 12 controls—however, the changes were qualitatively and quantitatively much more severe in the former group); SA nodal architecture changes (in 3 of the 4 cows with long-term AF); and atrial dilatation (in 3 of the 4 cows with long-term AF). The results suggest that the fibrotic lesions of the right atrial myocardium may represent the anatomical changes that underlie idiopathic AF in dairy cows.

KEY WORDS: atrial fibrillation, bovine, heart, pathology.

FULL PAPER

Pathology

Atrial fibrillation (AF) is the most commonly observed arrhythmia of cattle [6, 21, 27]. It has been reported to develop in cattle with a variety of disease conditions, the most common being gastrointestinal disturbances including dysfunction of forestomachs and displacement of the abomasum [5–8, 20, 24, 27, 32]. Reflex vagotonia has been considered to be the inciting factor in these clinical incidents, with the reflex originating in the walls of the gastrointestinal tract [31], and evidence of underlying heart disease, therefore, cannot be found by routine clinical evaluation [24, 27]. Other cases of AF in cattle may be induced by heart diseases such as valvular endocarditis [5, 20, 32] or traumatic pericarditis [20, 32]. Thus, almost all animals with AF reported previously have had underlying disease conditions.

We evaluated 285 apparently healthy Holstein dairy cows serially for AF over an 18-month period and noted the arrhythmia in 7 cows with an incidence of 2.5% [21]. The results suggest that AF also develops in healthy dairy cows with no clinically demonstrable disease and that such cases of AF may reflect a condition similar to that referred to as idiopathic AF (or lone AF) in humans [12, 13, 15, 26].

The present paper reports histopathological observations on hearts from 9 cases of idiopathic AF in Holstein dairy cows in an attempt to find the histopathological basis for the arrhythmia.

MATERIALS AND METHODS

Animals: Nine Holstein dairy cows with AF included in this study (AF group) were selected at the time of necropsy or slaughter covering an 8-year period during which 33 bovine cases of AF were observed. Those chosen had no macroscopical evidence of underlying heart diseases, such as valvular endocarditis, traumatic pericarditis, or bovine leukemia, with the exception of atrial enlargement in 3 cases, and had clinical data which gave accurate information on the time of onset and duration of the arrhythmia. Furthermore, none of the 9 cows with AF had shown clinical signs of disease including gastrointestinal disturbances before the onset of AF. They had all produced a large quantity of milk (total milk yield during a lactation period of 305 days ranging from 8,500 to 11,700 kg), although their milk production decreased markedly during the period of AF. In all the cows, AF persisted until the time of necropsy or slaughter and was classified according to its duration; that is, 5 cases of short-term AF lasting a few days or weeks (Cases 1 to 5), and 4 cases of long-term AF lasting more than 1 month (Cases 6 to 9). Duration of AF was 3 to 24 days, with an average of 13.4 days for the short-term AF group, and 2 to 16 months, averaging 9.3 months for the long-term one (Table 1). The age of affected cattle ranged from 5 to 8 years (average 6.6 years) for the short-term AF group and 5 to 9 years (average 6.3 years) for the long-term one (Table 1).

In addition, a further 12 dairy cows with normal ECG and no cardiac disease, with ages ranging from 4 to 11 years (average 7.4 years), were used as a control group.

Histopathology: After examining it macroscopically, the whole heart was fixed in 10% phosphate-buffered formalin for at least a week. The atria were then dissected from the ventricles at the atroventricular sulcus. The right atrium was cut serially into 48 to 61 blocks perpendicular to the sulcus terminalis (at right angles to the long axis of the sinoatrial (SA) node) so that both the epicardium and endocardium, as well as the cranial vena cava and right atrial wall, were included [4]. In addition, 9 to 13 sections were taken from the left atrium transversely across the atrial appendage. For examination of ventricular myocardial lesions, 35 to 42 other blocks were taken from the left and
right ventricular free walls and the interventricular septum. Samples were embedded in paraffin wax, sectioned at 6 µm, and stained with hematoxylin and eosin (HE), elastica van Gieson, and Masson’s trichrome for light microscopical examination.

RESULTS

**Gross findings in the heart:** Atria were markedly dilated in 3 of the 4 cows with long-term AF. Case 6 had slight right atrial enlargement, Case 8 marked right atrial enlargement (Fig. 1), and Case 9 marked biatrial enlargement (Fig. 2). In addition, there was thinning of the right atrial wall in Case 8 and of biatrial walls in Case 9 due to muscle loss with apparent fibrous tissue replacement. No cows with short-term AF had recognizable gross heart lesions including atrial enlargement.

**Microscopical findings in the heart:** All the 9 cows with AF had significant cardio-histopathological changes in common. The main pathological conditions that occurred consistently in the present series included increased fibrous tissue in the myocardium and disruption of the muscle bundle architecture (myocardial fibrosis) in the right atrial wall. The foci of myocardial fibrosis were classified into two grades: mild to moderate and severe. Mild to moderate lesions were minute in size and characterized by relatively dense fibrous tissue with a loss of muscle fibers, and a conspicuously increased elastic tissue in the fibrosed area (Fig. 3). Severe lesions were characterized by an extensive loss of muscle fibers, which had been replaced by dense collagen and elastic fibers, indicating progressive and substitute fibrosis (Fig. 4). These lesions were occasionally accompanied by adipose tissue. In mild cases the lesions were usually focal and involved only small areas of the myocardium. In more severe forms involvement of the myocardium was more diffuse. In the most severe forms the individual lesions had become confluent and formed much larger ones.

In the right atrium of the AF group, as shown in Table 1, mild to moderate lesions were observed in Cases 2, 3, 5, 6 and 7, and severe lesions together with mild to moderate

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AF, atrial fibrillation; MF, myocardial fibrosis; Psl, posterolateral region; Anl, anterolateral region; Med, medial region; Aur, auricle; -, no lesion; +, mild to moderate lesion; ++, severe lesion.
Fig. 3. Photomicrograph of a section of the myocardium in the anterolateral region of the right atrium from a cow with short-term atrial fibrillation (Case 2). Note the mild to moderate lesions of myocardial fibrosis. Elastica van Gieson (EVG) stain, ×34.

Fig. 4. Photomicrograph of a section of the myocardium in the anterolateral region of the right atrium from a cow with short-term atrial fibrillation (Case 4). Note the severe lesions of myocardial fibrosis. EVG stain, ×34.

Fig. 5. Photomicrograph of a section of the myocardium in the medial region of the right atrium from a cow with short-term atrial fibrillation (Case 3). Note that focal lesions of myocardial fibrosis are located in the upper portion of the atrial wall, close to the sinus node (arrow). EVG stain, ×11.

Fig. 6. Photomicrograph of a section of the myocardium in the anterolateral region of the right atrium from a cow with long-term atrial fibrillation (Case 8). Note that the right atrial wall is severely sclerotic. EVG stain, ×13.
ones in Cases 1, 4, 8 and 9. In Cases 1, 2, 3, 5, 6 and 7, the lesions of myocardial fibrosis were located mainly in the upper portion of the anterolateral and medial regions of the right atrium and often found close to the SA node (Fig. 5). In Cases 4, 8 and 9, the right atrial wall was severely involved by the sclerotic process and showed extensive fibrosis, loss of muscle fibers and disruption of architecture (Fig. 6). In the right atrium of the control group, there were a few mild lesions in 2 animals, which were distributed similarly to those of the AF group. On the other hand, focal lesions of myocardial fibrosis composed mainly of collagen fibers were occasionally noted in other regions of the heart in both the AF and control groups, but they were qualitatively and quantitatively much milder than those in the right atrium.

Histological examination of the SA node revealed that in 3 of the 9 cases with AF there was a slight increase in fibrous tissue and a mild reduction of nodal cells (Case 6), a significant increase in fibrous tissue and a marked reduction of nodal cells (Cases 8 and 9). The remaining 6 cases with AF and all the 12 cows of the control group had morphologically normal SA nodes.

Changes in the intramural coronary arteries supplying both atria, namely, thickening of the vessel walls and a slight decrease in luminal size, were frequently observed in almost all cases of the AF and control groups. These abnormal vessels were also present in the ventricular walls. The wall thickening was due mainly to proliferation of smooth muscle and fibrous tissue in the intima and media. No apparent difference was seen in the severity or location of the vascular changes between the AF group and the control group. Moreover, the presence of the vascular changes was unrelated to the occurrence of the myocardial fibrotic lesions in the right atrium mentioned above.

**DISCUSSION**

Great emphasis has always been placed on the clinical features and clinicopathological basis of the arrhythmia of cattle AF because it has generally been regarded as a functional arrhythmia occurring without apparent cardiac pathological findings [24, 27]. Therefore, the association between AF and the histopathological changes of the heart has received considerably less attention.

Atrial dilatation was observed in 3 of the 4 cows with long-term AF. According to Falk [13], in human patients with recent-onset AF, right atrial volume was usually increased, whereas left atrial volume was less consistently increased. In contrast, biatrial enlargement was common in patients with a history of chronic arrhythmia. These findings substantially resembled those observed in the present study.

In human patients with mitral regurgitation, enlargement of the atria is well known to predispose them to developing AF [14, 23, 33]. This is because the larger the atria the greater the number of re-entry circuits that can be accommodated [28]. As for our bovine cases of AF, however, atrial dilatation was taken to be the result of AF but not the cause, because atrial dilatation was found only in the long-term AF group and not in the short-term AF group. This is supported by the finding that echocardiography indicates a detrimental effect of AF on atrial structure by documenting a progressive increase in atrial size in human patients with sustained arrhythmia [29]. Moreover, the fact that restoration of sinus rhythm results in a small but significant decrease in atrial volume may imply that the arrhythmia itself may result in atrial enlargement [22].

There have been many histological studies of human AF. Results have consistently shown conspicuous alterations of the atrial wall with involvement of the SA node: pathological changes in atrial myocardium [2, 9, 10, 17]; degenerative or ischemic lesions of the SA node [3, 10, 16, 18]; and dilatation of the atria [10]. Patchy, focal degeneration, necrosis and fibrosis in the atria predispose to delayed and inhomogeneous conduction, which are electrophysiologic prerequisites for AF [28]. Thus, the relationships between histological disorders of the atria including the SA node and AF have been relatively clearly defined in human patients.

The present study has provided a relatively clear picture of the close relationship between cardiac lesions in cattle and the presence of AF. The histopathologically significant findings common to all the 9 cows with AF were multifocal or fairly large areas of myocardial fibrosis in the right atrium. Fibrotic areas in the atrial myocardium lead to impaired intra-atrial conduction which, in the thin atrial wall, predisposes to inhomogeneity of atrial repolarization or conduction and may thus set the stage for AF [11, 13]. In the present series, therefore, it seems reasonable to imagine that the myocardial lesions which constituted anatomical obstacles to conduction in the right atrium created a suitable background for the electrophysiological inhomogeneity favoring the development of AF.

While it is conventional to regard the focal myocardial lesions in the right atrium as the cause of AF, it is also possible that they result from the arrhythmia and consequent disordered function of the chamber [10, 25, 34, 35]. In the present study, the atrial myocardial lesions observed in the long-term AF group were not qualitatively different from those in the short-term AF group. The similarity of the myocardial lesions observed in the right atrium in cases with varying duration of AF may suggest that the histological alterations are the cause of AF.

Although the etiology of the atrial myocardial lesions is not clear, it is interesting that they largely occupied a similar location being mainly in the upper portion of the anterolateral and medial regions of the right atrium. All the 9 cows with AF in this study had produced a large quantity of milk before the onset of AF. Also in our previous study on the incidence of AF in apparently healthy Holstein dairy cows, the genesis of AF were all observed in high-producing ones [21]. These facts suggest the possibility that an increased hemodynamic load imposed continuously on the heart, associated with an increase in total volume of systemic blood flow during lactation for milk production, has been related
to the occurrence of the myocardial lesions in the thin right atrial wall. Moreover, the anatomical structure of the right atrium may be such that its upper portion of the anterolateral and medial regions would be most affected by this increased hemodynamic load and would develop most lesions. Interestingly, such location of myocardial fibrotic lesions in the right atrial wall has also been observed in racehorses with AF [1, 19]. Study of the SA node revealed that an increase in fibrous tissue and a reduction of muscle tissue were marked when cows were suffering from long-standing AF. Controversy exists about the responsibility of organic lesions of the SA node in the genesis of AF. Many observations showed that AF was related to lesions in the SA node [3, 10, 16, 18]. On the other hand, according to Davies and Pomerance [10], the SA node was normal in short-term AF, whereas nodal tissue was reduced in long-term AF. The results of the present study corroborate these authors’ findings that SA node lesions do not comprise an essential factor for AF to develop. It is therefore possible that in cattle AF is a cause of histopathological changes in the SA node. Intriguingly, it has been reported that, in experiments on dog hearts, AF was easily produced by some drugs when the SA node was intact, but was difficult to produce when the SA node was injured [30]. In conclusion, we consider that the histopathological lesions of the right atrial myocardium may be the anatomical substratum for AF of idiopathic etiologies in Holstein dairy cows.

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REFERENCES


