NOTE Internal Medicine

Serum Amyloid A and Haptoglobin Levels in Bovine Amyloidosis

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(Received 21 September 2006/Accepted 17 November 2006)

ABSTRACT. Serum amyloid A (SAA) and haptoglobin (Hp) levels were determined in 25 cows suffering from amyloidosis. SAA levels in cows with amyloidosis ranged between < 0.3 and 225.8 μg/ml, with a median level of 105.1 μg/ml, and Hp levels ranged between < 20 and 1860 μg/ml, with a median level of 950 μg/ml. These levels were significantly higher than the levels observed in healthy cows (SAA levels ranged from < 0.3 to 13.5 μg/ml, with median of 1.4 μg/ml, and Hp levels were undetectable in all cases), but were not significantly different from the levels observed in control cows with chronic inflammation. There was a significant correlation between SAA and Hp levels in cows with chronic inflammation, but not in cows with amyloidosis. It was concluded that the serum SAA levels in cows with amyloidosis might be changed by some factor other than inflammation.

KEY WORDS: amyloidosis, haptoglobin, serum amyloid A.


Bovine amyloidosis is a relatively rare disease, with main symptoms of persistent diarrhea and edema. The clinical signs, clinical pathology and pathology of the disease have been reported by many authors. Epidemiologically, the disease is more common in aged cows, occurs subsequent to chronic inflammatory diseases such as chronic arthritis and chronic mastitis [4, 13, 14], but the etiology is not clear. Moreover, at present it can be diagnosed clinically only at the terminal stage showing nephrotic syndrome, and the establishment of ways to enable on early diagnosis and elucidation of the mechanism of the onset of the disease are needed.

The amyloid protein deposited in bovine amyloidosis is amyloid A (AA), and the precursor protein of AA is serum amyloid A (SAA). SAA is one of the acute phase reactive proteins contained in the serum of various animal species, including cattle and humans, and has a molecular weight of approximately 12–14 kD. SAA is usually degraded rapidly by enzymes which are present on the surface of macrophages, but when this degradation process is obstructed, SAA is partially degraded, producing AA, which has a molecular weight of approximately 8–9 kD. AA is polymerized, becomes fibrotic, and is extensively deposited in various organs, causing amyloidosis [6].

In humans, persistent high SAA levels in serum are considered a risk factor for amyloidosis, however, high SAA levels are not diagnostic of amyloidosis [16]. SAA levels in cows with various diseases have been reported only recently [2, 3, 5, 8, 9], but the levels are not routinely measured yet, and there has been only one publication on the determination of the serum SAA level in a cow with amyloidosis [1].

In the present study, we determined SAA levels in cows suffering from amyloidosis and evaluated the diagnostic value of the SAA level. Moreover, we determined the levels of serum haptoglobin (Hp), which, like SAA, is a more sensitive marker of inflammation than other acute phase reactants in cows [8, 12], and examined the correlation of SAA and Hp levels with amyloidosis in order to confirm whether or not the SAA level in cows with amyloidosis was increased in the presence of inflammation.

The animals studied were 25 Holstein dairy cows which were diagnosed by histopathological examination as suffering from amyloidosis. Eighteen cows with chronic inflammatory diseases (13 cows with chronic arthritis, five cows with chronic mastitis) and 10 healthy cows as judged using clinical and clinicopathological examinations were used as control animals.

SAA levels were determined with a commercial ELISA kit (Serum Amyloid A assay, Tridelta Development) [10]. Serum Hp levels were determined using a commercial assay kit (Bovine Hp Plate, Ecos Laboratory) based on the SRID method [11]. SAA and Hp levels in healthy cows, the cows suffering from amyloidosis and the cows with chronic inflammatory diseases were compared by Mann-Whitney’s U-test at the significance level of p<0.05. Spearman’s order correlation coefficient (r²) was calculated between SAA and Hp levels in cows with amyloidosis, and in cows with chronic inflammation, at the significance level of p<0.05.

SAA levels were above the limit detection of 0.3 μg/ml in 24 of 25 cows with amyloidosis, with a median level of 105.1 μg/ml and a range between 8.0 and 225.8 μg/ml. SAA levels in healthy cows were above 0.3 μg/ml in 8 of 10 cows examined, with a median level of 1.4 μg/ml and a range between 0.3 and 13.5 μg/ml. The difference between the cows with amyloidosis and the healthy cows was significant. The SAA level in cows with chronic inflammatory diseases showed a median level of 87.6 μg/ml and a range between 17.1 and 298.2 μg/ml. The difference between these cows and the healthy cows was significant, while the difference between these cows and the cows suffering from
Amyloidosis was not significant. Serum Hp levels were above the limit of detection of 20 µg/ml in 22 of 25 cows with amyloidosis, with a median level of 950 µg/ml and a range between 60 and 1,860 µg/ml. The serum Hp level in cows with chronic inflammatory diseases showed a median level of 455 µg/ml and a range between 180 and 2,000 µg/ml, and the difference between these cows and the cows with amyloidosis was not significant. The serum Hp levels in healthy cows were all below the limit of detection, and significantly lower than the levels in cows with amyloidosis and chronic inflammatory diseases (Table 1).

The correlation between SAA and Hp levels in cows with chronic inflammations was significant (r=0.74, p<0.01). On the other hand, there was no significant correlation between SAA and Hp levels in cows with amyloidosis (r=0.04, p>0.05) with Spearman’s test.

Table 1. Median and ranges of concentrations of serum amyloid A (SAA) and serum haptoglobin (Hp) of healthy cows and cows with amyloidosis and chronic inflammatory disease

<table>
<thead>
<tr>
<th>Group</th>
<th>Samples detectable*</th>
<th>Median (µg/ml)</th>
<th>Range (µg/ml)</th>
<th>Samples detectable*</th>
<th>Median (µg/ml)</th>
<th>Range (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amyloidosis (n=25)</td>
<td>24/25</td>
<td>105.1 a)</td>
<td>8.0–225.8</td>
<td>22/25</td>
<td>950 b)</td>
<td>60–1860</td>
</tr>
<tr>
<td>Chronic inflammatory disease* (n=18)</td>
<td>17/18</td>
<td>87.6 a)</td>
<td>17.1–298.2</td>
<td>16/18</td>
<td>455 c)</td>
<td>180–2000</td>
</tr>
<tr>
<td>Healthy cows (n=10)</td>
<td>8/10</td>
<td>1.4 b)</td>
<td>0.3–13.5</td>
<td>0/10</td>
<td>ND d)</td>
<td>ND</td>
</tr>
</tbody>
</table>

* Number of samples with a concentration greater than the lower limit of detection of the assay used/total number of samples.
** include chronic arthritis (n=13) and chronic mastitis (n=5).

Significant difference between a) and b) c) and d) (p<0.01, Mann-Whitney test). ND: Not detectable.

Fig. 1. Relationship between serum haptoglobin (Hp) and serum amyloid A (SAA) levels in cows with (A) amyloidosis and (B) chronic inflammatory diseases including 5 cases with chronic mastitis and 13 cases with chronic arthritis. Correlation is shown between Hp and SAA levels in cows with chronic inflammatory disease (r=0.74, p<0.01) but no correlation is shown with amyloidosis (r=0.04, p>0.05) with Spearman’s test.
eases including amyloidosis. On the other hand, only SAA2, which is one of the isoforms, seems to be the precursor of AA in the mouse [15]. Alsemgeest [1] reported that bovine SAA has some specific isoform expression patterns, and the sera obtained from cows with different diseases showed variable ratios of the isoforms, and furthermore, only one isoform was detectable in the serum of a cow suffering from spontaneous AA-amyloidosis. Thus, there is a possibility that differences of the isoform expression patterns cause the total SAA levels in cows with amyloidosis to change. In the future, analyse of the isoforms of SAA will be necessary in order to clarify the cause of bovine amyloidosis.

ACKNOWLEDGEMENTS. We thank the veterinarians who belong to the Tokachi Agricultural Mutual Aid Association in Hokkaido, Japan, for the collection of samples from cows with amyloidosis.

REFERENCES