Degenerative Changes in the Endometrial Vasculature of the Mare Detected by Videoendoscopic Examination

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The endoscopical appearance of small arteries under the endometrium (SAUE) reflected the degree of sclerotic change in the intima and adventitia. There was a clear correlation between the appearance of SAUE and age, and the degree of endometrosis was more severe in mares in which SAUE was more clearly recognized. Authors’ Address: Equine Medical Center, Hidaka Horse Breeders Association, Kamimori 175, Shizunai, Hokkaido 056-0002, Japan. © 2000 AAEP.

Introduction

In mares, as well as chronic infiltrative endometritis (CLE), endometrosis represented by glandular degenerative changes (i.e., gland ‘nests’ and/or gland ‘cysts’), formation of endometrial cysts, and periglandular and/or diffuse stromal fibrosis, are significant histopathologic features for their fertility. Endometrial biopsy is the most widely used technique for evaluating the severity of degenerative changes. However, this technique is invasive and time-consuming.

Recently, there have been some reports on hysteroscopy. Although the major advantage of hysteroscopy is such that it allows visualization of the entire mucosal surface of the uterus in vivo, Bracher and Allen concluded that hysteroscopy cannot replace a biopsy to evaluate the endometrium. In our experience, videoendoscopy is a relatively simple, non-invasive, and useful technique for detecting macroscopical lesions (i.e., endometrial cysts, fluid accumulation, adhesions, and tumors), although it is difficult to evaluate the severity of degenerative changes from macroscopical findings.

In videoendoscopy, small arteries observed under the endometrium (SAUE) tend to be whiter in older mares and are therefore clearly visible. In humans and in some mammals, the uterine wall arteries have been reported to show pregnancy sclerosis. In mares, Oikawa et al. reported that the uterine wall arteries of mares with repeated pregnancy failure exhibited elastosis of the intima and/or adventitia.

In this study, the relationship between the endoscopical appearance of SAUE and their histological features were investigated. And comparing with the degree of endometrosis evaluated by the biopsy examination, videoendoscopic evaluation of degenerative changes in the endometrium was also carried out.
Materials and Methods

Experiment 1

A maiden (mare A) and six barren (mare B to G) thoroughbred mares were examined from September to December of each year 1994, 1995 and 1996. The mares were restrained in stocks and tranquilized with IV injections of 20 mg xylazine. The tail of each mare was bandaged and the perineal area was cleaned by a surgical procedure. An operator wearing sterile surgical gloves over the sleeve inserted the top of a videoendoscope with a length of 160 cm. The videoendoscope was used in combination with a videoprocessor. The uterus was expanded by continuous insufflation of filtered air from the endoscope. The entire surface of the endometrium was observed and the endoscopical appearance of SAUE was inspected. The endometria were classified into three groups according to the appearance of SAUE: SAUE not distinguishable from surrounding endometrial tissues in the entire endometrium (Group A, Fig. 1), SAUE slightly visible as white lines but not clearly in some parts of or the entire endometrium (Group B, Fig. 2), and SAUE clearly visible in the entire endometrium (Group C, Fig. 3).

After the mares were euthanized, the uterus of each mare was removed immediately. Tissue samples included whole layers of the uterus from three segments (anterior, middle, and posterior) of the three major portions of the uterus (right horn, left horn, and body). The tissue specimens were fixed in 10% neutral buffered formalin solution. Hematoxylin-eosin (HE) and elastica van Gieson’s stain were used for microscopic examination of the uterine tissues, especially for SAUE of more than 200 μm in external diameter which can be distinguished endoscopically. External diameter of each SAUE was measured, and the degree of lesions in each SAUE was evaluated and classified into four types: no significant lesions were observed (type I, Fig. 4), intima was thickened due to multiplication of layers of intimal elastic lamina. No lesions were observed in the media and adventitia (type II, Fig. 5), moderate elastotic change characterized by the intimal thickening and a slight increase in the amount of elastic fibers in the adventitia (type III, Fig. 6) and severe elastotic change was observed in both the intima and adventitia (type IV, Fig. 7).
Experiment 2

Four hundred twenty-three maiden and barren Thoroughbred and Anglo-Arabian mares, aged from 4 to 20 yr, were examined from September to December of each year from 1994 through 1999.

Rectal palpation and ultrasound examination of the uterus and both ovaries were performed, and the cervix was observed for evaluation of the estrus cycle. A visual assessment of the appearance of SAUE was performed by the same procedure described in Experiment 1.

At the end of the examination, biopsy sampling was performed at the corpus-cornual junction under endoscopic observation using normal-sized endometrial biopsy forceps for mares. The tissue specimens were fixed in 10% neutral buffered formalin solution, and HE stain was used for microscopic evaluation.

Fig. 4. Microscopic view of type I SAUE. Although edematous swelling of the intima was observed, no significant lesions were found. EVG ×200.

Fig. 5. Microscopic view of type II SAUE. The intima was thickened due to multiplication of the layers of this intimal elastic lamina. No lesions were observed in the media and adventitia. EVG ×200.

Fig. 6. Microscopic view of type III SAUE. Moderate elastotic change characterized by the intimal thickening and a slight increase in the amount of elastic fibers in the adventitia. EVG ×200.

Fig. 7. Microscopic view of type IV SAUE. Severe elastotic change was observed in both the intima and adventitia. The media was almost absent. EVG ×100.
The degree of endometrosis was divided into four groups (Groups 1 to 4) according to the similar criteria of Ricketts and Alonso: Group 1: No histopathological abnormality. Group 2: Occasional gland nests (<2 per 5 mm linear field) with minimal associated periglandular and no diffuse stromal fibrosis. Group 3: Diffuse gland nests (2–4 per 5 mm linear field) with associated moderate periglandular but no diffuse stromal fibrosis. Group 4: Diffuse gland nests (>4 per 5 mm linear field) and/or cysts with associated severe periglandular or diffuse stromal fibrosis.

A χ²-test for independence was used for statistical analysis and significance was determined at a level of p < 0.01.

Results

Experiment 1

Of seven mares, a maiden mare (mare A) was classified as Group A (Table 1). The endometrial tissue of this mare showed moderate mononuclear cell infiltration and moderate degenerative changes that were categorized as Group 2 (Table 1). Ten SAUE of more than 200 μm were observed. Although edematous swelling of the intima was observed in some of the small arteries, no significant lesions were found in all of the ten SAUE (type I, Fig. 4; Table 1).

Three mares (mares B, C, D) were classified as Group B and their endometrial tissue were group 1 or Group 2 (Table 1). Type II SAUE (Fig. 5) were observed in mares B (4/7, 57.1%) and C (1/9, 11.1%) (Table 1). Type III SAUE (Fig. 6) were recognized in mares B (2/7, 28.6%), C (7/9, 77.8%) and D (7/9, 77.8%), respectively (Table 1).

The endometrial tissues of three mares (mares E, F, G) in Group C were classified as Group 2 or Group 3 (Table 1). Except for a SAUE in mare F, the degree of elastosis in both the intima and adventitia was severe in all of the SAUE in this group. The media was almost absent and it was difficult to distinguish from the intima and/or adventitia (type IV, Fig. 7) (Table 1).

Experiment 2

The relationship between the appearance of SAUE and the age of the mares is shown in Fig. 8. In the 4- to 6-year-old group, SAUE was not visible in 41 of 55 mares (74.5%). The ratio of mares in group A decreased in older age groups, on the contrary, the ratio of group C mares gradually increased in older age groups. SAUE were observed more clearly in older mares (p < 0.01).

Table 1. Endoscopic Appearance and Microscopical Features of SAUE, and Degree of Endometrosis in Endometrial Tissue Samples from Seven Mares in Experiment 1

<table>
<thead>
<tr>
<th>Mare</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
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<tbody>
<tr>
<td>Age</td>
<td>5</td>
<td>8</td>
<td>9</td>
<td>15</td>
<td>13</td>
<td>16</td>
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<tr>
<td>SAUE</td>
<td></td>
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</tr>
<tr>
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<td>0</td>
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<td>0</td>
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<td>0</td>
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<td>0</td>
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<tr>
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<td>7</td>
<td>0</td>
<td>1</td>
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<td>0</td>
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<tr>
<td>Type IV</td>
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<td>1</td>
<td>2</td>
<td>8</td>
<td>8</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>10</td>
<td>7</td>
<td>9</td>
<td>9</td>
<td>8</td>
<td>9</td>
<td>21</td>
</tr>
<tr>
<td>Diameter (μm, mean ± SD)</td>
<td>216 ± 17</td>
<td>213 ± 19</td>
<td>204 ± 5</td>
<td>229 ± 16</td>
<td>246 ± 58</td>
<td>273 ± 85</td>
<td>227 ± 36</td>
</tr>
<tr>
<td>Endometrosis</td>
<td>Group 2</td>
<td>Group 1</td>
<td>Group 1</td>
<td>Group 2</td>
<td>Group 2</td>
<td>Group 2</td>
<td>Group 3</td>
</tr>
</tbody>
</table>

Fig. 8. Relationship between appearance of SAUE (groups A, B, and C) and age. The mares were divided into five age groups. The ratio of mares in group A decreased in older age groups, on the contrary, the ratio of group C mares gradually increased in older age groups. SAUE were observed more clearly in older mares (p < 0.01).
C. From this result, SAUE were observed more clearly in older mares \( (p < 0.01) \).

Group 1 endometrial tissues were found in 58 of 93 (62.4%), 50 of 171 (29.2%) and 30 of 159 (18.9%) mares in Groups A, B and C, respectively (Fig. 9). The percentage of Group 2 peaked at 58.8% (92 of 171) in group B (Fig. 9). In Group C, 50 of 159 (31.4%) were classified as Group 3, and only three mares (1.9%) in Group C had Group 4 endometrial tissues (Fig. 9). Degenerative change in endometrial tissues, therefore, was more severe in the group in which SAUE was more clearly recognized \( (p < 0.01) \).

Discussion

The results of Experiment 1 revealed that the endoscopic appearance of SAUE reflects the degree of sclerotic change in the intima and adventitia. Although there are few reports on the relationship between the macroscopic appearance and sclerotic change in the artery, in many animal species, arteriosclerosis is found in the abdominal aorta and other elastic arteries, and lesions are observed grossly as slightly raised, firm, white plaques.

The results of Experiment 2 suggested that the sclerotic change of SAUE is associated with aging. It has been reported that small arteries in the uterine wall show age-related sclerotic changes such as elastosis in the intima and adventitia, which result in luminal narrowing.\(^4,5\) Our findings agree with the previous work.

The present study demonstrated that there is a clear relationship between the degree of sclerotic change in SAUE and the degree of endometrosis in the endometrium. This finding was noted previously\(^5\) and was confirmed in the present study. Many researchers have suggested that endometrosis is a response to aging, chronic inflammation by infection, and possibly endocrinological factors.\(^2,6\)

Degenerative change in endometrial tissues was more severe in this group in which SAUE was more clearly recognized. Since individual differences were observed in the progression of sclerotic change and the degree of endometrosis, it could not be determined if SAUE sclerosis was a direct cause of endometrosis. The relationships between uterine environment, age and sclerosis and how these factors relate to endometrosis are not clear. Pathological changes in the uterus produced by SAUE sclerosis may contribute to endometrosis or the sclerotic change in SAUE and the progression of endometrosis may occur simultaneously as a result of aging.

Videoendoscopy is a non-invasive, relatively simple technique for evaluation of endometrium in mares. Ricketts and Alonso concluded, by using a statistically meaningful number of endometrial biopsy samples, that the development of endometrosis is associated with age.\(^2\) In order to predict the reproductive ability, it is very important to consider the age of the mare. In addition, endoscopic evaluation of SAUE is considered useful for estimation of the degree of endometrosis and a prediction of the reproductive ability of mares.

References and Notes


\(^a\) Olympus, Model CF200L.

\(^b\) Olympus, EVIS system.