DISSECTING ANEURYSM DURING PREGNANCY
AND THE PUERPERIUM

YUTAKA KONISHI, NORIKAZU TATSUTA, KAORU KUMADA,
KAZUAKI MINAMI, KATSUHIKO MATSUDA, ARI0 YAMASATO,
NORIHKO USUI, TOMOHIKO MURAGUCHI, YORINORI HIKASA,
EIICHI OKAMOTO,* RYOJI WATANABE**

According to Schnitker, Mandel, Hirst and their associates, approximately
half of the dissecting aneurysms in women under 40 years of age are associat-
ed with pregnancy. This significant relationship between dissecting aneurysm
and pregnancy has been discussed by considering hemodynamic stress and
also the hormonal changes of pregnancy. In this report, we describe five
patients with dissecting aneurysm during pregnancy or the puerperium,
review the literature and discuss the influence of pregnancy on the patho-
genesis of this disease.

ALTHOUGH dissection of the aorta is more
frequent in males than in females and is
more common between the ages of 40 and 70; it can occur in younger females. Schnitker; Mandel; Hirst and their associates pointed out
that approximately half of the cases of dissecting aneurysm in women under 40 years of age were
associated with pregnancy. In addition, aneu-
rysms or ruptures of the cerebral artery, splenic
artery, coronary artery, renal artery and
ovarian artery in relation to pregnancy have
also been reported. Thus, the significant associa-
tion between pregnancy and dissecting aneu-
rysms or vascular accidents has been discussed by
a number of authors. It is generally accepted
that medial degeneration is the basic requisite
for dissection of the aorta. Alterations of the
arterial wall due to hormonal and hemodynamic
changes during pregnancy may lead to medial
defects and aneurysm formation.

In the past 13 years, we have treated five
patients with dissecting aneurysms which devel-
oped during pregnancy or the puerperium. Four
were operated on, and there was one operative
death. This report reviews the literature and
describes the characteristic features of dissecting
aneurysm during pregnancy or the puerperium.
The resected aortic wall was examined histologi-
cally for pregnancy-related pathologic changes
that might predispose it to dissection.

CASE REPORTS

Patient I: A 39-year-old woman suddenly
developed severe chest pain six weeks after her
first delivery. She was known to have had hyper-
tension for two years. Chest x-rays revealed an
abnormal mass in the left upper lung field. No

Key Words:
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Pregnancy
Pathogenesis of dissecting aneurysm
Acid mucopolysaccharide
Elastic fiber and smooth muscle of the aorta

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Second Department of Surgery, Kyoto University School of Medicine, Kyoto
*First Department of Pathology, Kyoto University School of Medicine, Kyoto
**First Department of Medicine, Wakayama Red Cross Hospital, Wakayama

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Dissecting Aneurysm during Pregnancy and Puerperium

TABLE I  SUMMARY OF DATA IN EACH CASE

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yrs)</th>
<th>Parity</th>
<th>Hypertension</th>
<th>Time of</th>
<th>DeBakey's Type</th>
<th>Shape of Aneurysm</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>39</td>
<td>0</td>
<td>+</td>
<td>1.5 mo.</td>
<td>16 mo.</td>
<td>post p.</td>
<td>post p.</td>
</tr>
<tr>
<td>2</td>
<td>32</td>
<td>2</td>
<td>+</td>
<td>9 mo.</td>
<td>1 mo.</td>
<td>preg.</td>
<td>post p.</td>
</tr>
<tr>
<td>3</td>
<td>34</td>
<td>1</td>
<td>–</td>
<td>5 mo.</td>
<td>1 mo.</td>
<td>preg.</td>
<td>post p.</td>
</tr>
<tr>
<td>4</td>
<td>45</td>
<td>2</td>
<td>–</td>
<td>4 mo.</td>
<td>4 mo.</td>
<td>preg.</td>
<td>preg.</td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>0</td>
<td>–</td>
<td>2 d.</td>
<td>6 mo.</td>
<td>post p.</td>
<td>post p.</td>
</tr>
</tbody>
</table>

\(d.:\) day(s), \(m.o.:\) month(s), \(Preg.:\) pregnancy, \(post p.:\) post partum

Further examination was performed. One year later, in May 1966, the patient underwent aortography because of persistent left back pain as well as the abnormal shadow in the chest film and was found to have a Type III dissecting aneurysm. In June 1966, operation was performed under cardiopulmonary bypass, and the aneurysmal descending aorta was replaced with a 25 mm-Teflon graft. Unfortunately, the patient died because of uncontrollable bleeding from the operative field.

Patient 2: A 32-year-old para 2, who had been pregnant for 36 weeks, was admitted to Wakayama Red Cross Hospital on December 1, 1973, complaining of severe back pain which was followed by a tight sensation over the anterior chest. Her blood pressure had been slightly high since the 28th week of pregnancy and was 158/86 on admission. Although no heart murmur was audible on admission, a grade 3/6 diastolic murmur and a 2/6 systolic murmur began to be heard at the third and fourth left intercostal spaces three days later, and the blood pressure was 170/0. A chest film revealed slight enlargement of the heart and widening of the aortic arch. Dissecting aneurysm combined with aortic insufficiency was suspected. With intensive drug therapy to control blood pressure, cesarean section was performed on December 8, 1973, and a normal infant was delivered. One week later, the aortic arch was further enlarged in a plain chest x-ray, and the patient was referred to our clinic. Aortography demonstrated a DeBakey Type I dissecting aneurysm combined with aortic regurgitation of grade III. Operation on February 4, 1974, revealed an aneurysm of the ascending aorta, 68 mm in length and 63 mm in diameter. Dissection did not extend to the aortic ring. Therefore, the aortic insufficiency appeared to be due to dilatation of the aortic annulus. The aortic valve was replaced with a 10A Starr-Edwards prosthesis, and the ascending aorta was replaced with a 30 mm woven Dacron graft. The postoperative course was com-
TABLE II SUMMARY OF HISTOLOGIC CHANGES, MINIMUM (+) TO MAXIMUM (+++)

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yrs)</th>
<th>Acid Mucopolysaccharide</th>
<th>Disruption of elastic fibers</th>
<th>Hypertrophy of smooth muscle</th>
<th>Calcification</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>39</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>32</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>34</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>45</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>cell infiltration</td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>50</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>++</td>
<td>atherosclerosis</td>
</tr>
<tr>
<td>7</td>
<td>44</td>
<td>++</td>
<td>+</td>
<td>–</td>
<td>++</td>
<td>atherosclerosis</td>
</tr>
</tbody>
</table>

Cases 6 and 7 are non-pregnant controls: Case 6, dissecting aneurysm; Case 7, true aneurysm. Surgery was not done in Case 5.

Complicated by mental disturbance but recovery was complete after hyperbaric therapy.

**Patient 3:** A primipara, aged 34 years, was admitted to Kochi Hospital in Kochi City with severe back pain and dyspnea. She was in the 20th week of pregnancy. Her symptoms subsided spontaneously soon after admission, although dull pain in the left back remained, and she was discharged with a diagnosis of pancreatitis. She delivered a normal female infant on March 28, 1978. Three days after delivery, she complained of severe back pain again and x-ray examination showed a possible thoracic aneurysm. The patient was transferred to our clinic and further examination confirmed a Type III dissecting aneurysm. She denied a history of hypertension. A temporary bypass was established between the ascending aorta and the right iliac artery, and the descending aorta was replaced with a 22 mm Dacron graft. The postoperative course was uneventful.

**Patient 4:** A 45-year-old para 2 suddenly developed severe pain in the back and anterior chest while driving in June, 1978. The pain continued intermittently. She was admitted to Tomita Hospital in Kyoto. A plain chest x-ray showed an abnormal shadow in the left upper lung field. Blood pressure was normal but laboratory examinations revealed abnormally high values of alkaline phosphatase (ALP), leucine aminopeptidase (LAP), and γ-glutamyl peptidase (γ-GPT). Therefore, thoracic aneurysm and liver dysfunction were suspected. The patient was referred to our clinic. Aortography showed a Type III dissecting aneurysm. Liver function tests were almost normal except for the abnormal values of ALP, LAP and γ-GPT. At this time, she first stated that her menstruation has been irregular and her last menses had been five months earlier. Gynecologic consultation revealed that she was in the 16th week of pregnancy. Surgical abortion with hysterectomy was done. Subsequently, the aneurysm became progressively bigger and produced atelectasis of the left upper lobe and increased back pain. On October 20, 1978, ten days after hysterectomy, surgical repair of the aneurysm was performed. The aneurysm involved the whole thoracic descending aorta, from the origin of the left subclavian artery to the level of the diaphragm. It was 100 mm in width. At the middle of the aneurysm, the aortic wall was very thin, adhesions to the chest wall had prevented rupture. The descending aorta was replaced with a 20 mm Sauvage graft during temporary aorto-iliac bypass. Postoperative recovery was smooth.

**Patient 5:** A 22-year-old patient had a normal delivery on January 6, 1976. On the second post partum day, she suddenly felt sharp chest pain radiating to the back and had a temperature of 38.5°C, but the symptoms disappeared spontaneously two days later. She was admitted to Wakayama Red Cross Hospital, and a diagnosis of Type III dissecting aneurysm was made by aortography. There was no history of hypertension. A repeat aortography performed eight days later at our clinic showed that the false lumen had apparently already been closed by a thrombus. It was decided, therefore, that the patient should be followed without surgery. She has done well to date.

None of the patients had Marfan's syndrome.
Fig. 1. Elastic van-Gieson stain (x 200). Disruption or fragmentation of the elastic fibers was seen in both pregnant (Fig. 1a, Case 4) and non-pregnant woman (Fig. 1b, Case 6). However, in the former changes were much more severe with loss of the elastic fibers. The accumulation of collagen is demonstrated by red coloration.

Fig. 2. Hematoxylin-eosin stain (x 200). With the same magnification, smooth muscle cells and fibers appear to be increased in number and size in Figure 2a (Case 3), but not in Figure 2b (Case 6). A large amount of a blue-white interstitial substance is seen in both figures. It probably represents the accumulation of acid mucopolysaccharide.

Fig. 3. Alcian-blue stain (x 200). The blue coloration, indicating acid mucopolysaccharide, was seen both in pregnant (Fig. 3a, Case 3) and in non-pregnant patients (Fig. 3b, Case 6). However, it is more intense in the former.
TABLE III  ANALYSIS OF DISSECTING ANEURYSM OF THE AORTA DURING PREGNANCY REPORTED IN THE LITERATURE, THE NUMBER OF CASES IS DIFFERENT IN EACH TABLE BECAUSE OF INCOMPLETE RECORDING OF SOME OF THE PARAMETERS

<table>
<thead>
<tr>
<th>* Age</th>
<th>20–29</th>
<th>30–39</th>
<th>40–46</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Case</td>
<td>52</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>21 (40%)</td>
<td>25 (48%)</td>
<td>6 (12%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>* Parity</th>
<th>Nullipara</th>
<th>Multipara</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Case</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9 (23%)</td>
<td>30 (77%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>* Time of Onset</th>
<th>Months of Pregnancy</th>
<th>Labor</th>
<th>Puerperium</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Case</td>
<td>28</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2–4</td>
<td>5–7</td>
<td>8–10</td>
</tr>
<tr>
<td></td>
<td>5 (18%)</td>
<td>2 (7%)</td>
<td>16 (57%)</td>
</tr>
<tr>
<td></td>
<td>2 (7%)</td>
<td>3 (11%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>* Time of Rupture</th>
<th>Months of Pregnancy</th>
<th>Labor</th>
<th>Puerperium</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Case</td>
<td>51</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2–4</td>
<td>5–7</td>
<td>8–10</td>
</tr>
<tr>
<td></td>
<td>3 (6%)</td>
<td>5 (10%)</td>
<td>26 (51%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7 (14%)</td>
<td>10 (20%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>* DeBakey’s Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Case</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td>27</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>* Associated Anomalies</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Case</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td>31</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>* History of Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Case</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td>28</td>
</tr>
</tbody>
</table>

syphilis, or congenital cardiovascular anomalies. The data are briefly summarized in Table I.

HISTOLOGIC STUDY

Sections of the aorta were obtained at operation from the four patients who had surgical repair, and the elastic fibers, smooth muscle and acid mucopolysaccharide were carefully examined and compared with two other specimens from non-pregnant women, one with a dissecting aneurysm and the other with a true fusiform aneurysm. Specimens were taken from unsplit or
least split part of the aorta adjacent to aneurysm where were usually at the site of anastomosis.

Elastic Fibers: Van Gieson elastic stain showed the elastic fibers clearly. Although disruption or fragmentation of the elastic fibers was seen in all specimens, including those from the non-pregnant women, it was most severe in Case 1 and Case 4 in which there was even loss of elastic fibers (Figures 1a and 1b).

Smooth Muscle: Both hypertrophy and hyperplasia of smooth muscle cells and fibers were usually seen in the pregnant patients and greater in Cases 1, 2 and 3 (Figures 2a and 2b).

Acid Mucopolysaccharide: Acid mucopolysaccharide was clearly shown with Alcian-blue stain, although it could be identified as a blue-white substance with Hematoxylin-eosin stain (Figures 2a and 2b). The amount of acid mucopolysaccharide appeared to be increased in all patients, but the blue coloration was most intense in Cases 1, 3 and 4 (Figures 3a and 3b).

In order to summarize the histologic changes due to pregnancy, the pathologic findings of each specimen were graded, from minimum (+) to maximum (+++), on the basis of severity as well as extent of the changes (Table II).

**DISCUSSION**

A search of the literature revealed a total of 54 cases of dissecting aneurysm in pregnant women reported between 1832 and 1977 (Table III). Most of the cases were collected by Pedowitz et al.15 and additional cases were reported by Hirst1, Hume14, Kitchen15, Stellwag-Carion16 and their associates. Most of these patients were multipara under forty years of age. The time of onset or of rupture of the aneurysm was most often during the third trimester and, contrary to what we would expect, relatively rare during labor. Thus, the stress of labor appeared to have little effect on the occurrence of this catastrophe. On the other hand, an increase in cardiac output and blood volume, which are usually observed in the later months of pregnancy17,18 are significant factors in the precipitation of this vascular accident. Hypertension was noted in 16 of the 28 cases in which the blood pressure was recorded, but in five cases hypertension first developed after pregnancy. Congenital anomalies, such as coarctation of the aorta or bicuspid aortic valve or Marfan’s syndrome, were present in 12 of 31 cases (36%). Type I of DeBakey’s classification was most common (70%).

In our cases, the time of onset varied, two were in the second trimester, two in the post partum period and only one in the third trimester, although there were no ruptured aneurysms, and in all cases there was adequate time for aortographic diagnosis. It was very lucky, however, that Case 3 had a normal uneventful delivery before diagnosis. Since most pregnant women refuse x-ray examinations for fear of adverse effects on the fetus, diagnosis of the aneurysm during pregnancy is rather difficult. In Case 4, however, the patient did not know that she was pregnant, so earlier diagnosis and treatment were possible. In four of our five cases onset was early in pregnancy or after delivery; in one third of the
reported cases rupture occurred during these periods. From the standpoint of the hemodynamic changes during pregnancy, it is hard to explain why many dissecting aneurysms develop or rupture in early pregnancy or in the puerperium when circulatory stress is minimal. Hormonal influences on the aorta might be an additional etiologic factor. During pregnancy, both estrogen and progesterone levels increase progressively, reaching a peak at term, and then abruptly fall\textsuperscript{19} (Figure 4). Gestational changes in the aorta were examined in rabbits by Danforth et al\textsuperscript{20} and in human beings by Manalo-Estrella et al\textsuperscript{21} and the following histologic features were noted: 1) fragmentation and disruption of the elastic fibers of the media, 2) hypertrophy and hyperplasia of the smooth muscle cells or fibers, and 3) decrease in the amount of interstitial acid mucopolysaccharides. Cavazo et al\textsuperscript{22} on the other hand, failed to find any such differences between pregnant and non-pregnant women. In most of the 54 cases published in which histologic studies were done, there were also so-called "Erdheim's" lesions or the equivalent, such as an accumulation of acid mucopolysaccharide and a decrease of elastic fibers. The presence of acid mucopolysaccharide within the aorta is not always pathologic and it generally increases with age\textsuperscript{23}. According to Asboe-Hansen et al\textsuperscript{24} and Likar et al\textsuperscript{25} the decrease in acid mucopolysaccharide during pregnancy appeared to be induced by progesterone and to be counteracted by estrogen. This decrease was clinically demonstrated only by Manalo-Estrella et al\textsuperscript{21} in pregnant women without dissecting aneurysms. On the contrary, an increase in acid mucopolysaccharide was generally found in our cases as well as in most of the other series of pregnant women with or without dissecting aneurysm! Recent opinion interprets focal collections of mucoid substances to be a secondary reparative or reactive phenomenon following degeneration of elastic fibers and smooth muscle! This is in contrast to the old study of Erdheim\textsuperscript{26} who suggested a primary overproduction of this substance. Kunita\textsuperscript{27} assumed, on the other hand, that the diminution of metachromatic substances might be the most important etiologic factor in dissecting aneurysm in patients under 40 years of age, whether pregnant or not. For lack of basic knowledge concerning the mucoid changes in the pathogenesis of dissecting aneurysm, further studies, including histochemical identification of acid mucopolysaccharide, will be needed to determine the role of this substance.

Degeneration of elastic fibers, perhaps the initial lesion of dissecting aneurysm, was seen in all reported cases, including ours. However, no clear evidence exists to implicate hormonal changes of gestation as a specific precipitator of the disruption or fragmentation of elastic fibers.

Hypertrophy and hyperplasia of smooth muscle, which have been reported to be characteristic features of pregnancy\textsuperscript{28,29} were rarely seen in any of the cases of dissecting aneurysm reported, but were present in various degrees in each of our cases. Since the aorta is predominantly an elastic artery, smooth muscle appears to be less important in the development of dissecting aneurysm of the aorta. Nevertheless, some authors\textsuperscript{29,30} have considered that a smooth muscle defect is the cause of dissecting aneurysm rather than hypertrophy or hyperplasia.

Hypertension, Marfan's syndrome and coarctation of the aorta were associated with dissecting aneurysm with almost the same frequency in both pregnant and nonpregnant patients! In our series, however, there were no cases of the latter two diseases.

In conclusion, statistical analysis has disclosed a positive correlation between dissecting aneurysm in young women and pregnancy. The hormonal changes of pregnancy probably affect the aortic wall to some degree, but it is not known whether this influence is so intense as to induce dissection of the aorta. Hemodynamic stress during pregnancy is probably a precipitating factor in the formation and rupture of dissecting aneurysms.

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