

Endometriosis in Rhesus Monkeys

Bo S. Lindberg¹ and Christer Busch²

¹*Primate Laboratory, Department of Obstetrics and Gynaecology and*

²*Department of Pathology, University Hospital, Uppsala, Sweden*

ABSTRACT

Endometriosis was present in five out of six Rhesus monkeys who had to be sacrificed because of disease in a colony of 90. The monkeys lost appetite and became constipated. The abdomen was distended and often a pelvic mass could be palpated. At autopsy, 300-500 ml of blood-stained fluid was found in the abdomen together with intestinal or pelvic endometriosis.

The etiology of endometriosis in Rhesus monkeys is unknown. The most probable explanation is intraabdominal implantation of endometrial tissue through retrograde menstruation. The lesion is rare in animals in free ranging colonies. It is not known whether this is due to a higher frequency of pregnancies in animals with free access to matings or to its consequences, i.e. more infrequent menstruations.

INTRODUCTION

Endometriosis is a disease which affects only menstruating individuals, humans as well as other primates. It has been reported in cynomolgulus (6), pig-tailed macaques (3), Rhesus monkeys (1), and in baboons (5).

The epidemiology of diseases such as endometriosis in laboratory animals is difficult to study. Instead, case reports might be of particular value. Furthermore, findings in non-human primates might give some clues to the etiology of the condition even in women. The present report gives the details of five cases from the Primate laboratory in Uppsala.

MATERIALS

The primate colony in Uppsala consists of about 90 Rhesus monkeys (*Macaca mulatta*). The animals are kept in individual cages and given free access to water. The food is composed of pellets, vegetables and fruits.

During the last two years, six animals have had to be sacrificed because of diseases. They were all received from commercial importers more than 10 years ago and were at least 15 years old. All had received synthetic oestrogens or gestagens for maximally a month ten years ago. The menstrual cycles were regular as judged by observation of blood on the floor of the cage. Only one of them (104; Table 1) had been pregnant (one delivery and one spontaneous abortion). They had not undergone caesarean section or irradiation.

Their behaviour was similar when the disease was observed. They usually ceased eating and were constipated. Laboratory investigations usually revealed anemia. On examination, the abdomen was found to be distended and often a pelvic tumour was palpated.

Laparotomy was performed in anaesthesia. In all cases except No 119, the abdominal cavity contained 300-500 ml of dark fluid consisting mostly of blood. Data on the findings at the operation are given in Table 1.

Table 1. Clinical and histological findings.

<u>Monkey</u>	<u>Tumour</u>	<u>Histological findings</u>
63	Intestinal	Endometriosis of the intestine causing obstruction.
68	Genital	Endometriosis embedding ovaries, uterus and omentum. The endometrium in proliferative phase. Sero-papillary ovarian tumour.
80	Genital	Endometriosis embedding ovaries, uterus and rectum. The endometrium autolytic.
104	Genital	Endometriosis embedding ovaries, uterus and rectum. The endometrium in proliferative phase.
119	Intestinal	Endometriosis of the intestine causing obstruction.
150	Genital	Necrotic, malignant epithelial tumour filling the pelvis.

HISTOLOGICAL FINDINGS

Appropriate blocks were fixed in 10 % formalin and embedded in paraffin. Five μm sections were stained with haematoxylin-eosin and Weigert-van Giesson. The macro- and microscopic findings are summarized in Table 1. Thus in 5/6 of the cases, the "tumour" appeared to be a classical endometriosis (Fig. 1), in two of the cases the lesion was confined to the large intestine (63 and 119), causing obstruction and ileus. Two other cases (80 and 104) showed massive pelvic endometriosis embedding ovaries and uterus in a partially necrotic mass. Also these lesions proved to be endometriosis on microscopic examination. The sixth case presented a necrotic pelvic mass which was judged as a malignant epithelial tumour of uncertain origin.

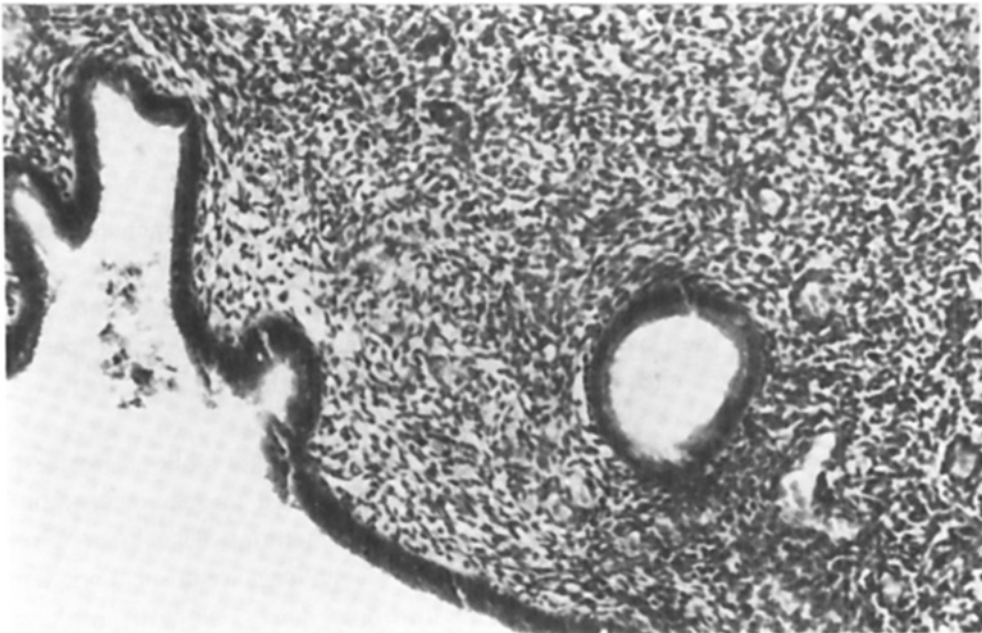


Fig. 1. Section from the tumour-like lesion of monkey 68. Typical endometriosis. H. & E x 40 (original magnification).

DISCUSSION

Since being first described in 1899 by Russell at Johns Hopkins Hospital (9), endometriosis has continued to intrigue observers. Many theories have been proposed for its etiology.

The implantation theory of endometriosis was proposed by Sampson in 1921 (10). Menstrual blood containing viable endometrial tissue was transported in

retrograde direction through the fallopian tubes and then implanted on extra-uterine abdominal organs. This theory was strongly supported by the work of TeLinde and Scott in 1950 (13). These authors surgically prepared 10 monkeys by transecting the uterus through the cervix below the internal os and turning it 180 degrees, while preserving the ovarian and uterine blood supply. Thus, they created a communication such that the animals menstruated from the endometrial cavity into the abdominal cavity. Four animals died of intercurrent diseases, while the remaining six developed endometriosis within two and a half months to three years.

Intraabdominal endometriosis in women has also been attributed to celomic metaplasia (8), which implies that the celomic lining of the peritoneal cavity was transformed by the blood through metaplasia to a paramesonephric type of epithelium and stroma. This theory was refuted by Scott and coworkers in 1953 (11). They injected blood obtained from Rhesus monkeys at the time of menstruation into the peritoneal cavity. Their only finding was adhesions and they were not able to induce endometriosis.

Endometriosis is common in the Rhesus monkey. A previous report cited a prevalence of 33 per cent in 63 animals (7). The prevalence increased with parity, age, increasing number of hysterotomies and increasing time since last pregnancy. Whether the increasing time since last pregnancy is a result rather than the cause of endometriosis remains to be settled.

Several explanations have been given to the occurrence of endometriosis in Rhesus monkeys. Frequent irradiations have been reported in some cases, but seem to be an unusual cause (12). In a report by Bertens et al, (1), a correlation between endometriosis and a previous early caesarean section was noted. However, this operation may not be the only cause, since in monkeys which only underwent repeated caesarean sections, not more than one case in 18 was found. In animals treated with ovarian steroids after the caesarean section, the incidence was highest (5 out of 8 animals). Ovarian steroids may have enhanced the endometriosis after the sections. In a group treated with ovarian steroids without operation, endometriosis was found in 2 out of 6 animals.

The theory of enhancement of endometriosis with ovarian steroids after caesarean section is also supported by Dizerega et al. (2), who were able to induce endometriosis in castrated Rhesus monkeys by seeding endometrial tissue in the abdominal cavity and afterwards treating the animals with ovarian steroids.

In a majority of the reported cases of endometriosis among monkeys, the animals have been housed in individual cages (3) as in our laboratory and they had not been mated. Animals living in free ranging colonies and given access to free matings seem to have less risk of endometriosis (4). However, whether this protection is due to the pregnancy itself or to its consequences, i.e. more infrequent menstruations, remains to be investigated. Another explanation may be that animals in free ranging colonies succumb earlier to diseases. Their ability to struggle for food may be reduced by the early symptoms of endometriosis.

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Address for reprints:

Bo Lindberg, M.D.
Department of Obstetrics & Gynaecology
University Hospital
S-751 85 UPPSALA SWEDEN