

Histological Variations of Canine Deciduoma Induced in Non Pregnant Horn at Different Stages of Unilateral Pregnancy

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ABSTRACT. Histological variations of canine deciduoma which was induced in the non pregnant horn at several stages of unilateral pregnancy were examined. In the first half of the unilateral pregnancy, deciduoma was characterized by the cystic glandular hyperplasia corresponding to each of the stages in normal early placentation. In the second half, deciduoma could not be induced and few histological reactions were recognized. The endometrium looked normal for late diestrus with no growth of the uterine glands. These differences might reflect the latent strength of the uterine glands to proliferate and dilate in the stimulated periods. — **KEY WORDS:** canine deciduoma, histological variation, stimulation phase.

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In our previous reports, we have examined whether deciduoma can be induced in canine and what kind of histological reactions will occur. These results showed that canine deciduoma could be induced also by almost the same methods as those in rodentia, however, the histological characteristics of the deciduoma were very different from rodentia. They did not originate from endometrial stromal cells but showed a similar structure to that of normal canine placentation (physiological decidual reaction), which is characterized by uterine glandular proliferation and dilatation [6–9]. Since then, we have continued to clarify the other properties of canine deciduoma, i.e., what sorts of stimuli can produce the reactions, what sorts of reactions can be seen [10, 11], and whether canine deciduoma is dependent on corpora lutea [12, 13].

In the present study, as a part of the continuing work on clarifying the characteristics of canine deciduoma, it was planned to discuss how the histological reactions are influenced by the differences of the stages for the stimulation.

Thirty mongrel bitches in the estrus were used for this experiment. They were divided into 6 groups according to the difference of the timing of the suture insertion, and each group consisted of 5 bitches. Before experimental treatments, all bitches were laparotomized, and the bifurcation of the left uterine horn and left oviduct were ligated to prevent the transport of fertilized eggs into the left horn. They were permitted to copulate with males freely, and to be impregnated in the right horn only. After that, these bitches were checked daily with vaginal smears (V.S.) to determine the first day of diestrus (Day 1) [4]. Each bitch received an insertion of a silk suture in the non-pregnant left horn. The suture insertion was performed at day 1 in group 1, day 5 in group 2, day 10 in group 3, day 20 in group 4, day 30 in group 5 and day 40 in group 6 respectively. A surgical silk suture was inserted through the uterine lumen near the junction of the cranial and middle thirds of the left uterine horn. The cranial one-third of the left horn was left intact as a control. Each bitch received a daily injection of antibiotic (aminophenylacetamido

penicillanic acid 10 mg/kg/day) until the experiment was terminated.

Twelve days after inserting the silk suture, a routine ovariohysterectomy was performed on the bitches. The removed ovaries and uteri were fixed in 10% buffered formalin solution immediately after macroscopic observation, embedded in paraffin and sectioned for histological preparations. On the evaluation of the histological changes, a positive was recorded when a stronger degree of glandular endometrial hyperplasia was observed in the left horn compared with that of the control part (intact cranial one-third of the left horn). Moreover, the degree of the placentation in the right pregnant horn was used for the comparative estimation of the latent ability for proliferation in the left uterine glands at each of the stimulated stages.

The results of the histological examination are shown in Table 1. The groups in the first half of the experiment (from day 1 to day 20) formed remarkable proliferation and dilatation of the uterine glands and the histological structure looked like “Swiss cheese endometrium” (Fig. 1). This histological tendency could be recognized most strongly in the groups 3 and 4 (day 10 and day 20). These histological structures resembled the normal histology of early placentation (Fig. 2). On the other hand, the proliferation

Table 1. Histological changes of the canine deciduoma in the non pregnant horn at several stages of unilateral pregnancy

Groups	Day ^{a)} of insertion and (hysterectomy)	Histological findings ^{b)} of glandular proliferation and dilatation in the		
		superficial	functional	basal layer
1	1 (13)	+	+	+
2	5 (17)	+	++	++
3	10 (22)	+	+++	+++
4	20 (32)	–	+++	++
5	30 (42)	–	–	–
6	40 (52)	–	–	–

a) Days after the first day of diestrus. b) –: no findings, ±: slight, +: weak, ++: moderate, +++: marked.

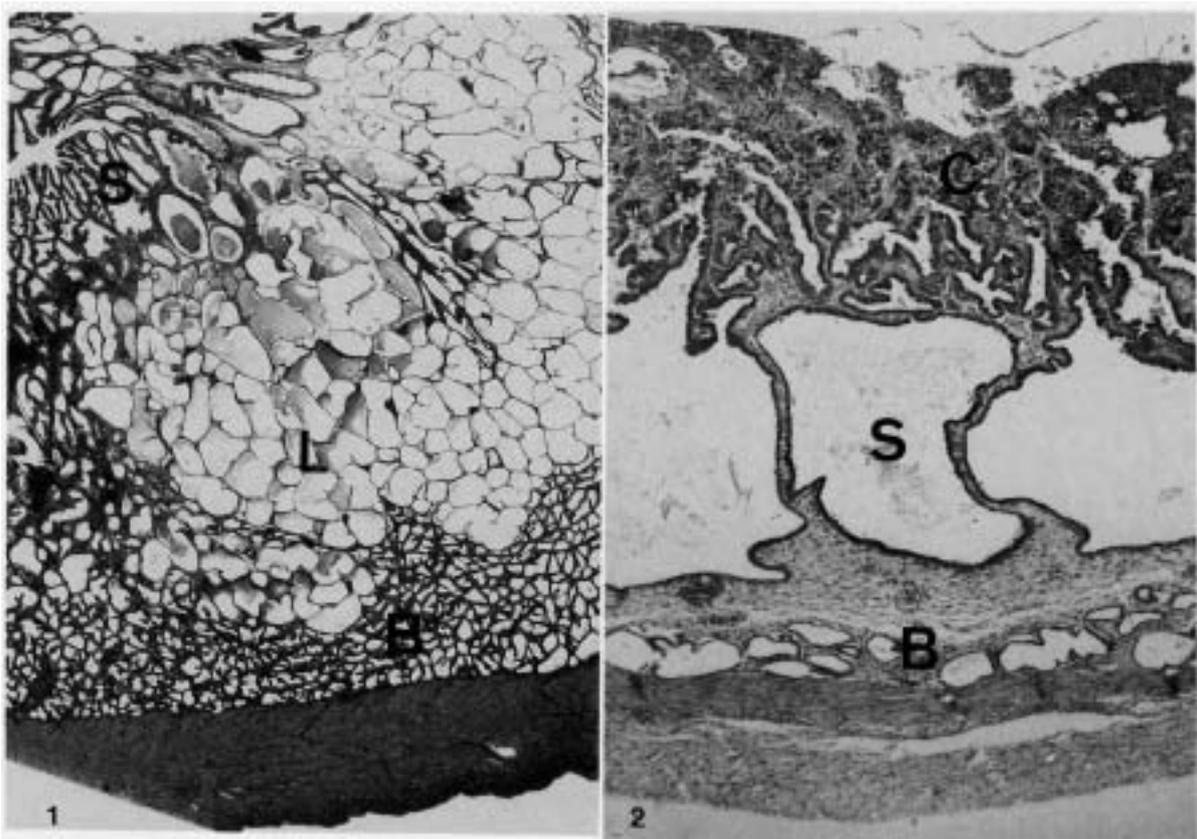


Fig. 1. Endometrial hyperplasia with cystic glandular dilatation (Canine deciduoma) which was induced in the bitch by inserting a suture during the first phase of the experiment (Day 10) is shown. Histological tendency of the glandular proliferation and dilatation in this deciduoma has resemblance to that in middle placentation (Fig. 2.). S: superficial hyperplasia of the glands. L: lacunar dilatation of the intermediate glands. B: cystic dilatation of the basal glands. H&E stain.

Fig. 2. The right pregnant horn in the same bitch in the Fig. 1. The normal middle placentation (Day 24) is shown. C: compact layer. L: layer of lacunar formation. B: basal glandular layer. H&E stain.

and dilatation of uterine glands could not be observed in the latter half of the experiment [almost all cases in group 5 (day 30) and all cases in group 6 (day 40)]. The histological findings of these cases showed a similar pattern to the normal late diestrous endometrium except a small reaction which was shown by the flattening and pseudostratification of the epithelia around glandular openings in the attached endometrium with inserted silk suture (Fig. 3).

From the results, the experimental groups could be classified into 2 types by the uterine histological changes, those showing cystic endometrial hyperplasia (CEH) and not those. The first four groups belonged to the CEH type (Fig. 1) and the later two groups belonged to the non CEH type (Fig. 3). They were clearly separated by the difference of the stage of stimulation.

The right horns in each bitch showed histologically the placental structures according to the days after the V.S. change (Day 1 [4]). Those of the groups from day 1 to day 20 showed the strong uterine glandular growth and differentiation. They showed several steps in the early placentation, and varied in structure from early spongy layer formation to incomplete endotheliochorial placenta

according to the time course after V.S. change (Fig. 2). However, those of the groups after day 30 showed no growth of new uterine glands and had a complete endotheliochorial pattern in the placentation (Fig. 4).

Each ovary at the ovariectomy showed normal histological findings corresponding to the time course after diestrus. Each bitch in the groups from day 1 to day 20 had some ripe corpora lutea in the ovary. However, some bitches in the groups of day 30 and day 40 had some degenerated corpora lutea which showed irregular outlines and contained some small vacuolated luteal cells with pycnotic nuclei among the normal ripe luteal cells.

In our previous reports, canine deciduoma usually have been shown by the histological characteristics of the uterine glandular hyperplasia and dilatation (cystic endometrial hyperplasia) [6-11].

In the present experiment, in the first period (Day 1-Day 20) canine deciduoma showed the typical structure of cystic endometrial hyperplasia (CEH) (Fig. 1). This phase, in the normal estrous cycle corresponds to the stage from early to middle diestrus when the level of the blood progesterone gradually increases and reaches the highest level [2, 3, 5].

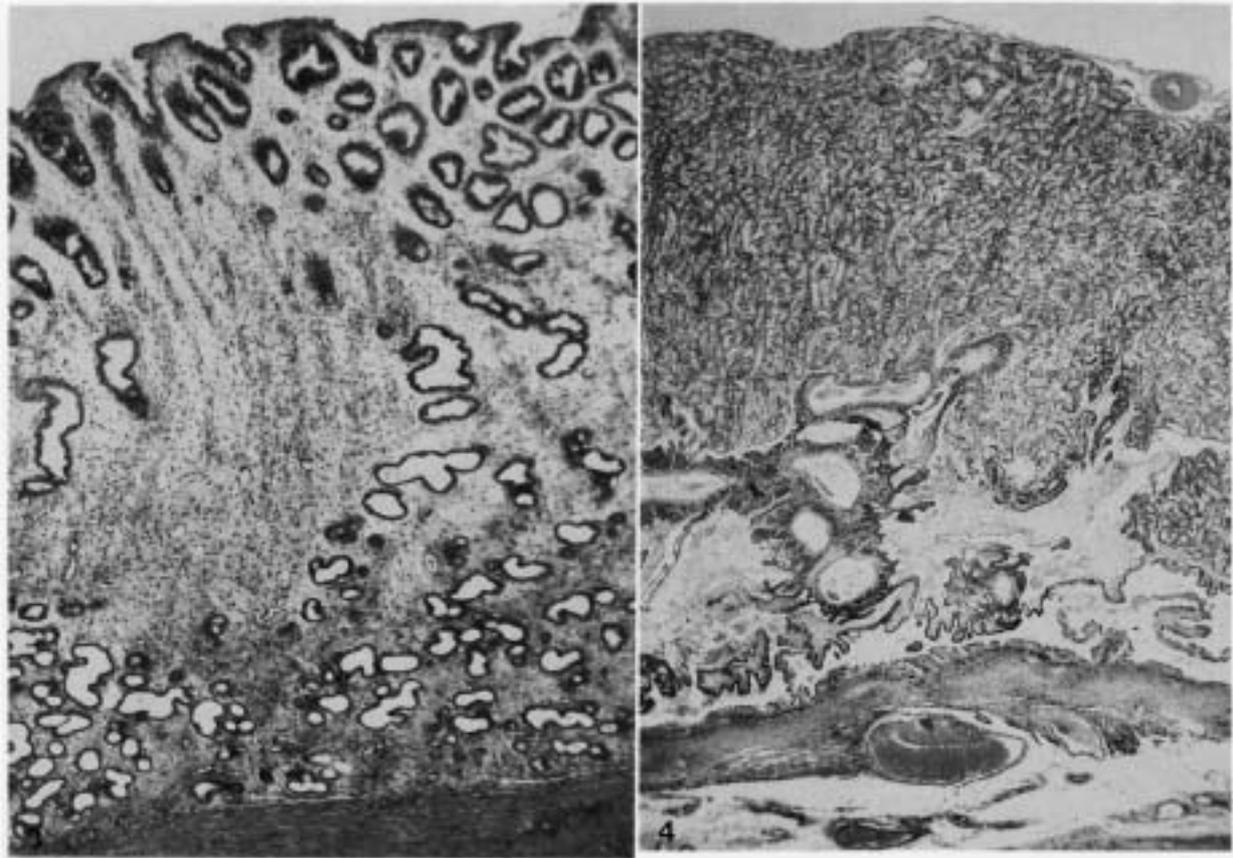


Fig. 3. Endometrium in the bitch stimulated in the late stage of the experiment (Day 40) resembles the normal endometrium in the late diestrus. The uterine glands show few reactions in the contrast with those of the contralateral pregnant endometrium (Fig. 4). H&E stain.

Fig. 4. The right horn of the same bitch in the Fig. 3 shows the normal placental structure near the terminated phase of pregnancy (Day 52). The uterine glands had already matured and do not show proliferation or dilatation such as in the early phase of placentation. H&E stain.

It is generally supposed that this phase has the highest sensitivity and shows the strongest potential power for the uterine glands to grow and differentiate (Fig. 2).

On the other hand, in the second period of the experiment (Day 30–Day 40), almost all cases except one showed no cystic endometrial hyperplasia (non CEH) (Fig. 3). Usually it is known that the growth of the canine uterine glands is dependent upon the ascending level of progesterone [1]. This phase in the normal estrous cycle corresponds to the decreasing stage of the blood progesterone level [2, 3]. So, canine deciduoma might no longer be induced under these circumstances. Histological reactions from this period of the experiment showed almost the same conditions as those of late diestrus which involves no proliferation and dilatation of the glands (non CEH) (Fig. 4).

Thus, in the present experiment, the histological characteristics of the reactions were clearly divided into two types by whether they showed CEH or not. The former groups in this experiment formed deciduoma, but the latter did not. This suggests whether canine deciduoma can be induced or not may be reflected by the endometrial circumstances especially the strength in the growth of

uterine glands. Therefore, it is estimated that near day 30 in this experiment may correspond to the turning point of the growth of the uterine glands in the endotheliochorial placentation, in other words, day 30 may be a turning point as to whether canine deciduoma can be formed or not.

Our previous reports mainly have dealt with the histological variations on the deciduoma caused by different stimuli [6–11]. In the present experiment it was shown that the histological strength of the canine decidual reactions were also changeable depending upon the stages of the stimulation in the diestrus.

In conclusion, it is suggested that canine deciduoma also has similar characteristics to those of rodentia. However, canine endometrial responsiveness could be clearly divided into two types by the stage of stimulation. Moreover, including the results of previous reports [6–13], understanding the behavior of the canine endometrium response to stimulation might be helpful in analyzing the pathology of the canine uterus. Especially in the pathogenesis of the canine pyometra, these uterine behavior will give us some important suggestions, i.e., canine pyometra may be a kind of a naturally occurring deciduoma

accompanying with infection, or contrary uterine infection may bring about a decidualoma and the differences in the opportunity of the infection may introduce the different histological types of canine pyometra. In future studies, we will examine these points by induction of the canine decidualoma by injection of bacterial solution into the uterine lumen.

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