DYNAMICS OF TISSUE AND VASCULAR CHANGES IN THE FRAGMENT OF OVARY REMAINING AFTER REMOVAL OF THE WHOLE OF ONE OVARY AND PART OF THE OTHER

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Numerous investigations have been made of regeneration of the ovary [1-3], but the dynamics of the histological changes taking place in its structural elements have not been fully elucidated, nor have the processes of reconstruction of the blood vessels and lymphatics of the residual part of the organ been studied.

Because of reports in the literature that the ovaries of rats and mice are unsuitable as test objects on account of their small size, the large number of follicles which they contain, and the development of cyclic processes in the sexually immature animals, experiments were carried out on the ovaries of rabbits.

EXPERIMENTAL METHOD

Operations were performed on 25 rabbits, previously isolated from males for 3-4 weeks (the duration of pregnancy in rabbits is 30 days), under ether anesthesia. One ovary was removed entirely, and the cranial or caudal part of the other was resected. Using a sterile slide caliper, simultaneous measurements were made of the removed ovary and of the resected and residual parts of the other ovary. The animals were sacrificed between 6 and 104 days after the operation, when the operation areas were inspected and the residual part of the ovary was measured, especially its length. The blood vessels (through the abdominal aorta, with ink) and the lymphatics (Gerota's blue mass, injected into the tissues) of the ovary, together with their capillaries, were then injected. The injected preparations were fixed, dehydrated in alcohols of rising concentration, and cut into thick(100-150 μ) sections, which were cleared in methyl salicylate; thin sections (10-15μ) were stained by Van Gieson's method. Some sections also were impregnated by Snesarev's method in order to demonstrate the argyrophilic stroma of the ovary.

EXPERIMENTAL RESULTS

At autopsy on the rabbits following the operation, the residual part of the organ in most cases was immured in the tissue conglomerate consisting of the oviduct, the parietal peritoneum, and cellular tissue. In about half the cases adhesions were found between the divided end of the ovary and loops of large intestine. The large vessels of the abdominal cavity were moderately hyperemic. The tip of the ovary was oval and elongated in shape, like the ovary of the nonpregnant rabbit, a feature observed in some cases by the 6th-7th day after the operation; in other cases the site of section was clearly visible even 15-20 days after the operation.

In most experiments the residual ovarian fragment was appreciably enlarged by the 15th-30th day after the operation. At longer intervals after the operation the ovary was smaller than initially, and this reduction in size was more clearly seen during the last days of the experiment.

The results given in the table show that the length of the regenerating ovary increased from the first days after the operation. In no case, however, did it regain its original length. The results of a few measurements of the width and height of the organ show that these dimensions also increased during regeneration. Hence, 10-35 days after the operation, the organ had almost regained its original volume, although its dimensions were changed. This

Changes in Measurements of Residual Part of Ovary at Different Periods after Removal of One Ovary and Part of the Other from a Rabbit

Time after operation (in days)	Dimensions of ovary wholly removed at operation	Dimensions of part of second ovary removed at operation	Length of part of ovary left behind at operation	Dimensions of ovary in animals at autopsy	Difference in length of residual part of ovary during operation and at autopsy
	In cm				
6	1,25×0,55×0,46	0,91×0,64×0,42	0,50	0,56×0,54	+0,06
10	1,48×0,40×0,36	0,81×0,47×0,37	0,88	0,98×0,52	+0,10
10	1,23×0,45×0,28	0,55×0,42×0,23	0,91	1,03×0,46	+0,12
11	0,90×0,36×0,34	0,41×0,32×0,37	0,60	0,45×0,36	—0,15
13	1,92×0,29×0,23	0,92	0,60	0,64×0,30	+0,04
14	1,45×0,60×0,44	0,61×0,43×0,29	0,54	0,72×0,35×0,31	+0,18
15	1,08×0,52×0,32	0,48×0,43×0,38	0,44	0,72×0,36	+0,28
15	1,29×0,29×0,30	0,62×0,33×0,27	0,71	0,64×0,31	—0,07
16	1,33×0,37×0,32	0,63×0,33×0,31	0,67	0,34×0,54	—0,33
17	1,09×0,39×0,28	0,51×0,36×0,23	0,78	0,86×0,42×0,37	+0,08
19	1,27×0,43×0,30	0,64×0,50×0,32	0,50	0,61×0,31×0,28	+0,11
20	1,15×0,47×0,36	0,66	0,55	0,62×0,54	+0,07
20	1,01×0,21×0,24	0,58×0,27×0,26	0,54	0,70×0,38	+0,16
25	1,35×0,46×0,24	0,42×0,38×0,25	0,60	0,91×0,41	+0,31
25	1,58×0,53×0,47	0,73×0,50×0,50	0,69	0,74×0,50	+0,05
30	1,06×0,45×0,34	0,49×0,45×0,38	0,56	0,67×0,46	+0,11
30	1,64×0,38×0,31	0,68×0,36×0,34	0,73	0,91×0,44×0,27	+0,18
35	1,16×0,44×0,27	0,62×0,40×0,29	0,66	0,66×0,44	0,00
35	1,25×0,39×0,27	0,68×0,45×0,27	0,60	0,61×0,40	+0,01
40	1,04×0,45×0,41	0,53×0,46×0,43	0,63	0,60×0,46	—0,03
50	1,08×0,37×0,28	0,68×0,23×0,23	0,55	0,30×0,25	—0,25
97	1,04×0,37×0,30	0,53×0,40×0,33	0,50	0,27×0,27	—0,23
98	1,00×0,31×0,20	0,50×0,29×0,27	0,57	0,36×0,31	—0,21
98	1,10×0,28×0,31	0,48×0,30×0,34	0,63	0,59×0,24	—0,04
104	1,13×0,17×0,27	0,53×0,24×0,30	0,54	0,31×0,30	—0,23

demonstrates that regeneration of the ovary is not brought about by the spread of tissues out from the wound surface, but by an increase in the size of the remnant of the organ as a whole, i. e., by regeneration hypertrophy. At the later periods atrophy of the organ was proceeding.

Corresponding to the changes described above, affecting the size of the organ, transformation of its macro- and microscopic appearance took place. These changes showed a very great variety, especially in the early periods after the operation.

Hypertrophy of the ovary was shown morphologically by proliferation of the stroma, intensive ripening of follicles, and enlargement of the corpora lutea. Whereas during the operation large Graafian follicles were present in the ovary, at autopsy on the animals 11-15 days later an intensive luteinization of the organ was observed. In the region of the operation field there was marked proliferation of connective-tissue fibers, branching out from the adjacent intact portions of the tunica albuginea and the large connective-tissue trabeculae of the medullary layer. At these periods the bundles of fibers mentioned above did not compress the generative elements, lying in the space between them. In the hypertrophied ovary the blood and lymphatic capillaries were correspondingly dilated within the medullary layer, in the connective-tissue trabeculae, and in the specific membrane of the vesicular follicles.

In the 3 observed cases of "early" atrophy death of the majority of the interstitial cells of the ovary was observed, and some of the remaining cells were enlarged to twice or three times their original size, and underwent vacuolation. At the same time, massive death of primordial follicles and thickening of the thecal membrane of the vesicular follicles were observed in the ovary. With respect to the blood and lymphatic capillaries, signs of reduction were observed. The capillaries of the cortical layer were preserved only in individual connective-tissue septa, at the periphery of solitary enlarged interstitial cells, and in the membrane of the follicles.

On approximately the 30th-35th day, hemorrhagic follicles or cysts were seen to project from the surface of the organ. The previously functioning generative elements were replaced by connective-tissue fibers. The interstitial cells were undergoing replacement by small, apparently compressed connective-tissue cells, or some cells were observed to be dead while others showed signs of swelling or cystic hypertrophy. Both processes were accompanied

by a marked reduction in the capillary system of the organ. Blood and lymphatic capillaries remained only in the relatively large bundles of fibers and they did not surround every cell, as is normally observed.

A progressive connective-tissue degeneration of the ovary was occurring. The fibers of the stroma were tortuous, thickened in places, and sometimes intertwined haphazardly. The vessels of the medullary layer were considerably dilated, the cortical layer was atrophied, and the tunica albuginea was thickened. The interstitial cells, either solitary or grouped into round foci, were abundantly vascularized.

The changes in the follicular apparatus consisted, not only of the development in certain cases of hemorrhagic follicles and cysts, but also of degeneration of the oocytes, large-scale atresia, and persistence of solitary follicles. The latter usually had a hypertrophied, abundantly vascularized, connective-tissue membrane.

Distinctive processes were taking place in the corpora lutea. In the period immediately after the operation the lutein cells were well developed, and were surrounded by three-dimensional plexuses of blood and lymphatic capillaries. One month after the operation changes were taking place in the corpora lutea. Sometimes atrophy of the majority of the lutein cells and hypertrophy of the remainder were seen. In these cases the group of residual lutein cells was surrounded by connective-tissue fibers and was highly vascularized. The residual cells were conventionally called "secondarily hypertrophied" cells, for the "primary" process involved the whole corpus luteum uniformly. Total atrophy of the lutein cells of the corpora lutea sometimes developed. A marked enlargement of the corpus luteum and of all its structural elements was observed. Such corpora lutea were distinguished by the presence of large cystic cavities, often with blood-stained contents, of smaller slit-like spaces, arranged haphazardly among the lutein cells, but largest at the periphery of corpus luteum, and a greatly enlarged connective-tissue center by comparison with the usual dimensions.

The processes of cystic degeneration of the lutein cells and interstitial elements were accompanied by a sharp reduction in the number of bundles of connective-tissue in the stroma of the organ and by the appearance of characteristic cystic cavities. Corresponding changes took place in the system of blood and lymphatic capillaries within the ovary. This process occurred in two different ways: either as the atrophy and disappearance of a large proportion of the capillaries or as the atrophy of some capillaries and hypertrophy of the few remaining vessels. In the latter case the greatly dilated capillaries persisted in the thick bundles of fibers of the connective-tissue membrane of the cortex of the ovary. Marked dilation of the blood and lymphatic capillaries and, in particular, of the vessels was observed in the medulla.

The most obvious tissue disturbances developed against a background of general atrophy of the organ in places where previously follicles, corpora fibrosa, and corpora lutea had been. Whereas in ordinary conditions the normal function of the organ is restored within a short time, in the partially resected ovaries this process either did not take place at all, or it developed very slowly.

Distinctive changes took place in the theca folliculi. Although initially it was hypertrophied during growth of the organ, the theca subsequently underwent atrophy with atresia of the follicles. By the 30-40th day the thickened theca interna could be seen only in the solitary persistent follicles and cysts, but by the 60th-100th day it had undergone complete atrophy in both. The only explanation that could be given was that the persistent follicles and cysts initially performed a definite hormonal, partially compensatory function against the background of general atrophy of the whole organ, but these mechanisms also gradually disappeared.

The processes described above were associated with sharp changes in the anatomy of the blood vessels and lymphatics within the ovary. At first the capillaries and larger vessels were able to develop, but in some cases the walls of the larger vessels began to thicken, and this was followed by partial obliteration of the capillaries, which was particularly marked in the cortex of the organ. These findings give indirect evidence of a local decrease in the intensity of metabolism. Oxygen lack, and accumulation of metabolic products, evoked a compensatory dilation of the residual blood and lymphatic capillaries, and an uneven filling of the larger vessels with blood. The disturbances of tissue metabolism also led to an increase in permeability, for the destruction of the argyrophilic substance of the stroma, described above, also affected the argyrophilic elements of the vessel walls. This was evidently related to the phenomenon of dystonia, manifested by the variations in caliber and the tortuosity of the capillaries and larger vessels.

Hence, 10-15 days after the operation, either signs of regeneration hypertrophy (in most cases) or signs of "early atrophy" of the ovaries developed. Regeneration hypertrophy was observed until approximately the 30th-35th day after the operation, and then gave way to atrophy, which was conventionally called "late atrophy."

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