REGENERATION OF LYMPHATICS AFTER EXTIRPATION OF LYMPH GLANDS

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Regeneration of lymphatics was discovered after extirpation of the popliteal lymph gland in dogs, with complete restoration of the lymph flow. No regeneration of the lymph gland was observed.

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The possibility of regeneration of lymphatics after removal of lymph glands is of great practical importance because extensive extirpation of these glands is constantly being undertaken during the surgical treatment of malignant tumors. The problems has often been discussed but is still far from being solved, and opinions of investigators differ [1-4, 8-13, 16]. Meanwhile, solution of this problem may help not only to explain some of the causes of postoperative complications, but also to prevent them. For this purpose 40 experiments were carried out on 20 dogs.

EXPERIMENTAL METHOD

Under thiopental anesthesia, 2-3 ml of a 0.4% solution of indigocarmine was injected very slowly into the digital pulp of the hind limb of the dog. The operation field was prepared and a skin incision 4-5 cm made in the region of the popliteal fossa. The lymphatics located in the upper third of the leg and draining into the popliteal gland served as guides for the projection and location of this gland. These lymphatics were colored blue 4-5 min after injection of 3-4 ml of 0.4% indigocarmine into the digital pulps. The lymph gland was separated from the surrounding fatty areolar tissue partly by sharp, but more especially by blunt dissection, and after division of the afferent and efferent lymphatics the gland was removed. The operation wound was closed in layers without drainage. Continuous intravital observations on the state of the lymphatic system of the dog's hind limb after the removal of the lymph gland were carried out by intravital lymphography using 70% diodone solution.

Every 10 days after the operation a group of animals (2 or 3) was sacrificed. The longest period of observation was 540 days. Immediately after autopsy the lymphatic system of the dog's limb was injected with No. 2 Gerota–Akilova fluid (modified by Zerbino [5]), and then fixed in 12% neutral formalin. After injection and fixation, the lymphatics were dissected and macroscopic and microscopic preparations made and studied, using the MBS-1 binocular microscope. A histological investigation was also made of the region of extirpation of the lymph gland. Pieces of tissue cut from the cleared preparation were washed by Kraev's method [7], dehydrated, soaked in celloidin, and stained with hematoxylin-eosin or by Van Gieson's method.

EXPERIMENTAL RESULTS

Ten days after extirpation of the lymph gland, the lymphatics were seen to come to a halt at the operation site, and no further movement of the contrast medium occurred. On the 20th day after the operation, collateral lymphatics began to appear. The main trunk also was restored, and the newly formed capillaries and vessels connecting the two divisions of the divided lymphatic trunk were particularly well marked in some experiments. Restoration of the lymph flow occurred after regeneration of lymphatic capillaries running from the stump of the divided lymphatics. Regeneration of the large lymphatics was due to several factors, an increase in pressure in the distal stumps of the divided lymphatics being among the most important [14, 15].

One month after complete extirpation of the popliteal lymph gland, almost the same picture was observed as in the earlier periods. It should be mentioned that the collateral channels observed after injury

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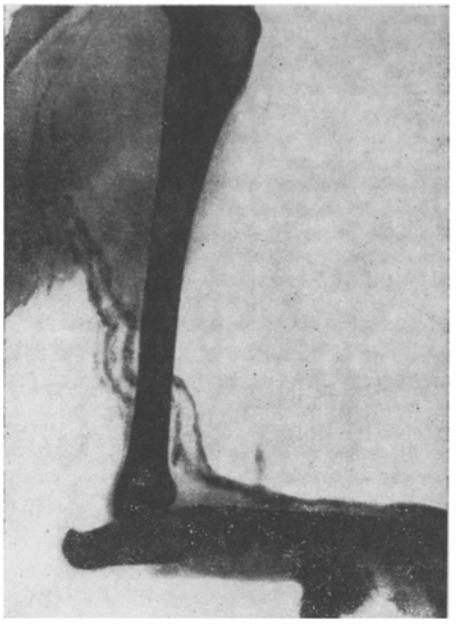

Fig. 1

Fig. 2

Fig. 1. Lymphatic capillaries and vessels connecting the lymphatic trunks are visible 50 days after removal of the lymph gland. Lymphography with 70% diodone solution; prints taken from roentgenogram.

Fig. 2. Structure resembling a lymph gland can be seen 8 months after operation in the region of the extirpated gland. Modified Gerota's medium. MBS-1, 8×.

Fig. 3. Structure resembling lymph gland can be seen 18 months after operation in region of extirpated gland. Modified Gerota's medium. MBS-1, 8×.

to the main trunk could arise as a result of: a) growth of capillaries, b) transformation of lymphatic capillaries into lymphatic vessels, and c) the opening up of reserve pathways already in existence but not detectable by injection. So far as pre-existing shunts are concerned, they were observed only after injury to the main lymphatic trunk, and otherwise they did not appear. Finally, newly formed anastomoses arising through regeneration of capillaries and restoration of direct communication between the stumps of the divided vessels must also be mentioned.

In the course of 1.5-2 months the vessels of the main trunk interrupted by removal of the lymph gland began to appear. By this time lymphatic capillaries and vessels could be seen between the proximal and distal stumps, bridging the gap between the divided segments of the lymphatic trunk of the limb. Initially the vessels were numerous, winding, and tangled, but later they became straighter and less numerous (Fig. 1).

Between 8 weeks and 6-8 months after the operation, further gradual differentiation of the lymphatic vessels took place at the site of the removed gland, so that the interrupted lymph flow was restored. The need for collateral lymphatic channels decreased, and some of them gradually ceased to fill with contrast material.

Being a macroscopic method, roentgenography does not completely solve the problem whether complete or partial regeneration of lymph glands can take place, but nevertheless it is worth mentioning that after total extirpation of the glands, in 3 cases structures resembling new lymph glands were detected on the roentgenograms.

Before these structures were detected, many roentgenograms had been taken, and they were seen for the first time in one case 8 months, in another 9, and in the third 18 months after the operation. The problem of whether these structures were in fact lymph glands could be finally solved only by detailed microscopic investigation.

Examination of cleared macroscopic and microscopic specimens taken from the region of the extirpated gland in the three cases described above revealed structures with fairly well defined outlines resembling lymph glands with afferent and efferent vessels between 30 and 500 μ in diameter (Figs, 2 and 3).

Histological examination of these "lymph glands" in one case revealed a lymph gland with well marked sinuses and capsule, and in another case part of a lymph gland was found with a well defined capsule and with sclerosis of the trabeculae. Side by side with the gland, in the fatty areolar tissue, dilated lymphatics filled with lymph were seen. Finally, in the third case, among the fatty areolar tissue at the site of removed gland many lymphatics were found with a fairly thick wall, including muscle fibers. No lymphocytes were present whatever. Great care is needed in interpreting the results of the first two of these observations as regards the possibility of new gland formation. It is quite possible that during the operation a small part of the gland was left behind, and that the structures described above regenerated from it. It could also be suggested that these glands existed in the dogs before the operation, but were not included in the main lymphatic channel under normal conditions of lymph flow. When the conditions were sharply modified, however, and stasis of lymph developed in the limb after the severe trauma to the lymphatic pathways, these glands then became incorporated and underwent vicarious hyperplasia [6].

In some cases (270-360 days), a plexus of lymphatics forming an elongated oval developed at the site of the extirpated gland. This plexus apparently replaced the extirpated gland, for all the lymph flowing along the main trunk passed through it. In other cases, 3 to 4 lymphatics (400-600μ in diameter) passed through the site of the extirpated gland at this time, and were completely indistinguishable from the proximal and distal portions of these vessels, being uniformly stained blue by the injection material, and with valves clearly visible in them. In other cases, 180-240 days after the operation, numerous lymphatics of different diameters could be seen at the site of the extirpated gland, anastomosing with each other and forming a network; the newly formed network connected the proximal and distal stumps of the divided lymphatics.

In no case, therefore, was regeneration of the extirpated lymph gland reliably observed. These experiments, it will be noted, are only the first steps in elucidation of the principles governing development and new formation of lymphatics in experimental animals, and their results cannot be applied to man without further intensive study.

The practical importance of the results of these experiments is determined by the possibility that lymphatic communication may be established between organs following changes in the conditions of the lymphatic circulation. This may subsequently influence both the pathways of spread of metastases of malignant tumors and also the course of infections developing in regions where operations have previously been performed on parts of the lymphatic system.

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