On the Behavior of the Bone Marrow Elements Transplanted into the Double-Ligated Segment of the Artery

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The endothelial cells of arteries or veins in the adult organism are generally believed to be highly differentiated cells. But it is also the consensus of opinion that they still retain the ability of active proliferation like the common connective tissue cells under special conditions, e.g., after ligation of the vessels (Baumgartner, 1876; Malyschew, 1929; Ferrara, 1950; and Mehrotra, 1953) and in in-vitro culture (Silberberg, 1929; Shibuya, 1931; Törö, 1937; and others). In the earlier experiments by Tagawa (1957a), it was confirmed that double ligation of the carotid artery of the adult rabbit elicits an extensive proliferation of the endothelial cells in the enclosed segment, resulting in a considerable intimal thickening. Since the vascular endothelium is thought to be a cell type closely related to the blood cells in its early developmental stage, the question then arises whether or not the blood cells, the immature forms in particular, when transplanted into the double-ligated segment of an artery, are able to grow like the endothelial cells in the enclosed segment. The present work is an attempt to answer this question.

Material and Methods

Twenty-three adult albino rabbits of both sexes weighing about 2 kg each were used. The right common carotid artery was tied by two ligatures about 10–15 mm apart, as described previously (Tagawa, 1957a). After 4, 8, 12 and 16 days, cellular elements or fragments of bone
marrow taken from the right femur of the same animal and suspended in saline, were injected in the double-ligated segment of the artery. Injection was easy until the 8th day after ligature, but thereafter it became difficult because the ligated arteries had turned very stiff by that time. In another series of rabbits, cellular elements or fragments of lymphatic tissue taken from the right popliteal lymph node of the same animal were injected into the ligated segment of the carotid artery. For all operative procedures sterile technic was employed.

At successive intervals from 12 hours to 13 days after injection, the double-ligated segments of the artery were excised, fixed in Zenker-formol, embedded in paraffin, sectioned serially at 6 μ and stained with Mayer's acid hemalum and eosin.

Results

Until 24 hours after injection of bone marrow, the nucleated marrow elements remained almost intact in the double-ligated segment of the carotid artery, but thereafter they gradually underwent degeneration. At the 48-hour stage, nuclear fragments derived from the disintegrated cells became very numerous and the nucleated marrow elements disappeared almost completely by the 96th hour after injection of bone marrow, with the exception of a few myelocytes and fat cells remaining in the enclosed arterial segments (Figs. 2-3). At stages later than the 96th hour, neither myelocytes nor other immature blood cells were found anywhere in the ligated segment of the artery.

In the cases in which cellular elements or fragments of lymphatic tissue taken from the right popliteal lymph node had been injected in the ligated segments of the carotid artery, the injected lymphoid cells also did not show any tendency toward proliferation in the enclosed arterial segments.

The endothelial cells of the ligated artery, on the other hand, were in active proliferation from the 7th day on after ligature, as described in a preceding paper by Tagawa (1957a).

Discussion

The present experiments have shown that the injected immature blood cells of bone marrow were unable to grow in the double-ligated segment of the carotid artery, although the endothelial cells in the enclosed segment showed active proliferation. In his earlier observations
on the reactions of the reticuloendothelial cells of the rat liver to trypan blue, Tagawa (1957b) demonstrated that repeated injections of the dye brought about an extensive proliferation of these cells, whereas the hemopoietic activity of bone marrow was considerably decreased thereby. These findings would indicate that, so far as their proliferative reactions to certain stimuli are concerned, no close relation is to be seen between the endothelium and the blood cells. This is partly understandable in view of the fact that in the adult the endothelial cells show no signs of mitosis under physiologic conditions, whereas the immature blood cells are normally in active proliferation. In this respect, the endothelial cells closely resemble the common connective tissue cells.

It is generally believed, on the other hand, that in its early developmental stage the young endothelium has the property of forming blood cells. Some investigators as Syssojev (1926), Malyshev (1927, 1929) and Altschul (1947) further claim that the vascular endothelium of the adult organism may turn into blood cells through its proliferative processes. Of especial interest in this connection is the work of Malyshev (1929), who observed the occurrence of myelocytes and, rarely, of erythroblasts inside of the ligated segment of the carotid artery of adult rabbits. This author assumed that these cells stem from the proliferated endothelium. This view, however, was vigorously opposed by the majority of workers (e.g., Clark, 1927; Falk, 1928; Goss, 1928; Ehrlich, 1934).

In an earlier investigation, Tagawa (1957a) followed up the experiments of Malyshev as closely as possible but failed to confirm the appearance of immature blood cells in the double ligated segment of the rabbit carotid artery. Yet the possibility still remains to be considered that the immature blood cells trapped in the ligated segment of arteries might proliferate therein. The results of the present experiments indicate that such a possibility is very slight.

Summary

In a series of adult albino rabbits, the common carotid artery was tied by two ligatures about 10–15 mm apart. After 4, 8, 12 and 16 days, cellular elements or fragments of bone marrow and those of lymph node of the same animal were injected into the double-ligated segment of the artery. It was disclosed that neither the immature blood cell of bone marrow nor the lymphoid cells of lymph node
injected into the ligated artery showed any tendency toward growth therein. In contrast, the endothelial cells in the enclosed segment of the artery were in active proliferation from the 7th day on after ligature.

Reference


Explanation of Figures

Plate I

1. Cross-section of the double-ligated segment of the carotid artery, showing
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nucleated marrow elements remaining almost intact in the enclosed segment. Twenty-four hours after injection of bone marrow (120 hours after ligature). Notice that the many pseudoeosinophil leukocytes which are migrating through the wall of the artery show a circular arrangement along the elastic fibers. \( \times 100. \)

2. Cross-section of the double-ligated segment of the carotid artery, illustrating the disintergrated marrow cells with a decreased number of fat cells. Ninety-six hours after injection of bone marrow (12 days after ligation). \( \times 100. \)

3. Greater magnification of a few marrow elements (myelocytes) remaining intact in the double-ligated segment of the carotid artery until 96 hours after injection of bone marrow (8 days after ligation). \( \times 400. \)