CAPILLARY PATTERN OF THE THYROID GLAND IN THE RAT IN FUNCTIONAL BLOCK

By

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ABSTRACT

1. The capillary pattern of the thyroid gland was studied in the rat: one group had undergone hemithyroidectomy, one was treated with propyl thiouracil, and one subjected to both these experimental measures. Histological and microangiographic observations were compared with those in an intact control group.

2. Epithelial hyperplasia and other morphological signs of activity were seen to a moderate extent in the hemithyroidectomized group, were marked in the rats treated with thiouracil, and most marked in the group subjected to both thiouracil medication and hemithyroidectomy.

3. The appearances of the interfollicular capillaries showed no perceptible changes in the group subjected solely to hemithyroidectomy.

4. Changes of the interfollicular capillaries were marked in all the animals treated with propyl thiouracil. In the group only treated with propyl thiouracil, the capillaries were dilated to sinusoid-like blood pools in limited segments between which the capillaries were of normal width. In the group subjected to both hemithyroidectomy and propyl thiouracil treatment the interfollicular capillaries were dilated throughout their course.

5. The significance of these morphological and microangiographic observations is discussed.

The thyroid gland has long been known as an organ with a very abundant blood supply. Its vascular anatomy has been studied by Major (1909), Modell (1933), and recently by Johnson (1955), and others. These investigations have shown that the distribution of vessels in the gland corresponds in general to its lobular structure, so that each lobule is supplied by an artery and its individual follicles by capillaries originating in that artery.
This normal vascular pattern is altered in some respects when the gland is changed into a nodular goitre. In such altered tissue Wangensteen (1929) observed large sinusoidal vessels, and Johnson (1955) demonstrated similar vessels – »giant vessels« – in nodules the histological features of which corresponded to those of a foetal adenoma.

Since the vascular, and especially the capillary, pattern of the thyroid gland appears in some measure to be dependent on the functional state of the gland, we thought it of interest to study the vascular pattern microangiographically in connection with operative reduction of the thyroid parenchyma. after a certain period of thiouracil treatment, and also with a combination of these two experimental measures.

The effect of thiouracil on the vascular bed of the thyroid gland in the rat was studied by Thomas (1945), who reported very large interfollicular capillaries – »giant capillaries«. Furthermore, he described two capillary systems in the thyroid: one interfollicular identical with that mentioned above and assumed by others to be the capillary bed of the individual follicles, and one intra-epithelial originating in the former, whose existence has been questioned by Johnson (1955) and others.

Apart from these studies, we have failed to find in the literature any reports on the reaction of the vascular pattern of the thyroid gland to factors such as reduction of the parenchyma and thiouracil medication. This led us to believe that an investigation of these matters was warranted.

MAT E R I A L AND METHODS

Forty white laboratory rats were used, their weights ranging from 250 to 400 g at the start of the experiments. The series was divided into four groups of ten rats each according to the experimental conditions described below. The experimental period lasted 30 days.

1) Normal control group – intact rats receiving no treatment during the experimental period – »C-group«.
2) Thiouracil group – intact animals receiving a daily dose of 0.05 g of propyl thiouracil during the experimental period – »T-group«.
3) Operation group – rats subjected to hemithyroidectomy at the start of the experimental period and subsequently not given thiouracil – »O-group«.
4) Thiouracil and operation group – hemithyroidectomized rats given a daily dose of 0.05 g of propyl thiouracil during the experimental period »TO-group«.

The procedure at hemithyroidectomy consisted of removal of the left lobe under open ether anaesthesia and sterile conditions.

The propyl thiouracil was distributed to the animals in daily feeds of grated cheese which was eagerly consumed.

After 30 days, the animals were sacrificed and the microangiographic examination described previously was performed (Nylander & Olerud 1960). The contrast medium was barium sulphate (Micropaque suspension). After its infusion, the animals were fixed for 48 hours in toto in 10 per cent formalin; the trachea together with the
thyroid gland was then excised and fixed for a further 24 hours. These specimens were examined roentgenographically (Ilford X-ray film).

Samples from all the experimental groups were incubated after ethanol dehydration in methyl salicylate according to Spalteholz (1914). air-evacuated, and examined stereoscopically in a dissection microscope. For detailed examination of the vascular pattern of the gland, thin sections of thyroid tissue were prepared from specimens treated according to the method of Spalteholz.

The remaining specimens were embedded in paraffin. 5-micron thick sections were prepared and stained with either haematoxylin-eosin or with Azan.

RESULTS

All the animals given propyl thiouracil became listless and apathetic, their fur was matted and they also shed a lot of hair. No weight losses, however, were recorded in the propyl thiouracil group or in the remaining animals in the experimental series.

After 30 days of propyl thiouracil treatment the thyroid in the T- and TO-groups was appreciably enlarged and had the character of nodular goitre – particularly in the TO-group. Identification of the thyroid gland, usually small in the rat, presented no difficulty microangiographically in the propyl thiouracil group owing to the size and considerably increased vascularization of the gland. The difference in these respects between the glands in the C-group and those in the T- and TO-groups is illustrated in Fig. 1.

In specimens treated according to the method of Spalteholz the increased contrast density of the enlarged thyroid glands in the propyl thiouracil group was found to be due to a marked dilatation of vessels, especially of the capillaries. Although the number of these vessels was largely unaltered per

Fig. 1.
Roentgenograms showing the size and contrast-density of the thyroid gland in a) C-group, b) T-group and c) TO-group.

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Fig. 2.
Sections of specimens treated with Spalteholz method in a) C-group and b) TO-group.
Direct light.
unit of gland volume, the calibre of the individual capillaries was markedly increased. The discrepancy between the normal thyroid gland (C-group), in which slender capillaries outlined the follicles, and the gland in rats given propyl thiouracil (T-group) where this harmonious arrangement was replaced by an irregular system of large-calibre vessels, is illustrated in Fig. 2.

Histological sections from the C-group showed the features normal to the rat thyroid gland, with colloid-filled follicles of various size. In the rat, the largest follicles are always situated at the periphery of the gland. The epithelium was low and cubical, and the colloid abundant, dense, and stained readily (Fig. 3 a).

The microangiographic appearances of these sections were characterized by capillary vessels originating in intralobular arterioles and outlining the individual follicles, whose epithelium – in the absence of basement membrane – lay in direct contact with the capillary wall. The capillary calibre was otherwise normal, having in all the specimens in this group a diameter corresponding to the red blood cell of the rat (Fig. 3 a).

Corresponding sections from the O-group showed similar, although in some respects deviating, features. The follicles were largely devoid of colloid, generally of small size even in the peripheral portions of the gland, and covered with appreciably higher epithelium (Figs. 3 b and 4 a).

The vascular pattern, on the other hand, corresponded fully with that in the C-group in that normal-calibre capillaries outlined the individual follicles, giving the impression that these were enclosed in a system of capillary loops (Figs. 3 b and 4 a).

Sections from the T-group differed in appearance both as regards general morphology and microangiographic features. Normal follicles containing colloid were as a rule absent. The histological features were chiefly distinguished by epithelial hyperplasia with epithelial cells of differing size and shape arranged in such a manner that individual follicular formations – always deficient of colloid – were identified only with difficulty (Fig. 3 c).

The microangiograms were distinguished by interfollicular capillaries, in parts showing great dilatation. Segments of these were enormously distended, forming large pools of contrast material enclosed by flat endothelial cells. Between these «cavernous» capillaries, interfollicular capillary loops of normal or slightly increased calibre were seen to mark the boundaries of the individual follicles against the surrounding structures (Fig. 3 c).

In the TO-group the specimens mainly showed similar changes which were, however, more pronounced in every respect. The hyperplastic epithelium had cells varying greatly in size and shape, arranged without any resemblance to the normal follicular pattern. As in the T-group specimens, stainable colloid was absent (Figs. 3 d and 4 b).

The normal capillary pattern was wholly absent. At no point were inter-
Fig. 3.

Histological sections demonstrating the morphological and microangiographic appearances in animals in a) C-group, b) O-group, c) T-group, and d) TO-group.

For details see text. Azan staining, magnification $\times 96$. 
Fig. 4.
Details of a) in Fig. 3 b, and b) in Fig. 3 d. Staining azan, magnification × 255.
follicular capillaries of normal calibre seen, but were everywhere replaced by extremely wide sinusoids surrounding irregularly arranged and hyperplastic aggregations of epithelial cells. These contrast-filled "giant capillaries" were lined with characteristically flat endothelial cells and formed the microangiographic foundation of the contrast density described previously in all the thiouracil-treated thyroid specimens (Figs. 3 d and 4 b).

DISCUSSION

Although the histological appearances one month after hemithyroidectomy were indicative of moderate glandular activity with small follicles poor in colloid and with fairly high epithelium, microangiographic examination of these specimens showed features which, as regards the capillary network, corresponded in principle with those of intact controls. The loss of half the thyroid gland had, after this period, resulted in a moderate reaction from the remaining parenchyma but had not led to any perceptible change in the appearances of the capillary bed.

After one month of propyl thiouracil treatment, however, the pronounced parenchymal hyperplasia was accompanied by marked changes in the capillary system of the thyroid. This reaction — like that of the parenchyma — was more marked in the rats subjected to both hemithyroidectomy and propyl thiouracil treatment than in those only given propyl thiouracil. While the capillary dilatation in the former category involved the entire capillary bed so that no loops of normal width were perceptible in the specimens, the interfolllicular capillaries in the latter group were distended only in limited segments between which relatively normal capillaries were seen to outline the follicles.

There seems to be agreement in the literature that the well known effect of propyl thiouracil on the morphology of the thyroid gland, also observed in the present study, is due to an increased secretion of thyroid-stimulating hormone (for references see Arosenius et al., in press 1962).

It seems to us probable that the capillary dilatation described in the above is of the same origin. The gradual increase in the dilatation of the capillary bed noted between the animals receiving propyl thiouracil alone and those subjected to both hemithyroidectomy and propyl thiouracil medication, and the parallel rise in the morphological effect of the thiouracil, strongly suggests that this is the case.

The capillary change induced by the propyl thiouracil medication was in principle the same as that previously described by Thomas (1945). However, Thomas expressed the view that these "giant capillaries" were the result of endothelial proliferation. No signs of such proliferation were detected anywhere in our samples. The impression was, rather, that the long and flat
endothelial cells had been stretched by an extremely marked capillary dilatation. This assumption was borne out by the microangiographic appearances of specimens from animals receiving solely propyl thiouracil medication, where distended capillary segments alternated with those of normal width – none of which showed signs of endothelial proliferation. The other capillary changes which supervened when operated rats were treated with propyl thiouracil appeared to be due to dilatation of these normal-calibre capillary segments.

Comparison of the capillary changes induced by propyl thiouracil with those previously described in nodular goitre by Wangensteen (1929) and Johnson (1955) is of some interest. The two types of changes show close similarities, and although the present study affords no evidence of a common causative factor in the form of increased TSH-activity, this should be regarded as probable.

From the point of view of practical surgery, the present study exemplifies experimentally the observation of all thyroid surgeons that goitres treated with thiouracil have a greater tendency to bleed at operation. Transection of a gland of this type opens the giant capillaries which, as seen in the present specimens, occupy an appreciable area of the incisional surface of the organ.

REFERENCES


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