THE POSSIBILITY OF INDUCTION OF MYELOID TISSUE IN IRRADIATED ANIMALS

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Myeloid tissue is distinguished by its high radiosensitivity. With a sufficiently large dose of whole-body irradiation, the injury to the bone marrow cells present in the body at the moment of irradiation is one of the most important links in the pathogenesis of radiation sickness. For this reason the attempts to transplant hemopoietic cells from healthy animals to irradiated recipients in order to replace the injured myeloid cells by repopulation of the bone marrow in the period preceding its regeneration are of such great interest [5]. One of the greatest difficulties in this procedure is caused by delayed secondary reactions, which are evidently due to immunological incompatibility of the foreign tissues [5].

The connective tissue of a normal animal is known to be capable of taking on a supplementary hemopoietic function, as is shown by the possible development of extramedullary hemopoiesis. The question arises whether the formation of myeloid tissue in an irradiated animal may be induced by a change in the direction of differentiation of those connective tissue cells which are relatively radioresistant and, in consequence of this, are not destroyed during irradiation sufficient to cause the death of the bone marrow cells.

Under experimental conditions the transitional epithelium of adult mammals possesses osteogenetic and myelogenetic activity [6, 7]. It has been shown [1-4] that substances with the histochemical properties of glycogen are secreted by transplantates of the mucous membrane of the urinary bladder and after ligation of the renal vessels, from the growing, undifferentiated layer of transitional epithelium into the surrounding tissue. This process is brought about as a result of buried areas of infiltration of this epithelium and of a specific secretory process, directed both through the surface of the layer and beneath it. The secretion of glycogen from the transitional epithelium is accompanied by induction of foci of ectopic bone formation and hemopoiesis in the adjacent connective tissue.

In the present communication we describe the findings concerning the inducing activity of transitional epithelium when transplanted into an irradiated recipient.

EXPERIMENTAL METHOD

The mucous membrane of the urinary bladder of guinea pigs, cut up finely with scissors, was homotransplanted into the anterior abdominal wall of 30 animals which had been irradiated 60-90 minutes beforehand with a dose of 250 r from a cobalt source EGO-2. After 8-21 days the transplantates were fixed by Helly's and Shabadash's methods and also with cooled acetone and were embedded in paraffin wax. Series of sections were stained with hematoxylin-eosin by the Dominici-Kodrovskii method, the periodic acid-Schiff method for alkaline phosphatase by Gomori's method and for RNA by Brachet's method.

EXPERIMENTAL RESULTS

Proliferation of the transplanted epithelium took place more intensively in the irradiated animals than in normal animals, and was accompanied by areas of buried infiltration. On the tenth day, in these areas, osteoblasts were differentiated from the connective tissue cells of the recipient and foci of ectopic bone developed. These had the typical appearance: The osteoblasts contained a large amount of RNA and alkaline phosphatase and the bone matrix showed the usual structure of integumentary anlagen. The inducing epithelium, as in transplantates in nonirradiated recipients [2-4], was rich in glycogen, which was secreted into the foci of induction. This process was accompanied by destruction of the cytoplasm of part of the epithelial cells invading the connective tissue; glycogen secretion could take place, however, without destruction of the cytoplasm of the epithelial cells, and it was directed both towards the underlying connective tissue and through the surface of the layer into the cavity of the epithelial cysts formed in the transplantates.

After the 17th day, foci of myeloid hemopoiesis were differentiated between the trabeculae of bone in the sites of induction, and on the 21st day actively proliferating hemopoietic tissue appeared here consisting of typical cells of the myeloid series with their charac-

teristic histochemical properties. The intensity of development of myeloid tissue in the irradiated animals was considerably in excess of that taking place by induction of hemopoiesis in transplantates in nonirradiated recipients. It was characteristic that, in contrast to the latter, in the irradiated animals myeloid tissue could also develop in the transplantates at points not in contact with osteogenic tissue, although always in direct proximity to transitional epithelium. On the 17th-21st day, transplantates were fixed from eight animals; in six transplantates induction of myeloid tissue was observed.

The histogenetic activity of transitional epithelium thus was apparent in irradiated animals also, in which it was shown in particular by induction of myeloid tissue. It is natural to consider that, immunologically speaking, the induced myeloid cells are not foreign to their own body. In this respect these findings concerning the possible induction of hemopoiesis in the connective tissue of irradiated animals by means of transitional epithelium may indicate one approach to the problem of the replacement of myeloid tissue injured by irradiation, by a method such as this in order to avoid delayed secondary reactions.

SUMMARY

Urinary blader mucosa was homotransplanted subcutaneously into guinea pigs irradiated with X-rays in a dose of 250 r, causing destruction of the bone marrow cells. Ectopic osteogenesis, with differentiation of foci of myeloid hemopoiesis, were observed in the irradiated animals under the effect of transplantation, this proving the preservation of the corresponding potentiality in the connective tissue of irradiated animals. The histogenetic activity of transitional epithelium is capable of inducing extramedullary myelopoiesis in irradiated animals.

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