Regeneration of Heterotopically Transplanted Autologous Splenic Tissue*

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Summary. Normal young pigs were splenectomized and thin slices of autologous splenic tissue grafted in pouches of the large omentum and underneath the fascia of the abdominal muscles. The regeneration of the transplanted splenic fragments was studied histologically. Within the first few days, the grafts underwent almost complete necrosis. After 14 days no signs of regeneration could be seen. All typical structures of splenic tissue could be found after 3 months but the red and white pulp were populated to a lesser extent than normal with lymphoid cells. After 6 months and 12 days after i.v. injection of sheep red blood cells, the number of follicles increased dramatically and all the morphological signs of an immune response could be seen. After heterotopic transplantation in young pigs splenic fragments regenerate to small splenules of normal appearance. The regeneration is less rapid and results in smaller masses of tissue than in rodents.

Key words: Spleen – Regeneration – Immune response – Pig.

For a long time it was taken for granted that the human spleen can be removed without serious side-effects. Recently however, the asplenic state has attracted considerable interest because of several reports of an increased incidence of overwhelming bacterial sepsis especially in infants (for review see Dickerman 1976; Trigg 1979). Splenic tissue can regenerate in humans especially after trauma of the spleen leading to multiple foci of splenic tissue, disseminated throughout the peritoneal cavity, so-called “splenosis” (for review see Fleming et al. 1976; Pearson et al. 1978). A prophylactic approach would be to transplant splenic fragments after splenectomy because of trauma in the hope that the transplanted tissue fragments...
regenerate and have a protective effect. The regeneration of splenic tissue has been studied in mice (Metcalf 1963, Ambrus et al. 1964), rats (Jacob et al. 1963; Perla 1936; Tavassoli et al. 1973) and rabbits (Williams 1950; Stutte et al. 1974). The autotransplanted tissue had a protective effect in some experiments (e.g. Likhite 1978; Schwartz et al. 1977; Dickerman et al. 1979); but not in others (Schwartz et al. 1978). It remains to be established how much splenic tissue, to which potential location and in which type of preparation it has to be grafted and to find out when a large enough mass of splenic tissue has regenerated.

However, prior to transplantation of splenic tissue in humans, the regenerative power of the spleen has to be tested in larger animals. In the first series of experiments the main purpose was to study the morphology of the regeneration of slices of splenic tissue transplanted into the larger omentum or beneath the fascia of abdominal muscles in young pigs. The splenic tissue developed less rapidly and grew to relatively smaller nodules than described for small laboratory animals. The splenic tissue, however, showed morphological signs of immune response after stimulation.

Materials and Methods

Sixteen normal young pigs of the German landrace were used (12–14 kg body weight, 8 weeks old at the beginning of the experiments). The animals were kept in conventional cages, were fed once a day with pelleted food and had water ad libitum. Atropine sulfate (0.5 mg) and 3 ml of azaperone (Stresnil®, Janssen, Düsseldorf, W.-Germany) were given i.m. as premedication. Anaesthesia was induced and maintained by successive doses of thiobarbital (Trapanal®, Byk-Gulden, Konstanz, W.-Germany). The abdomen was opened through a midline incision and the spleen removed. Slices of about 6 cm² of splenic tissue of about 2 mm thickness were cut with a scalpel. Three to five of these slices were placed in pockets of the larger omentum and fixed with two stitches at their borders in 10 animals. The omentum was attached to the anterior abdominal wall. Additionally, in five experiments one slice was placed underneath the fascia of the external oblique muscle of the abdomen. In six experiments only two slices of splenic tissue were implanted into the larger omentum and resected after 3 days in 4 animals and after 14 days in 2 animals. Five pigs were reoperated about 3 months after the transplantation, to check the growth of the splenic tissue. The number and size of splenic transplants were noted and one nodule resected for histology. In 10 experiments 5 × 10⁹ sheep red blood cells were injected intravenously and the animals killed 12 to 14 days later. In one pig 10 ml of colloidal carbon (C 11–143/a G. Wagner, Hannover, W.-Germany) was injected intravenously 3 h before death. The excised splenic nodules were fixed in Schaffer's solution or formalin, embedded in methacrylate or paraffin, cut at 2 μm or 5 μm and stained with Giemsa, hematoxylin-eosin, Turnbull's blue or Goldner's solution.

Results

Early Phase

Within the first 3 days after autotransplantation the general architecture of the splenic tissue was still recognizable. The red pulp was devoid of lymphoid cells and the sinuses seemed to have collapsed. In the white pulp many pyknotic cells could be seen. There was evidence of necrosis throughout the entire slice of splenic tissue with the exception of a few small areas of lymphoid cells which appeared to be viable in the outer zone of the graft (Fig. 1). After 14 days the transplant was surrounded by the larger omentum and on the cut surface only a small rim of brown-red tissue