Long-term Follow-up after Heterotopic Splenic Autotransplantation for Traumatic Splenic Rupture

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The trapping function of the heterotopic splenic autotransplants (HSA) in 13 polytraumatized patients, aged 5–38 yr, was evaluated using heat damaged technetium-99m-labeled autologous red blood cells in early (1–7 mo) and late (3–4.5 yr) period after heterotopic autotransplantation to the omentum. The intensity of tracer accumulation was graded in comparison to the liver uptake. The splenic tissue surface was calculated on anterior projection each time. The shapes of the transplants were compared and new uptake foci suggesting spontaneous splenosis were looked for on both scans. The average surface of HSA was 28.2 (±14.7) cm^2 on early and 44.1 (±14.3) cm^2 on late examination ($p<0.003$) and the increase in intensity of tracer accumulation on both occasions was significant as well ($p<0.0001$). In three patients, some additional splenotic foci were found on follow-up scans. Howell-Jolly bodies in peripheral blood were detected in six of eight patients in early and remained detectable in lower number in three of eight patients on follow-up. No serious infection was noticed in our group of patients. Our work confirmed the excellent survival rates of HSA with improving trapping function and no important spread from original implantation site on long-term follow-up.

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There is no doubt about the importance of splenic tissue preservation after traumatic splenic rupture. A significant lifelong risk of overwhelming postsplenectomy infection (OPSI) exists, especially in splenectomized children. The overall incidence of OPSI is 0.5%–1.45% with extremely high mortality rates up to 85% (*1–3*). Splenic reparative surgery is advised; when it is not possible, the alternative is heterotopic splenic autotransplantation (*3–5*). Sufficient amount of tissue has to be replanted to support the immunologic function (*3,6,7*). In spite of the undoubted validity of the HSA, some uncertainties exist about the long-term survival of the transplant (*4*), its clearance and immunologic function (*8,9*). The aim of our study was to evaluate the survival and clearance function of heterotopic splenic autotransplant (HSA) in early (1–7 mo) and late (3–4.5 yr) stages after operation.

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PATIENTS AND METHODS

In 13 polytraumatized patients with splenic rupture, 11 men and 2 women, aged 5 to 38 yr, HSA to the omentum according to the modified method of Seufert and Boettcher (*10*) was performed. Selective splenic scintigraphy with heat damaged autologous red blood cells was accomplished 1–7 mo and 3–4.5 yr after HSA in every patient. Erythrocytes were labeled using in vivo/in vitro method. Half an hour after 1 mg of stannous pyrophosphate application 5 ml of venous blood was withdrawn and labeled with 80–120 MBq technetium-99m. The red blood cells were heated for 20 min at 49.5°C. By this method approximately 80% (97% in the work of Atkins 1972) red cells adopted spherocytic shape. The imaging was accomplished about 45 min after i.v. injection of labeled blood cells with a LFOV gamma camera (Picker Dyna 4) and computer (Digital PDP 11/34). The scans were performed in anterior, posterior and left lateral projections. The region of interest (ROI) was drawn around the HSA in the anterior projection to compare the size of the HSA on both examinations. The surface of HSA was calculated in square centimeters using a standard reference area. The shapes of the HSAs were compared on both scans as well and new uptake foci were looked for on the late scans. The splenic uptake intensity was graded as compared to the liver as follows:

0—the uptake was less intense than the liver.
1—the intensity was the same as the liver.
2–moderately higher than the liver.
3—much higher than the liver.

The Howell-Jolly bodies were counted in the peripheral blood in eight of our patients at the same period as the scans were performed.

RESULTS

Patient data are given in Table 1. Early scans were performed from 1 to 7 mo and later from 36 to 57 mo after operation. The mean HSA surface was 28.2 (±14.7) cm^2 on early and 44.1 (±14.3) cm^2 on late

TABLE 1
Patient Data Overview

Age (yr)	Sex	HSA surface (cm^2) Early	HSA surface (cm^2) Late	Uptake intensity Early	Uptake intensity Late	Time E–L (mo)
5	Male	29	30	1	3	30
8	Male	39	50	2	3	47
10	Male	4	28	1	3	31
15	Male	42	44	2	3	48
16	Male	17	55	1	3	50
18	Male	45	65	1	3	47
19	Male	14	21	1	3*	44
24	Male	22	42	1	3	46
29	Female	18	24	0	3	45
29	Male	43	50	2	3*	56
30	Male	40	52	2	3	57
36	Female	10	62	0	2*	52
38	Male	44	50	2	3	48
	$\bar{X}$	28.2	44.1	1.45	2.92	
	±1 s.d.	14.7	14.3	0.52	0.27	
		$p < 0.003$		$p < 0.0001$		

Time e–l = time lapse between the first (early) and the second (late) examination.

* New splenotic foci on the later scans in addition to the HSA. For explanation see text.

scans. The difference was significant ($p<0.003$) and the intensity of tracer uptake was significantly higher on later scans as well (1.45 ± 0.52 early, 2.92 ± 0.27 late scans; $p<0.0001$). Howell-Jolly bodies were positive in six of eight patients in early phase after operation, disappeared in three of them on follow-up, and decreased in number in the remaining patients. All attempted heterotransplantations were successful and no rejection was found.

DISCUSSION

Heterotopic splenic autotransplantation is an attempt to preserve part of splenic immunologic function after such traumatic damage that does not allow surgical reparation of the organ. Heterotopic splenic autotransplantation to omentum was selected in our patients. Experimental animal data about short- and long-term survival and function of HSA are abundant and various animals have been chosen for experimental work. Histologic studies (*6,12–14*) gave conflicting results about the time needed for reorganization of the transplants and their resemblance to the normal spleen, depending on the site of the heterotopic implantation and the experimental animal used. Biopsy verified histologically typical splenic tissue in splenotic nodules in man (*15*). Most studies in humans used an indirect method to test splenic transplant survival and function after HSA. Scintigraphic studies used technetium-labeled sulfur colloid (*1–3,15–17*) or human serum millimicrospheres (*6,10,18*) as a marker of splenic phagocytic function. Heat-damaged technetium-labeled autologous red cells were shown to be very sensitive agents for selective splenic scintigraphy (*7,11,17,19–21*).

The splenic trapping function as assessed with this method was quantified and compared to the direct measurements in animals and the accuracy of the method in humans was proven (*21*). The advantage of the method used in our study is lower or absent visualization of the liver, allowing imaging of even smaller and less intense accumulation of the tracer in the HSAs without the problem of eliminating too intense activity in the liver as occurs in sulphur colloid studies (*15,17,19*). Splenic function after heterotopic autotransplantation is primarily dependent on quantity of implanted tissue and its regenerative power. At least one-third of original organ weight is needed to provide sufficient bloodstream clearance in rats (*22*) and dogs (*16*). Corrazza (*7*) proposed a minimum of 20–30 cm^3 of functioning volume for efficient immunologic function of HSA. We did not try to calculate the transplant volume because of irregular shape of the transplants but we compared the surface area of the HSAs on repeated scans. A significant increase in transplant size on follow-up was shown in our study (Fig. 1).

The increase in the size of the HSAs on the repeated scans did not depend on the age of the patient. A kind of autoregulation seems to influence the final outcome of the transplants in rats (*2*). Previous studies with long-term follow-up in humans did not show excessive growth of HSAs (*7,21*), nor was this seen in our group of patients. All our patients had splenic removal for traumatic rupture. The surgical conditions were not as they are at the elective splenectomy and the tissue disruption predisposes to the spontaneous autotransplantation in addition to the controlled transplantation procedure. This fact is demonstrated in three of our

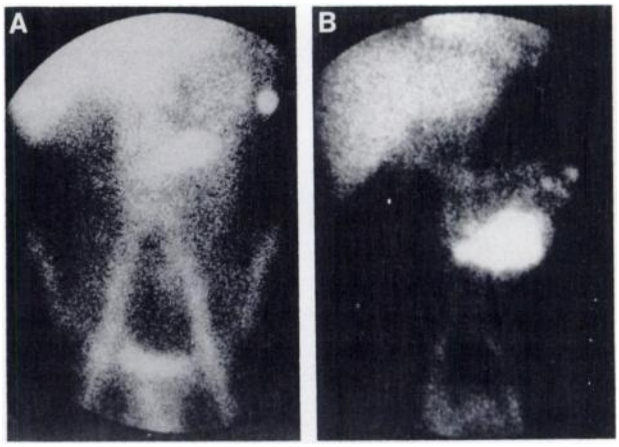

FIGURE 1
(A) Early and (B) late scans in a 24-yr-old male show an apparent increase in HSA surface (22–42 cm^2) and a striking increase in uptake intensity.

patients where new additional foci of intense tracer accumulation were found on later scans (Fig. 2). This is in accordance with Pearson's findings (*23*) of "born again" spleen after surgery for traumatic splenic damage and shown in other studies as well (*7,15,18*). Our findings differ from those of Corazza and Pearson, since we found splenosis in adults and not in children. This spontaneous splenosis after traumatic rupture is thought to account for lower incidences of infection and blood-borne sepsis after splenectomy for traumatic rupture even in cases without surgical reimplantation of splenic tissue although some fulminant infections are described in spite of splenotic foci found at autopsy (*9*).

In the remaining patients of our group, no additional foci were seen on later scans outside the surgically predicted site for implantation in the omentum. All attempted replants were viable on follow-up. The optimal imaging time after surgery is not known. It depends on the regenerative power of the transplanted tissue and the site of ectopic transplantation as well, which is faster in the omentum than in the subcutaneous tissue (24). The data in the literature are conflicting because different animal models were used, namely dogs (*6,12,16*), rats (*2,13,22,25*), mice (*26*), and rabbits (*24*). In humans, spontaneous splenotic foci were demonstrated 1.5 yr after splenectomy (*23*). In some of our patients, good imaging was achieved 1 mo after surgery, as previously reported by Abu-Nema (*17*).

The intensity of tracer accumulation in HSAs is a marker of trapping function. It therefore depends on HSA regeneration and tissue growth. In the first phase of transplant reorganization, the splenic tissue initially undergoes central necrosis and can not resume the phagocytic function (*13,25*). Perhaps this is an explanation of less intense uptake (grade 0 as compared to the liver) in both our female patients on early scans (1.5 and 2 mo, respectively). The regenerative processes with histologic resemblance to normal spleen are completed in 5 wk after subcutaneous implantation in rats (*25*) and in 4 mo in omentum implantation in dogs (*6*). In contrast, Moore (*13*) did not find histologic normal structure in rats after heterotopic autotransplantation and observed markedly deficient lymphoid content over 6 mo. Human splenotic nodules, biopsied at the time of laparotomy, were histologically normal three years after splenectomy (*15*).

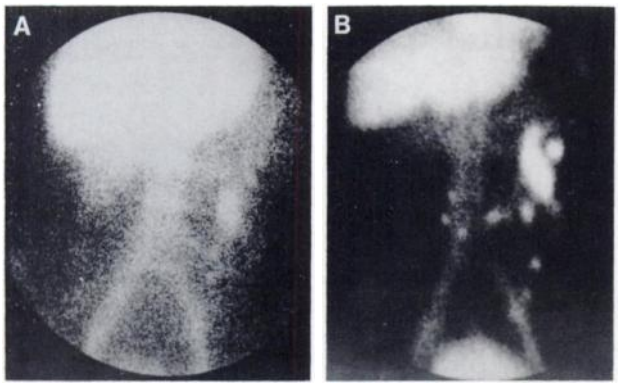

FIGURE 2
(A) Early (B) late scans in a 36-yr-old female show apparently "new" foci on later examination and moderate increase in uptake intensity.

The prolonged follow-up and different patients' age groups allowed some comparative conclusions to be drawn although the groups are not big enough to permit reliable statistical analysis. We did not find any important differences between the time of follow-up, size of the HSA or uptake intensity regarding the age of our patients as well as none of the above-mentioned conditions could predict the finding of Howell-Jolly bodies in red blood cells. The Howell-Jolly bodies present circulating nuclear fragments of newly-formed mature erythrocytes that are normally cleared from circulating blood by intact spleen. Their presence is considered a part of the normal post-splenectomy blood picture (*27*) and serves as a marker of returning splenic function after autotransplantation. Some studies had shown complete disappearance of these nuclear remnants in peripheral blood smears in dogs 3 mo (*16*) or 4 mo (*6*) after splenic tissue implantation. In humans, complete disappearance was seen after heterotopic splenic implantation in children (*28*). Unfortunately, not all of our patients had the peripheral blood smear examined for the presence of Howell-Jolly bodies, but in six of eight cases they were positive. They disappeared on follow-up in three of patients and in the remaining three they were less numerous. We can suppose that in the three patients with persistent Howell-Jolly bodies the function of the autotransplant was not fully restored at the time of examination although quantitative assessment of the degrees of splenic activity on the basis of relative number of those bodies is not fully approved (*23*).

No other additional immunologic testing was performed in our study. The patients were carefully clinically surveyed and no serious infection occurred during the follow-up period even without antibiotic prophylaxis or vaccination. Therefore, even the hypofunctioning heterotopic splenic tissue, as concluded from the presence of Howell-Jolly bodies, provided a substantial degree of immunologic function (*4,16*) during and up to 4.5 yr follow-up. The functioning heterotopic splenic tissue does not per se guarantee the immunologic adequacy of the tissue (*9,13*), but it is without doubt a valuable help in the host defense mechanisms as shown in most human studies.

In conclusion, we found excellent viability and short- and long-term trapping function of HSA after traumatic splenic rupture. The increase in size and intensity of

tracer uptake suggest improving transplant function on follow-up.

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EDITORIAL

Compensatory Splenic Growth: Role of Functional Indicators

The central nervous system, following partial resection, shows little compensatory growth in terms of either the number or size of the remaining cells. However, "regrowth" and at least partial restoration of function is demonstrated by a number of other organs. The mechanisms involved, however, may be quite varied. Protooncogene expression precedes compensatory growth in the liver, but apparently not in the ovary (*1*). Molecular signals involved in hepatic regeneration are multiple and are unraveled in much detail (*2*). Such information is nearly totally lacking as far as the spleen is concerned. The stimulus for splenic growth is uncertain, following resection of part of the organ; the same can be said for growth of accessory

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