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A simple method for predicting bone fractures in PBC patients after liver transplantation

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Abstract We introduce a simple serum test to predict which patients will have bone problems after liver transplantation. The crosslinked part of collagen I (s-ICTP) was measured in 21 patients with primary biliary cirrhosis before transplantation. Those with post-operative fractures had increased pretransplant values of s-ICTP compared with those without fractures.

Key words Primary biliary cirrhosis · Liver transplantation Bone fractures · Collagen

Introduction

Bone disease is common in end-stage cirrhotic patients and particularly in those with primary biliary cirrhosis (PBC) [5]. Liver transplantation often accentuates the bone problems which may even lead to fractures and compression of the vertebral column resulting in kyphosis. The fractures are often extremely painful and may lead to a substantial decrease in height and severely disable the patient [3, 4, 6]. There has been no simple and specific method to assess the risk for this complication. We describe a serum test that may be of prognostic value in the development of serious bone disease after transplantation [7].

The organic matrix of bone consists of up to 90% type I collagen. A peptide containing the crosslinked telopeptide part of type I collagen (ICTP) from decalcified human femoral bone has been isolated after digesting it with bacterial collagenase or trypsin [7]. The concentration of the ICTP antigen in serum correlates with bone resorption rate, measured using either histomorphometric or kinetic techniques [2]. The reference range for healthy adults is 1.7–5.0 μg/l.

Patients and methods

We measured serum-ICTP in 21 consecutive PBC patients (20 women and 1 man) before liver transplantation and up to 3 years after. Their age was 49 ± 7 (mean ± SD) years and s-bilirubin was 232 ± 105 μmol/l. After transplantation all patients were initially on triple immunosuppression therapy (steroids, azathioprine and cyclosporine). For prevention of bone problems they received calcium lactate and carbonate corresponding to a minimum daily dose of 1 g calcium. The 1-year patient survival rate was 86%.

Results

Before transplantation serum-ICTP was abnormal in all but two patients, the median value being 9.4 μg/l. After transplantation 10 patients developed fractures after a mean interval of 6 months (range 2–9 months). This group of patients had significantly higher s-ICTP values before transplantation than the 11 patients without post-transplant fractures, with median values of 11.6 μg/l and 6.3 μg/l, respectively (Mann-Whitney U-test, $P < 0.05$). A similar difference was seen after transplantation as the patients with fractures displayed increased median values throughout the 3-year post-transplant period (Table 1). In the patients without fractures s-ICTP was normal by 6

Table 1 Median serum-ICTP concentrations in patients with post-transplant serious bone complications (group 1) and those without complications (group 2). The number of serum samples measured at each time point ranged from 5 to 11

	Serum-ICTP concentration (μg/l)				
	Pretransplant	Post-transplant			
		2–3 months	6 months	1 year	2–3 years
Group 1 ($n=10$)	11.6	9.3	8.4	6.2	7.0
Group 2 ($n=11$)	6.3	9.7	4.6	4.1	3.2
P-value	<0.05	n.s.	<0.05	<0.05	<0.05

months after transplantation. Serum-ICTP did not correlate with subjective symptoms like bone pain. There was no difference between the two groups with respect to liver function or liver cell damage either before or after transplantation or with respect to the total dose of steroids or the frequency of other complications after transplantation.

Discussion

Bone complications are typical for liver patients undergoing transplantation, and particularly in those with PBC who already have osteoporosis-like changes prior to transplantation [5]. It is clear that the fractures cannot be related solely to immunosuppressive therapy as patients with renal transplants do not have such severe bone problems in the early postoperative period.

We conclude that PBC patients with a high pretransplant s-ICTP value are at risk of developing bone fractures and compression of the vertebral column after transplantation.

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