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Adynamic bone lesion in renal transplant recipients with normal renal function

F. Velasquez-Forero[1], A. Mondragón[2], B. Herrero[2] and José Carlos Peña[1,2]

[1]Departamento de Patología y Clinica de Osteoporosis y Metabolismo Mineral Hospital Mocel, México DF, and
[2]Departamento de Nefrología y Metabolismo Mineral, Instituto Nacional de la Nutrición Salvador Zubirán México DF, México

Abstract. Adynamic bone lesion has been defined as low bone turnover, normal or low osteoid volume and decreased bone formation rate (BFR). A prospective cross-sectional study was performed in 16 asymptomatic post-transplant kidney patients with normal renal function, to evaluate low bone mineral density. The mean age of the nine women and seven men was 33.9±7.3 years, the mean serum creatinine was 1.1±0.2 mg/dl and the mean creatinine clearance 71.5±13.8 ml/min/1.73 m^2. Six patients received triple immunosuppressive therapy for a period of 10.3±3.7 months and nine received double therapy. Eighty-four months after renal grafting, we carried out bone densitometry, biochemical markers and bone biopsy. Bone densitometry showed 78±8.7% and 80.4±8% for hip and lumbar spine, with a mean Z score of 1.79±0.72 and 1.88±0.78 (SD), significantly less than normal in the Hispanic young population for those two regions. Serum PTH (0.83±0.23 μg/ml normal range 0.32–0.65), urine cAMP (4.1±1.3, normal range 0.5–4.7 nmol/mg Cr) and total and nephrogenic fraction (3.1±1.1, normal range 0.29–2.9 nmol/100 ml GFR) were significantly greater than normal ($P<0.01$). The bone biopsy in 12/16 patients showed decreased percentage osteoid area (1.59±0.86% vs 3.19±0.82%), percentage mineralized area (13±4.7% vs 21.03±3.36%) and bone formation rate (505±237 vs 1275±168 $\mu m^2/mm^2$/day), with a P value <0.05 compared with 10 normal bone biopsies. The remaining four patients exhibited low bone turnover image with normal bone formation rate (1442±206 $\mu m^2/mm^2$/day). Iron deposits were demonstrated at the mineralization front in 10/16 patients. No aluminium or amyloid deposits were observed. The histomorphometric results showed the presence of adynamic bone lesion in 12 renal transplant recipients with normal renal function and osteopenia, which explains the low bone density. The long-term use of glucocorticoids and the presence of iron deposits may contribute to this bone lesion. The biochemical markers of bone remodelling showed abnormalities compatible with moderate increase in parathyroid function. The adynamic lesion in the presence of hyperparathyroid function may suggest down-regulation of PTH bone receptors, alterations of the bone microenvironment or both.

Key words: adynamic bone lesion; low bone turnover; renal osteodystrophy; renal transplant

Correspondence and offprint requests to: Dr F. Velasquez Forero or José Carlos Peña, Hospital Mocel, Clinica de Osteoporosis, Calle de Gelati No 29-304-A, Tacubaya, 11850 México DF, México.

Introduction

The most recently described bone remodelling lesion in patients with renal osteodystrophy is adynamic bone lesion. Sherrard *et al.* [1] in 1983 described this new lesion in dialysis patients with bone pain, pathological fractures and marked aluminium overload. Moriniere *et al.* [2] reported a group of uraemic patients with adynamic bone lesion without bone syptomatology and negative aluminium deposits According to Sherrard *et al.* [3] adynamic bone lesion is defined by a low bone turnover, normal or low osteoid volume, and decreased bone formation rate in patients with chronic renal failure with and without aluminium deposits. The same author found that in 60% of patients in peritoneal dialysis and in 36% of patients in haemodialysis, the bone biopsies showed adynamic bone lesion. In this group of 259 patients, 128 had adynamic bone lesion (49%). In these 128 dialysis patients Sherrard *et al.* [3] detected aluminium deposits at the bone surface spicula: more than 25% in 40 (31%), 5–25% in 39 (30%), and 0–5% in 49 (38%) out of 128 of patients studied. These data clearly show that these patients had a high incidence of aluminium at the bone mineralization front.

Katz and Epstein, in an editorial published in 1992 [4], state that post-transplantation bone disease is clearly recognized as a clinical entity, characterized by reduced bone density and histological changes of low turnover bone disease.

There is scanty information in the literature of bone

densitometric studies and bone biopsy in post-transplant patient recipients with normal renal function [5]. The purpose of this prospective, cross-sectional study was to evaluate the cause of the reduction in bone mineral density, detected with bone densitometry, in our patients with long-term renal transplantation and renal function within normal limits. To accomplish this goal we used bone remodelling biochemical markers and bone histomorphometry in 16 post-transplant asymptomatic kidney patients.

Subjects and methods

A prospective cross-sectional study was performed in 16 asymptomatic post-transplant patients with normal renal function and low bone mineral density. Fifteen renal allografts came from living related donors and one from a cadaveric donor. The mean age was 33.9 ± 7.3 years and there were nine women and seven men. Nine patients were on chronic peritoneal dialysis (CAPD) for a period of 30 ± 39 months and seven patients were in haemodialysis for 9.4 ± 10.1 months before renal transplantation. The cause of end-stage renal disease was chronic glomerulonephritis in 12, membrano-proliferative glomerulonephritis in two, membranous glomerulopathy in one and tubulointerstitial nephritis in one patient. History of diabetes mellitus, haemochromatosis and chronic liver disease, was absent in all patients. The mean serum creatinine was 1.1 ± 0.2 mg/dl and the mean creatinine clearance 71.5 ± 13.8 ml/min. All patients received variable quantities of aluminium hydroxide and oral calcium supplements, and no calcitriol, before renal transplantation. One of the patients with membrano-proliferative glomerulonephritis was on prednisone for 12 months before dialysis. Bone biopsy was taken after double tetracycline labelling, 84.2 ± 83.4 months with a range 7–226 months after renal transplantation. In the same week biochemical markers, bone desintometry and bone biopsy were carried out.

The study was approved by the Instituto Nacional de la Nutrición SZ Hospital Research Ethic Committee. Inform consent was obtained from each patient.

Immunosuppression

The main therapeutic regime was azathioprine (1.5–2 mg/kg/day) plus prednisone (10–15 mg/day) in 10 patients. Six received triple therapy with cyclosporing A (CsA 5 mg/kg/day) for 10.3 ± 3.7 months (range 6–16 months). Four patients were on CsA when the bone biopsy was obtained.

Laboratory measurements

Serum and urine calcium and magnesium were determined with atomic absorption (Perkin Elmer); serum and urine phosphorus [6] and creatinine, serum alkaline phophatase, and serum albumin were measured with a computarized Technicon Autoanalyzer. Serum concentrations of parathyroid hormone were obtained by middle molecule radioimmunoassay (INCAR kit; normal range 0.32–0.65 ng/ml). Cyclic AMP in blood and urine was determined by radioimmunoassay with a rabbit antibody (normal values in plasma 6–12 pmol/ml; total values in urine 0.5–4.7 nmol/mg Cr; and nephrogenic urine fraction 0.29–2.9 nmol/100 ml GFR). Serum calcidiol (25-OHD3) was determined with human transporter protein (normal range 15–50 ng/ml all year). Urine hydroxiproline (HOP) was determined using a colorimetric method (normal range 6–25 mg/g Cr) [7].

Bone densitometry

Vertebral (lumbar spine, L2–L4) and hip (femur neck) bone mineral density were measured with a Hologic DEXA, dual energy X-ray absorptiometry. For comparison we used tables for Hispanics from the softwear provided with the machine by Hologic Corporation. The results are expressed as bone mineral density in g/cm^2, and percentage of bone mass and number of standard deviations below or above the normal young population (Z score). Osteoporosis was defined as a Z score less than 2.5 SD [8] compared to the greatest bone peak mass attained by a normal Hispanic young population (30–40 years of age).

Bone histomorphometry

After double tetracycline labelling with a 10 day interval between doses, full thickness bone biopsy was obtained from the left anterior iliac bone. The non-decalcified bone specimen was fixed in ethanol and embedded in methylmethacrylate and sectioned for histomorphological examination. Bone specimens were stained with Goldner tricrome, aluminium according to a modification of Maloney *et al.*'s method [9], iron with Perls' method [10] and amyloid with Bennhol's congo red. We stained all bone sections for aluminium and iron using a control obtained from iliac bone of rats overloaded with these metals. The aluminium and iron deposits were evaluated in the mineralization front of the peripheral cancellous spicula surface. All histomorphometric analyses were done with the aid of a light microscope and a Merz Schenk reticle [11] and an eyepiece micrometer. Measurement of cancellous bone was divided into the following normal index values.

Static index. Percentage area of osteoid (OAr: $3.19 \pm 0.82\%$), percentage area of fibrosis (FbAr: $0.32 \pm 0.31\%$) and percentage area of mineralized bone (MbAr: $21.03 \pm 3.36\%$); percentage surface of osteoblasts (ObS: $5.40 \pm 1.30\%$) and percentage surface of osteoclasts (OcS: $1.40 \pm 0.72\%$).

Dynamic index. Mineralized appositioned rate (MAR: 1110 ± 0.170 μm/day), bone formation rate (BFR: 1275 ± 168 μm^2/mm^2/day).

We define adynamic bone lesion as: low bone turnover, decreased percentage of osteoid area ($\leqslant 3.2 \pm 0.8\%$), low BFR ($< 1275 \pm 168$ μm^2/mm^2/day), osteopenia (decreased percentage of mineralized bone area: $< 21.3 \pm 3.4\%$) and hypocellularity (percentage osteoblasts surface $< 5.4 \pm 1.3\%$ and percentage osteoclasts surface $< 1.4 \pm 0.7\%$). The normal bone biopsy indexes were obtained in bone specimens taken from 10 normal subjects of the same age and body weight, and studied with the same methodology in our laboratory. These normal subjects were submitted to surgery for monostotic benign bone dysplasias.

In reporting our histomorphometric data, the ASBMR histomorphometry nomeclature committee was followed [12].

Statistical analysis

All values are expressed as means ± standard deviation of the mean. Non-paired Student's t-test was utilized to analyse

the differences of static and dynamic indexes against the normal bone biopsies. P value <0.05 was considered significant.

Results

All patients included in the study had a kidney graft capable of maintaining mean serum creatinine at 1.1 ± 0.2 mg/dl (range 0.8–1.4) and creatinine clearance with 24 h urine collections of 71.5 ± 13.8 ml/min (range 49–87).

Table 1 depicts all serum biochemical values and Table 2 the 24 h urine values of bone remodelling, including creatinine clearance. Serum PTH (0.83 ± 0.23 μg/ml) values were twice normal in 5/16 patients; the mean values of all patients studied were significantly greater than normal ($P<0.01$). Serum calcium (9.5 ± 0.4 mg/dl), phosphorus (3.5 ± 0.6 mg/dl) and magnesium (1.6 ± 0.3 mg/dl) were within normal limits. Mean serum alkaline phosphatase (90.9 ± 42.3 U/l) was within normal limits; the highest value of this variable (207 U/l) corresponds to patient 14 with normal mineralization and low bone turnover (Table 4, group 2). Calcidiol values shown in Table 1 were all within the normal range except patient 11. Hypercalciuria (254 mg/24 h) was detected in a 25 year old female, patient 8 (Table 2), 9 months after renal transplantation; she was under triple immunosuppressive therapy. The cAMP, total and nephrogenic, was significantly greater than normal ($P<0.01$; Table 2). The mean values of the other urine variables, hydroxyproline, Ca/Cr, total urine calcium and phosphorous, were not different from the normal population (Table 2).

The results of bone densitometry for hip and lumbar spine are shown in Table 3. The majority of measurements demonstrated a substantial decrease in bone mass, with a percent decrease in hip to $78 \pm 8.7\%$ and in lumbar spine $80.4 \pm 8\%$, and a mean Z score of -1.79 ± 0.72 for hip and -1.88 ± 0.78 for lumbar spine. The risk of fracture was increased in all patients as a group in one or both regions. The diagnosis of osteoporosis was established for hip in two patients and for lumbar spine in three patients. Of our 16 patients, 13 were less than 39 years of age and three were between 40 and 43 years. The loss of mineral density in a very young population of nine females and seven males indicates severe abnormalities in bone formation. No significant differences in bone densitometry were found among gender groups.

Histomorphometric findings

The findings of the bone biopsies obtained simultaneously with the bone remodelling biochemical markers and bone densitometry are depicted in Table 4; all patients showed a typical low bone turnover pattern. Twelve patients (group 1) showed adynamic bone lesion with a significant decrease in percentage of osteoid area ($1.59 \pm 0.86\%$) and low bone formation rate (505 ± 237 $\mu^2/mm^2/day$). The adynamic bone lesion was associated with a low population in the percentage of bone cells, particularly osteoblasts ($4 \pm 1.7\%$) and osteoclasts ($0.3 \pm 0.4\%$), and with osteopenia, defined as a significant decrease in the percentage of mineralized trabecular bone area ($13 \pm 4.7\%$). Peritrabecular bone fibrosis was not observed. The other four subjects (group 2) exhibited in the static indexes a low bone turnover image, with normal bone formation rate (1442 ± 206 $\mu m^2/mm^2/day$); this lesion is different from the adynamic bone lesion described in group 1.

Iron deposits were demonstrated at the mineraliz-

Table 1. Serum biochemical values

Patient	Ca (mg/dl)	P (mg/dl)	Mg (mg/dl)	Cr (mg/dl)	Alb (g/dl)	AlkPh (U/l)	PTH (μg/ml)	cAMP (pmol/ml)	25-OHD3 (ng/ml)
1	9.33	3.92	1.72	1.10	4.4	139	0.64	11.7	
2	9.45	3.41	1.78	0.90	4.4	106	0.40	7.3	
3	9.01	4.38	1.09	0.80	4.2		0.37	11.5	34.1
4	9.00	3.88		0.80	4.4	61	0.41		25.2
5	9.65	3.32		0.90	4.4	49	0.49	6.18	30.5
6	9.47	3.52	1.59	0.90	4.4	64	0.47	10.9	36.5
7	9.77	2.92	2.00	1.00	4.7	60	0.65	3.8	15.1
8	10.01	4.17	1.20	1.10	4.4	84	1.00	11.4	28
10	9.52	2.53	1.45	1.30	4.1	108	1.04	17.1	15.7
11	8.84	3.65	1.59	1.00	4.1		0.42	9.7	74
12	10.00	4.13	1.25	1.40	4.2	112	0.64	12.5	19.5
13	9.17	3.25	1.69	1.40	4.9	63	0.71	9.7	38.2
14	9.84	2.96		1.20	4.9	207	0.79	8.3	32.3
15	9.15	2.71		0.90	4.1	62	0.46	3.6	
16	10.06	3.16		1.10	5.2	69	0.80	7.4	20.5
Mean	9.51	3.51	1.60	1.10	4.5	90.9	0.83*	9.44	33.8
SD	0.4	0.6	0.30	0.20	0.3	42.3	0.23	3.49	20.7
Normal range	8.7–10.4	2.5–4.8	1.7–2.8	0.5–1.3	3.5–5.0	50–112	0.32–0.65	6.0–12	15–50

*$P<0.01$ vs the normal population.

Table 2. Twenty-four hour urine values

Patients	UCa (mg/day)	UP (mg/day)	UCr (mg/day)	Cr Cl (ml/min)	OHPr (mg/g Cr)	cAMPtotal (nmol/mg Cr)	cAMPNephrog (nmol/100 ml GFR	Ca/Cr (24 h)
1	63	539	1373	87	9.30	3.02	2.15	0.05
2	112	555	1026	87		6.74	5.33	0.11
3	155	636	957	86	30.50	7.23	4.63	0.16
4	106	326	780	85				0.14
5	40	666	1050	82	15.30	2.78	1.88	0.04
6	145	799	1004	82	15.80	4.28	2.76	0.15
7	175	326	1025	79	30.70	4.68	4.30	0.17
8	254	860	1138	78	41.00	3.67	2.90	0.22
9	21	501	941	71	34.00	3.84	3.33	0.02
10	147	652	1303	70	16.70	3.00	1.68	0.11
11	8	225	1085	67	22.00	2.56	1.59	0.01
12	30	455	1122	63	18.20	3.63	2.74	0.03
13	14	475	1109	57	18.00	3.95	3.26	0.01
14	88	787	884	51	61.00	3.73	3.04	0.10
15	9	326	688	50		3.91	3.16	0.01
16	39	429	882	49	22.70	4.05	3.72	0.04
Mean	87.9	535	1023	71.5	25.80	4.1*	3.1*	0.10
SD	72.4	188	175	13.8	13.80	1.30	1.10	0.10
Normal range	50–250	500–1200	800–1500	60–100	6.1–25	0.5–4.7	0.29–2.9	<0.15

*$P < 0.01$ vs the normal population.

Table 3. Bone densitometry results

Patients	Hip neck (g/cm^2)	Hip neck (*Z* score)	Hip neck (%)	L1–L4 (g/cm^2)	L1–L4 (*Z* score)	L1–L4 (%)
1	0.877	−2.14	73	0.787	−2.76	72
2	0.941	−1.79	78	0.841	−2.28	77
3						
4	0.846	−2.14	74	0.785	−2.34	75
5	0.701	−3.19	61	0.788	−2.35	75
6	0.943	−1.41	83	0.917	−1.11	88
7	0.673	−3.27	60	0.891	−1.25	87
8	0.920	−1.58	81	0.847	−1.68	82
9	0.858	−2.07	75	0.786	−2.36	75
10	0.946	−1.40	82	0.738	−2.92	70
11	0.886	−1.90	76	0.793	−2.58	74
12	0.930	−1.43	82	0.991	−34.00	96
13	1.002	−1.28	84	0.871	−2.00	80
14	1.008	−1.55	81	0.941	−1.36	86
15	1.041	−0.64	92	0.772	−2.30	75
16	1.069	−1.00	88	1.022	−0.63	94
Mean	0.909	−1.79	78	0.851	−1.88	80.4
SD	0.111	0.72	8.76	0.780	0.78	8.1

ation front in 10 patients. In six of them the iron deposits occupied more than 25% of the peripheral spicula surface and less than 24% in the remaining four. Aluminium was not detected in any of the 16 bone biopsies; bone amyloid was also negative.

Discussion

The diagnosis of adynamic bone lesion rests mainly in the bone histomorphometric findings of low bone formation rate and normal or decreased osteoid area. Different values from the normal range of bone formation rate have been reported [5,13–16], reflecting intrinsic variability of the technique and differences in the selection of the control groups. The histomorphometric results in our study show the presence of adynamic bone lesion in 12 asymptomatic transplant recipients with normal renal function. This lesion was originally described in patients with chronic renal failure and aluminium deposits in 1983 [1]. In the past 10 years a similar lesion has been described in patients with chronic renal failure and without aluminium bone deposits [2]. In this study adynamic bone lesion was noted in transplant patients with normal renal function. This is in agreement with observations in 20 kidney transplant recipients studied by Julian *et al.* [5], with good renal function and with bone biopsy obtained 6

Table 4. Bone biopsy results

Patients	OAr (%)	MdAr (%)	FbAr (%)	ObS (%)	OcS (%)	MAR (μm/day)	BFR ($\mu m^2/mm^2$/day)
Group 1							
1	1.00	20.90	0.10	2.93	0.00	0.818	964
2	1.30	8.00	0.00	3.28	1.31	1.037	267
4	0.44	14.00	0.00	2.98	0.33	1.037	267
5	1.44	6.55	0.11	3.92	0.00	0.770	848
6	1.55	12.33	0.00	5.72	0.33	0.716	616
7	0.11	12.11	0.00	3.51	0.00	0.846	403
9	2.77	10.44	0.00	3.60	0.65	0.711	335
10	1.66	14.44	0.00	6.25	0.65	0.592	383
11	2.00	20.22	0.11	7.63	0.00	2.074	689
12	3.11	6.44	0.00	1.81	0.00	0.691	344
13	1.55	15.88	0.00	2.44	0.00	0.691	314
15	2.22	15.22	0.00	3.92	0.98	0.963	623
Mean	1.59*	13*	0.02*	4.00	0.3*	0.910	505*
SD	0.86	4.70	0.04	1.70	0.40	0.400	237
Group 2							
3	4.66	24.88	0.44	3.83	0.69	0.790	1273
8	0.22	14.22	0.22	6.25	0.62	1.092	1448
14	1.00	11.77	0.00	3.33	0.00	1.239	1317
16	2.55	8.00	0.00	2.70	0.00	2.024	1731
Mean	2.10	15.00	0.22	4.00	0.30	1.280	1442
SD	1.90	7.20	0.31	1.50	0.30	0.450	206
Normals ($n=10$)							
Mean	3.19	21.03	0.32	5.40	1.40	1.110	1275
SD	0.82	3.36	0.31	1.30	0.72	0.170	168

*$P<0.05$.

months after the renal alograft; the histological findings showed low turnover bone lesion, in the absence of aluminium deposits. The analysis of the histomorphometric indexes by Julian *et al.* fulfil the criteria established for the diagnosis of adynamic bone lesion (percentage osteoid area $4.7 \pm 2.3\%$; bone formation rate 23.1 ± 13.8 $\mu m^3/\mu^2$/year).

It is difficult to understand why this group of patients are not capable of forming bone as shown in Table 4. The explanation of this lesion in our transplanted patients is probably multiple. The use of high calcium dialysis fluid and high oral calcium supplements, calcitriol administration associated with hypercalcaemia, declining serum PTH levels and bone resistance to parathyroid hormone were considered among the causes of the low bone formation rate in adynamic bone lesion in patients with chronic renal failure [17,18]. Recently, intermittent oral or intraperitoneal calcitriol pulse therapy, independently of its PTH secretion suppressive effect, has been considered to play a role in this bone lesion [19]. The adynamic bone lesion has been described in patients before dialysis therapy [20]. The causes invoked to explain this lesion have been the therapy used (calcium, calcitriol, aluminium salts), serum PTH, systemic disease (diabetes mellitus), old age and uraemia [21]. Furthermore, the type of dialysis may also play a role in the pathogenesis of this low bone turnover lesion [3]. Patients with peritoneal dialysis were more prone to develop this lesion (60%) than patients on haemodialysis [3,16,19].

In our transplanted patients the duration of peritoneal dialysis and haemodialysis (pre-existing bone disease), the use of steroids, azathioprine and cyclosporin after transplantation [2,5] and the iron deposits in the mineralization front, may all contribute to the pathogenesis of this lesion. All our patients received low doses of prednisone. Glucocorticoids affect bone formation, altering the secretion of sex hormones, intestinal calcium absorption, calcitriol synthesis, renal excretion of calcium and phosphorus [22]. Glucocorticoids also locally decrease insulin growth factor, which inhibits osteoblastic activity and bone formation [23]. All our patients received low doses of prednisone. Osteoporosis has been the most common diagnosis associated with glucocorticoid treatment. It is important to emphasize that, from the histomorphometric analysis of the bone biopsy, it is difficult for us to differentiate adynamic bone lesion from osteoporosis.

Cyclosporin A has been implicated in the pathogenesis of high turnover osteopenia [24]. Only four of our cases were receiving CsA, and all had adynamic bone lesion.

Bone iron overload has not been described before in patients with adynamic bone lesion. In our laboratory we have found a high incidence of this metal at the mineralization front [25,26]. It is important to mention that iron overload has been described in chronic liver disease and haemochromatosis (none of our patients had a history of these diseases), and has been associated with decreased osteoblastic function

and osteoporosis [27]. Experimentally, Ittel *et al.* [28] in uraemic rats with iron overload showed a decreased bone formation rate, reduced osteoid volume and osteoid surface and adynamic bone lesion. We believe that though iron deposits were detected in the mineralization front in eight of our 12 patients, the absence of iron deposits in four patients suggests that this metal may participate, but is not the main cause of this lesion.

In a recent communication Kurz *et al.* [29] studied calcium kinetics in peritoneal dialysis patients with bone biopsy. The cases with low turnover bone lesion including adynamic bone lesion showed a normal or slightly decreased calcium efflux and calcium accretion rate together with a disproportionately low calcium retention. These findings demonstrate that patients with adynamic bone lesion have a decreased bone capacity to uptake calcium and have an inability to handle an extra calcium load.

The biochemical markers of bone remodelling showed mild abnormalities compatible with a slight increase in the parathyroid function (Tables 1 and 2). The absence of bone response to the elevated parathyroid function (PTH and cAMP in urine; Tables 1 and 2) in some of our cases suggests a resistance to PTH. The down-regulation of the PTH receptor (PTHr) in kidney and bone [30] has been postulated as a cause of the PTH resistance and also as the primary event in the secondary hyperparathyroidism of mild renal failure [17]. It is possible that our group of patients with all the indexes of adynamic bone lesion may not respond to the calciotropic hormones and to cytokines and growth stimulating factors of the bone microenviroment; this may be due to the presence of multiple factors acting together, such as glucocorticoid effect, iron deposits, alteration in the growth factors and a down-regulation of the PTHr in bone.

In patients 3, 8, 14 and 16 (group 2, Table 4) the bone biopsy findings showed a low bone turnover lesion identical to adynamic bone lesion according to static bone indexes, but with normal bone formation rate. This new form of low bone turnover bone lesion is compatible with a defect in the bone matrix formation (low osteoid) and normal mineralization. We do not have an explanation for this finding, but this group of patients may fall into a new category of adynamic bone lesion in the recovery phase. Furthermore, it is important to comment that patients 8, 14 and 16 showed the greatest PTH values (Table 1) of all 16 patients.

The decrease in bone mass clearly shown in the dual energy X-ray absorptiometry in this young population of nine women and seven men (Table 3) suggests that the bone loss occurred from the time of dialysis and continued after renal transplantation; these findings were also described by Julian *et al.* [5]. The majority of our patients probably never attained their bone mass peak. The biopsy clearly demonstrated osteopenia, correlating with the low densitometric findings. It is likely that such osteopenia may increase the risk of fracture in this population of patients.

In summary, the adynamic bone lesion in young transplanted individuals with normal renal function appears to be a relatively common disorder and may explain the low bone densitometric values in all our patients (Table 3). The long-term use of glucocorticoids may be a contributing factor to this lesion. The presence of iron deposits in the mineralization front may also participate in the pathogenesis of this lesion. The benign clinical course with slight abnormalities in the biochemical markers of bone remodelling, mainly hyperfunction of the parathyroid glands, and the lack of response of bone remodelling turnover mechanism, suggest a persistent PTHr down-regulation of bone, alteration of bone microenviroment regulators, or both.

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