Letters

Alendronate-associated focal segmental glomerulosclerosis

Sir,
Alendronate sodium, a bisphosphonate and commonly used pharmacologic agent for postmenopausal osteoporosis, has been rarely linked to renal toxicity [1] but not in association with focal segmental glomerulosclerosis (FSGS).

A 55-year-old Caucasian woman developed proteinuria and hypertension. Nine years earlier, she had been diagnosed with breast cancer treated with lumpectomy, radiotherapy and chemotherapy without evidence of recurrence. Two years later, she was diagnosed with osteoporosis and started on alendronate sodium 10 mg once daily for 3 years followed by 70 mg once weekly for 4 years and calcium plus vitamin D supplements. Other medications were multivitamins, primrose oil and venlafaxine for hot flushes. She had no other significant past medical history.

Blood pressure was 160/90 mmHg, with ankle oedema present. Serum creatinine was 106 mmol/dl with proteinuria of 10 g/day. HIV infection and viral hepatitis were ruled out. Computed tomography of the head, chest, abdomen and pelvis was negative for malignancy or metastatic disease. A renal biopsy contained 36 glomeruli present, none of which were globally sclerotic. Few glomeruli demonstrated mesangial hypercellularity with segmental areas of sclerosis with hyperplasia of visceral epithelial cells (podocytes) (Figure 1). A background of chronic interstitial inflammation and interstitial fibrosis was present. IgA, IgM, C3 and C1q were demonstrated on immunofluorescence in a globular segmental distribution. Electron microscopy supported this impression of FSGS with diffuse podocyte foot process effacement without immune-complex-type deposits (Figure 2). Alendronate was discontinued, and prednisone 1 mg/kg/day and lisinopril were started. Six weeks later, she went into partial remission (proteinuria 1.1 g/day).

Alendronate has an estimated terminal half-life in bone of >10 years, and only ~50% of a systemic dose is excreted unchanged in the urine within 3 days. Long-term drug excretion may cause renal toxicity through disruption of the podocyte cytoskeleton, a mechanism similar to that described in osteoclasts [2]. This beneficial effect of bisphosphonates on bone resorption has led to extensive use in several bone diseases. Pamidronate that is structurally almost identical to alendronate has been linked to FSGS. Studies in primary and recurrent FSGS implicate podocyte injury [3] and increased production of T-cell-derived lymphokines or 'permeability factors' [4] in the pathogenesis of segmental glomerular scarring. Drug dose and duration of treatment may influence the patient susceptibility to in-
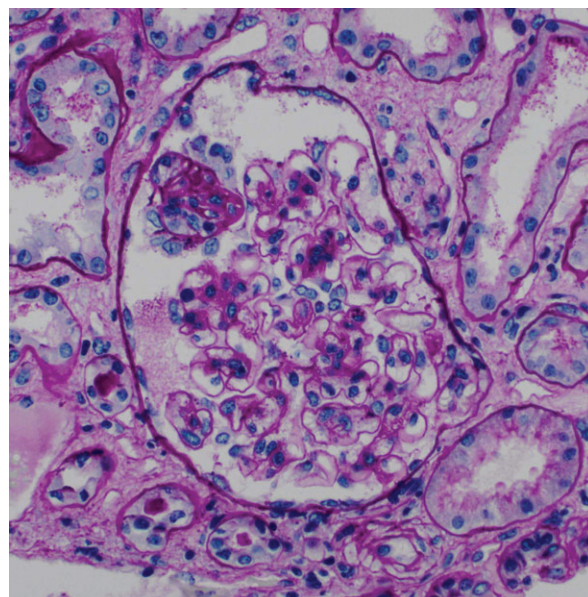

Fig. 1. PAS stain (400× magnification)—glomerulus with focal segmental sclerosis in the upper-left aspect of the glomerulus associated with visceral epithelial cell hyperplasia.
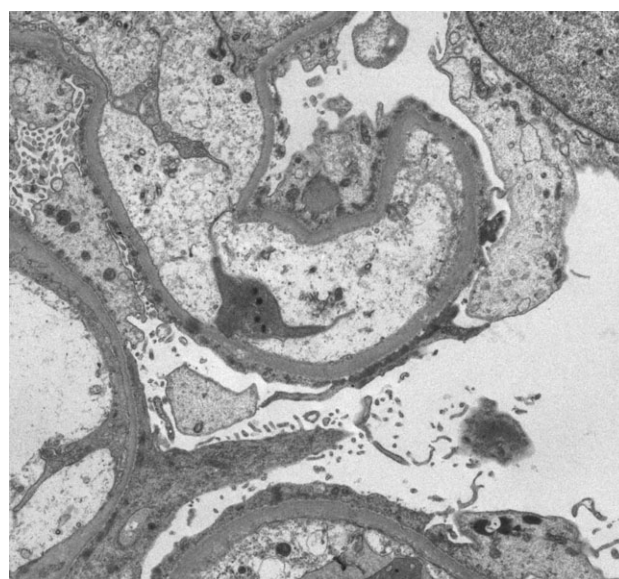

Fig. 2. Electron photomicrograph (2000×)—diffuse foot process effacement with villous transformation of epithelial cell cytoplasm.

jury [5]. Our patient was on the recommended dose of alendronate but for an extensive period of time (~7 years). This case suggests that alendronate, like pamidronate, may as well cause FSGS. While 'primary' or 'idiopathic' FSGS can obviously not be excluded, this entity is more commonly

seen in young adults, males and Afro-American individuals. We recommend frequent monitoring of urine protein excretion and renal function for early detection of renal injury.

Conflict of interest statement. None declared.

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Lack of correction of secondary hyperparathyroidism long term after kidney transplantation despite good graft function

Sir,

Secondary hyperparathyroidism (SHPT) and its associated bone and vascular complications are highly prevalent in patients undergoing renal replacement therapy. Whether successful kidney transplantation corrects SHPT in the majority of patients with a functioning graft is unclear. In the context of an ongoing, randomized study on the effects of vitamin D therapy in post-transplant patients, we reviewed the clinical data of 150 consecutive kidney or kidney–pancreas transplant recipients with a functioning graft a minimum of 1 year after transplantation at our institution. Table 1 presents patients' characteristics displayed according to a pre-transplantation iPTH level < or $\geq$65 pg/mL (upper limit of normal). As shown, despite a similar and acceptable post-transplant eGFR and optimal serum levels of calcium and phosphate, only 17% of the patients in the higher iPTH category regressed to normal, while 24% of the patients with low iPTH before transplantation moved to the higher category over time. In a multivariable model that included nine variables [age, gender, diabetes mellitus, iPTH< or $\geq$65 pg/mL at time of transplantation, most recent serum calcium (albumin corrected), most recent serum phosphorus, most recent creatinine, most recent eGFR and haemodialysis], we identified male gender [beta coefficient 2.67 (1.12–6.38); $P < 0.03$], pre-transplant haemodialysis

Table 1. Patients' characteristics according to pre-transplantation iPTH levels

Variable	Intact parathyroid hormone pre-transplant		
	$\geq$65 pg/mL ($N = 95$)	<65 pg/mL ($N = 55$)	*P* value
Age (years)	49.8 ± 14.3	45.0 ± 15.5	0.08
Male gender, *N* (%)	54 (57)	20 (36)	0.02
African American, *N* (%)	45 (48)	20 (36)	
Caucasian, *N* (%)	38 (40)	31 (56)	0.19
Other, *N* (%)	11 (12)	4 (8)	
Diabetes mellitus, *N* (%)	22 (24)	13 (26)	0.81
Hypertension, *N* (%)	66 (71)	42 (82)	0.13
Donor type, *N* (%)			
Cadaveric donor	70 (74)	36 (65)	0.29
Living donor	25 (26)	19 (34)	
Time from transplant (months)	41.7 ± 40.5	49.5 ± 30.8	0.27
Time on dialysis (years)	4.6 ± 11.7	2.8 ± 2.9	0.41
Haemodialysis	74%	47%	0.001
Peritoneal dialysis	21%	29%	0.49
Pre-emptive transplant	5%	24%	0.002
Serum creatinine (mg/dL)	1.93 ± 1.68	1.51 ± 1.17	0.14
eGFR (mL/min/1.73 m^2)	52.8 ± 22.4	56.6 ± 20.8	0.36
Most recent corrected serum calcium (mmol/L)	2.3 ± 0.3	2.3 ± 0.2	0.24
Pre-transplant corrected serum calcium (mmol/L)	2.3 ± 0.4	2.2 ± 0.3	0.68
Most recent serum phosphorus (mmol/L)	1.06 ± 0.42	1.16 ± 0.29	0.14
Pre-transplant serum phosphorus (mmol/L)	1.74 ± 0.58	1.77 ± 0.61	0.90
Serum albumin (g/dL)	3.6 ± 0.5	3.5 ± 0.6	0.33
Pre-transplant iPTH pg/mL	191 ± 203 (range 65–1613)	42 ± 11 (range 3–62)	0.0001
Follow-up iPTH pg/mL	239 ± 249 (range 28–1493)	107 ± 134 (range 13–739)	0.0001
Change in iPTH category	17 (18%)	12 (24%)	0.0001

Numbers are expressed as absolute values, percentages, mean ± SD and range where indicated.