Transplant Int (1992) 5 [Suppl 1]: S 98–99

TRANSPLANT
International

Early kidney transplantation may prevent aluminium-related bone disease

K. P. Nordal[1], E. Dahl[2], J. Halse[1], and A. Flatmark[2]

[1] Department of Medicine, and [2] Department of Surgery, The National Hospital, Rikshospitalet, Oslo, Norway

In uraemia patients aluminium (Al) accumulation in bone leads to low turn-over bone disease [4]. Al-related bone disease causes bone pain, non-traumatic fractures and hypercalcaemia, and does not respond to treatment with vitamin D compounds [9]. Al-contaminated dialysate and ingestion of Al-containing phosphate binding agents are the main risk factors for bone Al accumulation [6, 12].

Studies of selected patients have indicated that Al-related bone disease ameliorates after successful kidney transplantation [5, 10], but systematic studies of bone Al have not been reported. In a prospective study we investigated the effect of successful kidney transplantation on bone Al and clinical bone disease.

Key words: Kidney transplantation – Aluminium – Related bone disease

Subjects and methods

Consent to bone biopsy at transplantation was obtained from 84 kidney graft recipients with intact parathyroid glands. Of these patients, 19 (23%) had never been dialysed, and 65 (77%) had been treated by dialysis for 1–44 (median 9) months. After transplantation all were immunosuppressed with a low-dose corticosteroid and high-dose cyclosporin A regimen [7]. Eight recipients died and another 11 returned to dialysis. Of the remaining 65 recipients with a functioning graft, 55 (83%) consented to a second bone biopsy 1 year after transplantation.

Serum creatinine was measured by a standard technique. The transiliac bone biopsies were performed, processed and evaluated as previously described [1]. Aurin-tricarboxylic acid was used to detect stainable Al in bone [8], and Prussian blue to ensure that iron was not responsible for the purple lines.

Results

Seven predialysis (37%) and 50 dialysis (77%) recipients had stainable Al at Tx. In predialysis patients, Al-stained bone surface (AlS) correlated with daily intake of phosphate binders ($r = 0.57$, $P < 0.05$). AlS was correlated with dialysis duration ($r = 0.50$, $P < 0.01$) in dialysis patients, and multiple linear regression analysis using a model which comprised daily intake of phosphate binders, dialysis duration, tap-water Al concentration, and serum Al levels confirmed that only dialysis duration could explain the variability in AlS among dialysis patients ($P < 0.01$).

Four patients had symptomatic bone disease with fractures and/or skeletal pain at transplantation. They all had AlS exceeding 45%. All four had been treated with dialysis for more than 24 months, came from areas with high Al content in tap-water, and used phosphate binders. Five asymptomatic patients also had AlS exceeding 45%. All came from areas with high Al content in the water and used phosphate binders, but only one had been on dialysis for more than 12 months.

At follow-up 1 year after transplantation, serum creatinine ranged from 62 to 415 (median 168) μmol/l. AlS had decreased from 13% range 6–23% to 2% (0–3%) ($P < 0.01$), and correlated with AlS at follow-up ($r = 0.58$, $P < 0.0001$). Al had become undetectable in 16 recipients with stainable bone Al at transplantation. No relationship was found between serum creatinine and AlS at 1-year follow-up.

One recipient with symptomatic bone disease and one asymptomatic recipient with AlS >45% at transplantation had died of infection. Another one with bone pain at transplantation refused a second bone biopsy, but was then without bone pain. In the remaining two with symptomatic bone pain and in the another four with AlS >45% at transplantation, AlS had decreased (50 to 10%, 51 to 15%, 71 to 0%, 52 to 6%, 75 to 11%, and 60 to 53%, respectively).

Comments

Symptomatic Al-related bone disease is a feared complication of long-term dialysis [11], and increased mortality has been described in severely Al-intoxicated recipients even after transplantation [3]. The present study confirms that successful kidney transplantation cures Al-related

Offprint requests to: K. P. Nordal M. D., Med. Dept. B, The National Hospital, Rikshospitalet, N-0027 Oslo 1, Norway

bone disease [5]. Since Al deposition is related to duration of dialysis [2], the present study underscores the importance of early transplantation.

References

1. Dahl E, Nordal KP, Halse J, Attramadal A (1988) Histomorphometric analysis of normal bone from the iliac crest of Norwegian subjects. Bone Miner 3: 369–377
2. Dahl E, Nordal KP, Halse, Flatmark A (1990) The early effects of aluminium deposition and dialysis on bone in chronic renal failure: a cross-sectional bone-histomorphometric study. Nephrol Dial Transplant 5: 445–456
3. Davenport A, Davison AM, Will EJ, Toothill C, Newton KE, Giles GR (1989) Aluminium accumulation and immunosuppression. Br Med J 298: 458–459
4. Hodsman AB, Sherrard DJ, Alfrey AC, Ott S, Brickman AS, Miller NL, Maloney NA, Coburn JW (1982) Bone aluminum and histomorphometric features of renal osteodystrophy. J Clin Endocrinol Metab 54: 539–545
5. Ihle BU, Buchanan MRC, Stevens B, Becher GJ, Kincaid-Smith P (1982) The efficacy of various treatment modalities on aluminium associated bone disease. Proc Eur Dial Transplant Assoc Eur Ren Assoc 19: 195–202
6. Llack F, Felsenfeld AJ, Coleman MD, Keveney Jr JJ, Pederson JA, Medlock TR (1986) The natural course of dialysis osteomalacia. Kidney Int 29 [Suppl 18]: S 74–S 79
7. Lundgren G, Albrechtsen D, Flatmark A, Gabel H, Klintmalm G, Persson H, Groth CG, Brynger H, Frødin L, Husberg B, Maurer N, Thorsby E (1986) HLA-matching and pretransplant blood transfusions in cadaveric renal transplantation – A changing picture with cyclosporin. Lancet II: 66–69
8. Maloney NA, Ott SM, Alfrey AC, Miller NL, Coburn JW, Sherrard DJ (1982) Histological quantitation of aluminium in iliac bone from patients with renal failure. J Lab Clin Med 99: 206–216
9. Ott SM, Maloney NA, Coburn JW, Alfrey AC, Sherrard DJ (1982) The prevalence of bone aluminum deposition in renal osteodystrophy and its relation to the response to calcitriol therapy. N Engl J Med 307: 709–713
10. Poedenfant J, Salem N, Sypitkowski C, Frame B, Parfitt AM (1985) Reversal of aluminum-related dialysis osteomalacia after transplantation. Bone 6: 405
11. Smith AJ, Faugere M-C, Abreo K, Fanti P, Julian B, Malluche HH (1986) Aluminum-related bone disease in mild and advanced renal failure. Evidence for high prevalence and morbidity and studies on etiology and diagnosis. Am J Nephrol 6: 275–283
12. Ward MK, Feest TG, Ellis HA, Parkinson JS, Kerr DNS (1978) Osteomalacic dialysis osteodystrophy: evidence for a waterborne aetiological agent, probably aluminium. Lancet I: 841–845