



Fig. 1. Distribution of coronary artery calcification and stenosis in HD and non-HD patients. In the non-HD group, the site with the highest frequency of calcification corresponded to that with the highest frequency of stenosis, but in the HD group, stenosis was often observed distal to the site with the highest frequency of calcification.

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Is glucocorticoid-induced osteonecrosis after kidney transplantation related to osteoporosis?

Sir,
 Osteopenia and osteonecrosis (ON) cause important long-term morbidity in renal transplant (Tx) recipients with

increasing incidences because of longer graft survival and related drug exposure.

A 38-year-old woman who started on haemodialysis in November 2001 had a renal Tx from a live relative in March 2003 due to chronic pyelonephritis with vesicoureteral reflux related end-stage renal disease. She had persistent secondary amenorrhoea 2 months before dialysis treatment. Throughout this period she had calcitriol and phosphorus binders for controlling secondary hyperparathyroidism. Her pre-Tx serum parathyroid hormone (PTH) was 73.2 pg/ml and body mass index (BMI) was 18.4 kg/m². Post-Tx immunosuppressive treatment was prednisolone (500 mg initially, then 30 mg/day), tapered to 25 mg/day by post-operative day 14, mycophenolate mofetil (2 g/day), cyclosporin (CsA; 100 mg/d) and daclizumab (a dose of 1 mg/kg, totalling five dosages with 2-week intervals). After an uneventful 4 weeks she complained of severe leg pain and symptoms of muscle weakness in the previous 4 days. The dose of prednisolone was tapered to 15 mg/day, but pain developed in both shoulders. Diffuse ON was diagnosed by hip and shoulder magnetic resonance imaging (MRI). At the time of diagnosis the total cumulative doses of prednisolone and CsA were 1220 mg and 2925 mg in 4 weeks, respectively. Serum creatinine was 0.7 mg/dl, calcium 10.5 mg/dl, Alkaline phosphatase (ALP) 271 IU/l, PTH 84 pg/ml, calcitonin 27 pg/ml and calcitriol 22.9 ng/dl. Bone mineral densities (BMD) of the lumbar spine and the hip region by Dual x-ray absorptiometry (DEXA) after post-Tx 8 weeks were evaluated as osteoporosis with T scores of -3.2 and -3.9, respectively. Oral calcium, calcitriol and alendronate were added to the treatment. Her complaints regressed within 10 days. The dose of prednisolone was tapered to 10 mg/day at month 4 and to 5 mg/day at month 10. One year later, hip and shoulder MRIs showed normal findings. The respective post-Tx T scores of the lumbar spine and the femoral neck improved from -2.8 and -3.5 in the first year to -2.4 and -2.2 in the second year. Her serum creatinine level was 0.8 mg/dl with no complaint.

Multiple factors appear to contribute to osteopenia and ON, including persistent uraemia-induced abnormalities in calcium homeostasis and acquired defects in mineral metabolism induced by immunosuppressive medications, such as glucocorticoids (GC) [1]. There were no clinical or laboratory findings of adynamic bone disease in our patient during the pre-Tx period. She was in the early post-Tx period and on a low cumulative dose of GC. This may be considered a low dosage for treatment of renal Tx patients, but an average dose of 40.7 mg/day was a potential risk factor. Although long-term GC administration and possibly CsA treatment may chronically activate osteoclasts in spongy and/or cortical bone while osteoblast activity is inhibited, ON did not recur in our case and the bone loss was improved.

Bone loss occurs early and rapidly following Tx, and then continues in most patients, although at a much slower rate. BMD was not assessed in the pre-Tx period because she had no bone or articular pain and no history of steroid administration, hyperthyroidism, dyslipidaemia, alcohol and smoking habits, previously. The very first measurement performed at the post-Tx period evidenced severe osteoporosis, which is quite unusual for a woman of that age. An explanation for this might be the fact that chronic renal failure is frequently associated with endocrine disturbances in women leading to amenorrhoea. A recent study showed that persistent amenorrhoeic young women on dialysis have lower trabecular BMD and evidence of increased bone resorption when compared with normal menstruating women on dialysis [2]. This hypothesis supported the outcome of

gradually decreased bone loss with the improvement of her amenorrhoea in the post-Tx period together with the usage of antiresorptive agents, despite possible osteopenic immunosuppressive drug usage.

Although the pathology of GC-induced ON is unclear, one possible mechanism involves alterations in circulating lipids with resultant microemboli in the arteries supplying bone. Steroids induce changes in venous endothelial cells, leading to stasis, increased intraosseous pressure and eventual necrosis [3]. GC-induced adipogenesis might be important in the pathogenesis of ON. Statins were shown to preserve bone mass and simultaneously prevent ON, suggesting a close interrelation between osteoporosis and ON. Bone tissue necrosis could be the end result of a process that starts as osteoporosis and continues to ischaemia through trabecular microfracture and microvascular damage [4]. Our case's features can explain why only an unpredictable subset will develop ON among patients receiving a specific GC dose, which underscores the existence of individual variability in the action of GCs.

Our case is unusual in its presentation because of her low BMI, young age and relatively short interval between start of therapy and onset of symptoms, course of ON and the presence of severe osteoporosis early. Prospective studies should be focused on the effect of the state of bones and endocrine disturbances in uraemic patients prior to Tx, on the development of osteoporosis and ON.

Conflict of interest statement. None declared.

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Survival and infection rates of a polyurethane vascular access graft compared to tunnelled dialysis catheters and brachiobasilic arteriovenous fistulas

Sir,

The polyurethane graft can be used within 24 h and has improved haemostasis after cannulation [1,2]. It may be an alternative to central venous catheters in situations where