Transplant Osteonecrosis: Can it Be Due to Uremic Neuropathy?

M.	Massimo	Bertoli ^a
A.	Andrea	Meneghello ^b
A.	Annamaria	Ruffatti ^a
U.	Ugo	Vertolli ^a
G.F.	Gian Franco	Romagnoli ^a

^aDivisione di Nefrologia II and ^bServizio Radiologico II, Ospedale di Padova, Italy

Dott. Massimo Bertoli, Riviera S. Benedetto, 124, I-35100 Padova (Italy)

Dear Sir,

Aseptic osteonecrosis of the femur head, a disabling disease which strikes about 16% of renal transplant recipients, seems clearly related to steroid therapy as its incidence drops sharply with the use of new immunosuppressants such as cyclosporin [1]. Several etiological factors related to corticosteroid treatment have been implicated, such as fat embolism in the small subchondral arteries associated with hyperlipidemia, or steroid-induced osteoporosis due to reduced osteogenesis as well as reduced interstitial calcium absorption, which may aggravate secondary hyperparathyroidism. Hypercoagulability related to steroid therapy may also lead to thrombosis of the bone arterioles with consequent avascular osteonecrosis. However, a recent editorial concluded that 'there are no suitable biochemical or hormonal markers for predicting which patients will develop aseptic osteonecrosis after transplant surgery' [1].

In our opinion, uremic neuropathy may also facilitate the onset of transplant osteonecrosis, which, in fact, has been described in pathologic situations characterized by severe peripheral nervous system disease, such as alcoholism [2], diabetes [3], familial dysautonomia [4] and in the uremic patient undergoing periodic dialysis [5].

Sixteen patients, 12 males and 4 females, ranging in age from 24 to 57 years, underwent renal transplantation and were treated with conventional immunotherapy (prednisolone and azathioprine). In addition to routine periodic laboratory tests, an electromyogram of the external popliteal sciatic nerve (velocity of neuromotor conduction) was performed once annually before and at 6 months following transplantation.

Five patients in this group (31.2%) developed osteonecrosis; in 4 cases onset occurred within 10 months of transplantation, and in 1 after 38 months. One patient also developed aseptic necrosis of a metacarpal epiphysis. No significant differences were observed between patients with and without osteonecrosis regarding the biochemical parameters examined (hematocrit, serum alkaline phosphatase, calcium, phosphorus, cholesterol and triglycerides) and total steroid dose. From a neurological point of view, however, motor conduction velocity of the sciatic-popliteal nerve was significantly slower ($p < 0.05$) in patients with osteonecrosis before and also 6 months after renal transplantation (41.05 ± 1.4 and 41.25 ± 0.96 m/s, respectively), while in patients without osteonecrosis, values were 45.5 ± 1.96 and 46.8 ± 5.59 m/s, respectively.

The origin of osteonecrosis secondary to transplantation is most likely multifactorial, and our patient group is too small for a confident conclusion to be drawn. Nonetheless, our results suggest that uremic neuropathy and its persistence following transplantation may represent an important pre-existing cause in the development of osteonecrosis. The deficit in proprioception and sensitivity associated with imbalance in joint motion due to neuropathy make it impossible for the weight-bearing joint surfaces to perceive the minor chronic stress, thus leading to consequent joint abuse and trabecular fractures with final interruption in arterial flow and death of the osteocytes.

References

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