Excess Purine Degradation in Muscle of Chronic Hemodialysis Patients

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Dear Sir,

We read with interest the recent report by Cleminson et al. [1]. They found a lower energy charge ratio expressed as $([ATP] + \frac{1}{2} [ADP]) / ([ATP] + [ADP] + [AMP])$ and increased concentrations of ADP and AMP in muscle of patients with chronic renal failure and hemodialysis, which might be related to the patients' reduced exercise ability and their poor metabolic state. Although this finding is quite interesting, the direct measurement of adenine nucleotide concentrations and energy charge using muscle biopsy is hard to perform in many patients in order to evaluate the energy metabolism in their muscles. Instead of the direct measurement of ATP in the muscle using biopsy, the determination of changes in plasma hypoxanthine after exercise is useful to estimate the energy charge in the exercising muscle, as described by Mineo et al. [2]. Excess hypoxanthine release from exercising muscle results from either an 'absolute' or a 'relative' imbalance in the supply of ATP of the muscle through activation of the purine nucleotide cycle; the former is observed in patients with glycogen storage disease [2] and the latter is observed in patients with hyperthyroidism [3]. We found that an excess release of hypoxanthine from muscle occurred under conditions where energy charge was less than 0.8 (unpublished data). Therefore, to check whether the energy metabolism in exercising muscle of chronic hemodialysis patients is impaired or not, in 3 cases, we determined the changes in plasma hypoxanthine, ammonium and blood lactate before exercise and 2, 6, 12, and 60 min after semi-ischemic forearm test as described elsewhere [4]. As shown in figure 1,

case 1 had an excess elevation of plasma hypoxanthine accompanied by a remarkable elevation of both ammonium and lactate, however, cases 2 and 3 had normal elevation of plasma hypoxanthine (min)

Fig. 1. Increase in venous hypoxanthine concentration after ischemic forearm test in chronic hemodialysis patients. Each point represents an incremental increase in hypoxanthine concentration in 3 cases. The shaded area indicates the mean $\pm$ SD in control subjects (n = 4). The same as 4 normal subjects as indicated by the shaded area. Case 1 was a 58-year-old male patient who had had hemodialysis for 10 years, case 2 a 60-year-old female patient who had received hemodialysis for 1 month, and case 3 was a 57-year-old male patient with 5 years of dialysis. These results suggest that the excess release of hypoxanthine in case 1 could result from the activation of the purine nucleotide cycle due to 'relative' disturbance of ATP supply, i.e., the demand of ATP exceeding the supply of ATP via anaerobic glycolysis, as observed in a patient with either hyperthyroidism [3] or congestive heart failure.

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secondary to CRF and exceptional in infants. Before the extended clinical use of active vitamin D metabolites, its frequency had been estimated to be from 1.5 to 1.7% of adult patients [2, 3]. To our knowledge, this is the 4th case described in children with CRF, always in females [4-6]. The reasons why a very limited number of children with severe renal osteodystrophy develop brown tumors is unknown. In our case, the possibility that erythropoietin treatment could be involved in the occurrence of the tumor cannot be ruled out. However, this undesirable side effect of erythropoietin therapy has not been reported to date. Brown tumor treatment should include appropriate management of renal osteodystrophy and curettage or surgical mass removal [7]. Total or subtotal parathyroidectomy has been useful in all reported cases but one [8]. Renal transplant solved the problem in 1 child [6]. No surgical procedure was performed in our patient because of her poor general condition.

This report serves to emphasize that brown tumor should be included in the differential diagnosis of a bone mass in children with CRF. The prolonged survival of infants with ESRD may lead to a higher incidence of this unusual form of renal osteodystrophy in poorly controlled patients.

References

- 3 Hisatome I, Ishiko R, Takeuchi T, et al: Excess 5 Hisatome I, Ishiko R, Miyakoda H, et al: Excess
Clemenson WG, Manchester KL, Diesel WJ, et al: Adenine nucleotide concentrations and energy charge in muscle of chronic haemodialysis patients. *Nephron* 1992;60:232-234.
- Mineo I, Kono N, Shimizu T, et al: Excess purine degradation in exercising muscle of patients with glycogen storage disease type V and VII. *J Clin Invest* 1985;76:556-560.
- purine degradation in skeletal muscle with hyperthyroidism. *Muscle Nerve* 1990;13:558-559.
- 4 Hisatome I, Kitamura H, Miyakoda H, et al: Excess release of hypoxanthine from exercising muscle in two gout patients with partial HGPRTase deficiency: Lack of ammonium release. *Am J Med* 1991 ;90:533-535.
- purine degradation caused by an imbalance in the supply of adenosine triphosphate in patients with congestive heart failure. *Br Heart J* 1990; 64:359-361.
- 482 Kosaka/Hisatome/Ogino/Tanaka/Osaki/ Excess Purine Degradation in Muscle of
Kitamura/Omodani/Matsumoto/ Chronic Hemodialysis Patients
Miyakoda/Kotake/Mashiba/Ono/Inoue