Evolution of Anemia of Chronic Renal Failure after the Treatment of Hyperparathyroidism

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Dear Sir,

It is already known that one of the causes of severe anemia and lack of response to erythropoietin (r-huEPO) therapy in chronic uremic patients on hemodialysis is secondary hyperparathyroidism [1,2]. It is believed that the reason of this resistance to r-huEPO is the bone marrow fibrosis related to the hyperparathyroidism [3], although the inhibitory effect of parathyroid hormone, as an uremic toxin, on erythropoiesis has also been considered [4, 5]. We present here 2 patients with chronic renal failure on regular hemodialysis with severe hyperparathyroidism and anemia refractory to r-huEPO therapy which improved spectacularly after hyperparathyroidism treatment.

Case 1: A 45-year-old man with end-stage renal disease due to nephroangiosclerosis on hemodialysis for the last 11 years. Over the past few years severe secondary hyperparathyroidism developed with serum PTHi levels of 1,300-1,500 pg/ml (normal level 10-60 pg/ml), alkaline phosphatase 400 U/l, with normal calcium and phosphorus and radiological findings consistent with hyperparathyroidism. Within the last 2 years hemoglobin was between 4.9 and 7.4 g/dl (49-74 g/l) and hematocrit 15-23%. He was on r-huEPO therapy at a dose of 200 IU/kg body weight/week administered intravenously postdialysis. Despite this treatment he needed blood transfusions twice; no evidence of iron, vitamin B₁₂ or folic acid deficit or obvious bleeding was noted, aluminium intoxication and other causes of r-huE-PO resistance were excluded. After starting treatment with intravenous calcitriol, 1 µg administered postdialysis, a progressive decrease in PTHi levels was noted (below 500 pg/ml) with a simultaneous increase in hemoglobin up to 10.9 g/dl (109 g/l) and hematocrit to 34%. A reduction in the dose of r-huEPO to 150 IU/kg body weight/week was performed with steady values of hemoglobin up till now (fig. 1).

Case 2: A 55-year-old man with chronic renal failure secondary to renal lithiasis and primary hyperparathyroidism. Eleven years ago his left kidney was removed because of pyonephrosis, 1 year later a parathyroid adenoma was surgically removed. He has been on regular

hemodialysis for the last 5 years. Within the last few years a relapse of his hyperparathyroidism was observed with another adenoma being discovered by ultrasound; the serum PTHi level was 1,428 pg/ml, alkaline phosphatase 465 U/l, total calcium 2.7-3 mmol/l (10.8-12 mg/dl) and phosphorus 1.9-2.4 mmol/l (5.8-7.4 mg/dl). No bleeding history was noted, his serum hemoglobin was 6-7.5 g/dl (60-75 g/l) and hematocrit 14-25% needing blood transfusions on some occasions even though he was receiving 250 IU/kg body weight/week of r-huEPO given intravenously postdialysis. Other recognized causes of r-huEPO resistance had been corrected or excluded. A total parathyroidectomy with gland implant in the forearm was performed; after surgery hypocalcemia developed and calcium and oral calcitriol were started. There was a normalization of the alkaline phosphatase levels and a PTHi decrease to values below normal (5 pg/ml). We observed a quick increase in hemoglobin level up to 10 g/dl (100 g/l) and hematocrit to 32%, values that have been in steady state in spite of a reduction in the dose of r-huEPO to 155 IU/kg body weight/ week (fig. 1).

One of the already described reasons for the resistance to r-huEPO therapy is hyperparathyroidism [1, 2]. This resistance has been related to parathyroid hormone-induced myelofibrosis [3], some authors have also pointed out the direct inhibitory effect of PTH on erythropoiesis [4, 5]. In our 2 patients an improvement in their anemia after the effective treatment of hyperparathyroidism was observed; this has already been found by some authors after parathyroidectomy [6-8]. The regression of myelofibrosis after parathyroidectomy is only effective after 6 months of the procedure [9], this is the explanation given by some authors for the improvement of anemia in their patients 6 months after parathyroidectomy [10]. Although we have not performed bone biopsy in our patients to prove the degree of bone marrow fibrosis, the quick improvement in hemoglobin and hematocrit after the decrease in serum PTH level suggests a role by its direct inhibitory effect on erythropoiesis rather than the regression of fibrosis itself.

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PTHi

• Patient 1: O Patient 2:
1,500 pg/ml 1,428 pg/ml

P1H1

• Patient 1: 500 pg/ml O Patient 2: 5 pg/ml

11-10-9-1

10 11

Fig. 1. Evolution of hemoglobin after i.v. calcitriol therapy in patient 1 (•) and after parathyroidectomy in patient 2 (O). Erythropoietin dosage of patient 1 (A) and patient 2 (Δ). Tf = Blood transfusions.

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10

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Anemia Hyperparathyroidism
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 445