

The resolution of anemia after curative parathyroidectomy is sustained even after a decade

Sir,

We had previously reported that 53% of patients with symptomatic primary hyperparathyroidism (PHPT) had anemia, and bone marrow fibrosis was observed in 75% of them.^[1] Patients with hematological parameters/peripheral smear suggestive of anemia due to iron, folate or B12 deficiency, were excluded and none of the patients were on iron, B12 or folate supplements during the study period. The reticulin stain was done for the assessment and distribution of bone marrow fibrosis. It was quantified as Grade 0: No reticulin fibers demonstrable, Grade 1: occasional fine individual fibers and foci of fine fiber network, Grade 2: fine fiber network in most of the section, Grade 3: diffuse fiber network with scattered thick coarse fibers and Grade 4: diffuse and often coarse fiber network with areas of collagenization. Perls stain was performed for assessment of iron stores and the mean score of bone marrow iron score was 1.75 before surgery and it did not change after surgery. After curative parathyroidectomy, there was an improvement in both, marrow fibrosis and anemia, in all patients.^[1] Here, we share the follow-up of a same cohort of eight patients after 10 years of curative parathyroidectomy. These patients were invited for clinical evaluation and biochemical investigations. Body mass index, pallor, bone pain, fractures, and new onset renal stone disease were assessed. Preoperative, 1-year and 10 years hematological and biochemical parameters were compared which each other by nonparametric Wilcoxon signed ranks test and $P < 0.05$ was considered as significant.

At 10 years of follow-up, none of the patients had bone pain, fractures or new onset renal stone disease. Four patients initially presented with pancreatitis; none of them had a recurrence during follow-up. The mean (\pm standard deviation [SD]) body mass index of the patients, was 25.36 ± 6.0 kg/m² at baseline and 27.17 ± 3.6 kg/m² at 10 years. All patients had normal hemoglobin levels throughout follow-up of 10 years. The mean (\pm SD) hemoglobin at 10 years was significantly higher compared

to baseline (13.3 ± 1.5 vs. 11.5 ± 0.7 g/dl, $P = 0.035$). The biochemical parameters of the patients are summarized in Table 1.

It is known that elevated parathyroid hormone (PTH) levels correlate with anemia in patients with chronic kidney disease and this persistently elevated PTH leads to marrow fibrosis. Recently, Russo *et al.* have shown that serum intact PTH > 120.5 pg/ml is strongly associated with hemoglobin < 10 g/dl.^[2] Anemia is a dominating feature of PHPT patients in India.^[3] The mechanism of anemia in PHPT is multifactorial, including a direct inhibitory effect of PTH on erythropoietin synthesis and bone marrow erythroid progenitors, and PTH-induced bone marrow fibrosis, which is mediated by the effect of increased cytokines (interleukin-6 and tumor necrosis factor- α).^[4,5] In addition, loss of appetite, low Vitamin D and chronic pancreatitis-related malnutrition also contribute to anemia. Low levels of Vitamin D contribute to anemia directly by its effect on red blood cell precursors^[6] and indirectly by producing secondary hyperparathyroidism. Changes in the parathyroid proteome^[7] may also contribute.

None of our patients had a recurrence of anemia even after 10 years of curative parathyroidectomy, which suggest a causative role of elevated PTH for anemia. This calls for further studies with estimation of cytokines and erythropoietin levels before and after curative parathyroidectomy.

CONCLUSION

The follow-up of patients after curative parathyroidectomy provides useful information about anemia in PHPT: First, anemia in PHPT is related to elevated PTH; secondly,

Table 1: Biochemical parameters of the patients at baseline, 1-year and 10 years after curative parathyroidectomy

Parameter	Mean \pm SD		
	Baseline	After 1-year	After 10 years
Hemoglobin (g/dl)			
Males: >13	11.5 \pm 0.7	12.9 \pm 1.8*	13.3 \pm 1.5*
Females: >12			
Calcium (8.6-10.2 mg/dl)	10.4 \pm 0.6	8.68 \pm 0.6*	9.28 \pm 0.48*
Phosphorus (2.7-4.5 mg/dl)	2.97 \pm 0.34	3.56 \pm 0.4*	3.3 \pm 0.5
Creatinine (0.5-1.2 mg/dl)	0.77 \pm 0.19	1.14 \pm 0.4	0.78 \pm 0.12
Alkaline phosphatase (40-129 U/L)	388 \pm 532	125 \pm 68.9*	100 \pm 42.8*
iPTH (9-62 pg/ml)	1041 \pm 966	44.5 \pm 16.2*	52 \pm 35.7*
25 hydroxy Vitamin D (11.1-42.9 ng/ml)	18.7 \pm 9.7	20.39 \pm 12.3	20.4 \pm 17

* $P < 0.05$ as compared to baseline. iPTH: Intact parathyroid hormone, SD: Standard deviation

successful parathyroidectomy results in improvement of anemia, and finally, improvement in anemia is sustained even after a decade.

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Conflicts of interest

There are no conflicts of interest.

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