METABOLIC BONE DISEASE AND REVERSIBLE RENAL TUBULAR DYSFUNCTION IN A CHRONIC ALCOHOLIC

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Introduction

Alcohol is an important risk factor for various bone diseases. Amongst chronic alcoholics the most common metabolic bone disease is osteoporosis but rarely osteomalacia also occurs [1,2]. Possible etiological factors include poor nutrition, vitamin D malabsorption [3], defective hydroxylation of vitamin D to vitamin 25-OH D [4], and associated liver and renal dysfunction [5,6]. Alcohol bone disease has been reported in the absence of severe chronic liver damage. Here we report a case of hypophosphatemic osteomalacia with reversible renal tubular dysfunction in a chronic alcoholic patient.

Case Report

A 55-years-old male was admitted with complain of body pain and inability to walk since 1988. His X-ray pelvis revealed fracture of the left femur, for which he was put on traction for four months followed by rest for one month. After that he was unable to walk without a stick. In 1990 he was operated with plate fixation on the left femur, but had no improvement for two months and plates were removed. Since then he was unable to walk even with assistance. A bone biopsy from iliac crest was marked by sclerotic bone with normal marrow. In 1993 he was put on calcium and vitamin D₃ therapy without any improvement.

On admission in 1996 he was still unable to walk and bear weight and had diffuse body pain. There was good exposure to sunlight. Dietary review suggested that the daily intake of calories 2000 K cal, protein 64 gm/day and calcium 1.2 gm/day. He had no history suggestive of malabsorption, renal disease, hypercalcemia or tetany. In the past (1960) he had been operated for renal stone on left side and was treated for jaundice 20 years back, etiology of which is unknown. Family history was not contributory. He was a chronic smoker (one bundle of biddies per day) and was consuming alcohol about 180 ml/day for 33 years that he stopped on admission. In addition there was a history of treatment with steroids (prednisolone 5 mg/day) for one year in 1988.

On examination his height was 159 cm (previous documented height 166 cm) with upper/lower segment (73/86 cm) ratio of 0.85 (indicating loss of upper body height). His arm span was 176 cm. The length of left lower limb was 83 cm and right lower limb 87 cm (due to associated fracture of neck of left femur). His blood pressure was 150/96 mm of Hg. He had facial plethora, parotid enlargement and palmar erythema without icterus, clubbing,

edema or spider angioma. There was no evidence of conjunctival calcification, band keratopathy, Keyser-Fleischer ring or cataract on eye examination. Thyroid gland was not palpable. Chest expansion was 2 cm and there was diffuse tenderness of rib cage. There was no organomegaly. Per rectal examination was normal. There were tender swellings on the upper part of left and lower part of right tibia.

Investigations revealed haemoglobin 15.6 gm/dl, ESR 30 mm fall in 1st hour, Blood glucose fasting and postprandial 102 and 153 mg/dl, Blood urea 19 mg/dl, S creatinine 1.1 mg/dl, S sodium 142 meq/L, S potassium 3.9 meq/L, S bilirubin 1.2 mg/dl, SGOT and SGPT 84 and 99 IU/L, serum GGT 26.0 IU/L (8.0-38.0 IU/L), total protein 7.6 gm/dl, S albumin 4.8 gm/dl, S uric acid 7.0 mg/dl, S cholesterol 236 mg/dl and S acid phosphatase 6.1 IU/L (<6.5 IU/L).

Urine examination was normal with no Bence-Jones protein or aminoaciduria. Urine pH was 8.7 with blood pH of 7.331. Urine acidification test was done, which showed inability of kidney to lower urinary pH below 5.5 indicating defective acidification (Table-1).

TABLE 1
Biochemical Parameters

Parameters	Before treatment	After treatment	Normal range
Serum calcium (mg/dl)	9.0 - 9.3	9.0 - 9.3	8.8 - 10.8
Serum phosphate (mg/dl)	2.2 - 2.6	2.8 - 3.2	3.5 - 5.0
SAP (KAU/L)	66.9 - 69.5	150 - 157	3 - 13
Urine calcium (mg/kg/24 hr)	1.4 - 2.5	2.5 - 3.0	2.5 - 4.0
Urine phosphate (mg/kg/24 hr)	4.1 - 6.9	3.9 - 4.9	< 13
Blood pH - basal	7.331	7.387	7.34 - 7.44
- 4 hr after acidification	7.281	7.284	
Urinary pH - basal	8.7	5.7	
- 5 hr after acidification	7.485	5.192	< 5.5
TRP	75/dl	90/dl	> 85/dl
TmPO ₄ /100 ml of GFR	1.96	2.4	2.5 - 4.5
Parathyroid hormone (ng/L)	46.5	62.0	10 - 72

Serum calcium, phosphate, SAP alongwith 24-hour urinary calcium and phosphate were done for three consecutive days (Table-1). It revealed normal serum and urine calcium, low serum phosphates with increased phosphate excretion. Serum, urine and water fluoride were high-0.12, 3.0 and 3.8 ppm respectively (normal 0.02, 0.1 and 1.0 ppm). GFR measured with the help of 99Tc

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DTPA was 65 ml/min/1.73 m² (normal ref. laboratory range 106 ± 27) and effective renal plasma flow with ¹³¹I hippuran was 310 ml/min/1.73 m² (normal ref. laboratory range 573 ± 120).

Serum parathyroid hormone (PTH) was within normal range. Serum cortisol basal and post low dose dexamethasone was 205 ng/ml and 11.7 ng/ml respectively (normal basal 50-240 ng/ml and post dexamethasone suppression <50 ng/ml), and serum testosterone was 4.6 ng/ml (3.0-10.0 ng/ml).

Skeletal survey showed multiple pathological fracture in ribs, phalanges, neck femur, tibia and calcaneum associated with diffuse osteopenia in addition to osteosclerosis in the spine. There were Looser's zones at the upper rim of pubic rami and marked thinning of cortical bone. Ultrasonography of neck for thyroid or parathyroid was normal.

He was advised to change the source of water, abstinence from alcohol, oral calcium (1.5 gm/day), oral phosphate (1.0 gm/day), and vitamin alpha-D₃ 0.25 µg once a day and reviewed after two months. His clinical condition did not improve, rather he complained of increase in pains, which is well described in the early treatment phase. However a repeat urine acidification test revealed normal acidification and there was improvement in phosphate excretion indices (Table-1). He was advised to continue therapy.

Discussion

This patient presented with diffuse bone pain, multiple pathological fractures and pseudofractures, osteopenia at long bones of hands and pelvis and leg with osteosclerosis of the spine on radiological examination, normal serum calcium, low serum phosphorus with phosphaturia, raised SAP and renal acidification defect. A diagnosis of hypophosphatemic osteomalacia was made with etiological possibility of adult onset hypophosphatemic osteomalacia, renal tubular acidosis, oncogenic osteomalacia and alcoholic osteomalacia. Renal tubular function done in his son was normal with normal serum calcium and phosphorus levels. Clinical and radiological examination did not reveal any evidence of prostatic or mesenchymal tumor. However these tumor may escape detection for several years despite extensive investigations [7], hence diagnosis of oncogenic osteomalacia cannot be ruled out with certainty. Onset at late age and reversible renal acidification defect excluded renal tubular acidosis as primary cause. Though he had marginally raised SGOT and SGPT normal GGT level excluded significant alcohol related chronic liver disease contributing to osteomalacia.

Our patient also had various contributing factors like smoking, inactivity due to pain and fracture, steroid treatment and fluorosis that have aggravated the course of disease. He had osteosclerosis of spine on radiological examination that is not a common feature of alcoholic bone disease but can possibly be explained by high fluoride levels. Hypogonadism and hypercortisolism associated with alcoholism can also contribute to alcohol bone disease, however our pa-

tient had normal serum testosterone and serum cortisol levels.

Alcoholic bone disease often presents with idiopathic osteoporosis discovered by chance on radiological assessment [1,2]. Though impaired renal tubular dysfunction has been reported in the chronic alcoholics [5,6,8,9], its relation or association with alcoholic bone disease is not clear. Labib et al in 1989 reported impairment of renal tubular function in 40% of patients assessed by urinary excretion of albumin, and retinol binding protein [6]. Various workers [5,8,9] have reported hypophosphatemia in chronic alcoholics. Angeli et al reported hypophosphatemia in 35% of alcoholics with liver disease and 29% without liver disease [8]. De Marchi documented it in 30% patients [9]. Hypophosphatemia in chronic alcoholics is contributed by increased renal phosphate loss as documented in this case and also observed by others [5,9]. Renal phosphate excretion is dependent on phosphate intake and PTH levels. In this patient increased phosphate loss in presence of normal PTH suggest either direct effect of ethanol on the renal handling of phosphate [9] or its effect on other unknown humoral factor responsible for phosphorus homeostasis [7]. Our patient had defect in renal acidification and mild metabolic acidosis, which reversed after abstinence of alcohol. Similarly De Marchi et al also observed defect in renal acidification in 28% of patients which was reversible after four weeks of abstinence from alcohol. However, they did not observe alcohol bone disease in their patient. Relation of these defects to alcohol bone disease is unclear.

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