CASE REPORTS

OSTEOMALACIA DUE TO TYPE-I RENAL TUBULAR ACIDOSIS IN A MIDDLE AGED PAKISTANI WOMAN

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INTRODUCTION

Osteomalacia, one of the causes of reduced bone density, is a disorder of mineralization of newly formed bone matrix in adults. Though it is an uncommon disease in western world, but it is not that infrequent in Indian subcontinent. Though dietary deficiency of vitamin-D is responsible for the vast majority of osteomalacia cases worldwide, but renal diseases can lead to osteomalacia in variety of ways including reduced formation of calcitriol, renal tubular acidosis (RTA) and secondary hyperparathyroidism. Among RTAs, it is seen most often with proximal RTA (type-II) and occasionally with distal RTA (type-I). We report a case of osteomalacia in a middle age Pakistani woman with type-I RTA and tubular interstitial nephritis (TIN) that appear to be induced by streptomycin.

CASE REPORT

A 32-year-old woman was admitted in medical unit of Military Hospital Rawalpindi with history of generalized body aches and bony pain for last two years and muscular weakness for six months. Her pain was generalized, continuous, and aggravated on movement. The intensity of pain gradually worsened and became so severe that she became bed bound with in six months. She had profound muscular weakness and could not get up from squatting position, comb her hair, or change her clothes unaided. She was dependent on other family members for her mobility and daily needs. There was no history of cough, rash, arthralgias, fever, anorexia, vomiting, diarrhea or alteration in her bowel habits. Though she belonged to conservative family, but there was adequate exposure to sunlight. Her nutritional history was satisfactory. She did not suffer from diabetes, hypertension, or any other renal disease. She was diagnosed to be suffering from pulmonary tuberculosis two years prior to her admission and took rifampicin, isoniazid for nine months and pyrazinamide, injection streptomycin for initial two months. On detailed questioning, she attributed her illness to the use of anti-tuberculosis chemotherapy particularly streptomycin. Over the past two years, she had been regularly taking variety of analgesics and non-steroidal anti-inflammatory drugs (NSAID) for relief of pain. She was married and had three children delivered per vaginum normally. Her menarche was at the age of 13 and her menstrual history was normal till one year ago when she developed amenorrhea. Her family history was non contributory. On examination she was lean, weak and emaciated. She had pallor and her skin was dry and wrinkled. Her thyroid was not enlarged and lymph nodes were not palpable. Her blood pressure and body core temperature were normal. Her ribs were tender to touch and there were crepitations at right lung base. Her muscles were tender, and wasted, with power of 3/5 proximally and 4/5 distally. Muscle tone was normal and her gait was waddling. Reflexes were intact bilaterally and planters were down going. Liver, spleen and kidneys were not enlarged. Investigations revealed hemoglobin 10 g/l, microcytic and hypochromic, with erythrocyte sedimentation rate of 30 mm of fall at the end of first hour. Renal profile showed serum urea of 9 mmol/l, serum creatinine of 137micro mol/l, serum potassium of 3 mmol/l, serum sodium of 136 mmol/l. Bone profile revealed serum ionized calcium 0.98 mol/l, serum total calcium 2.29mol/l, serum phosphate 0.84 mol/l,

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alkaline phosphatase 570 u/l. Her serum albumin was 36g/l and thyroid function was normal. Her urine protein excretion rate was 1651 mg/24 hrs where as creatinine clearance was 40 ml/1.732m/24hrs. Her chest x-ray showed patch of bronchiectasis in right lower zone and there were pseudo fractures of ribs with callus formation. Her x-ray lumbo-sacral spine and hip showed osteopenia, cod fish deformity of vertebrae and callus formation at hip (fig.1). X-ray abdomen (kidneys and bladder) was normal. There was a small calculus of 0.2 cm at lower pole of right kidney on ultrasonography along with grade-I renal parenchymal disease. Bone scan showed increased uptake in the spine and long bones. Her plasma parathormone (PTH) was raised to12.8 pmol/l and vitamin-D was 14 pg/l. Bone biopsy histologically confirmed diagnosis of osteomalacias (fig.2). On arterial blood gas analysis, she was found to have metabolic acidosis with pH of 7.19, pCO2 30 mm of Hg and bicarbonate of 11mmol. Her anion gap was 18 and serum chloride was raised to 110 mmol/l. Serial measurements of her urine pH remained above 6.5 in spite of being in acidosis. Her 24 hour urine electrolytes were; calcium of 5.07 (1.25–6.0 mmol/ 24hrs), sodium 69.1 (40 - 220 mmol/day), potassium 24.3 (25 -125 mmol/d), chloride 34 (110 - 250mmol/d). Her urinary anion gap was increased which favored the diagnosis of distal type of RTA (type I). Her urine for glucose and amino acid were negative that ruled out multiple tubular defects. Her hepatitis-B and hepatitis-C profile were also negative. Renal biopsy was performed for her unexplained proteinurea that showed sclerosis of 8 out of 13 glomeruli, hyalinization of renal tubules and infiltration of interstitium with lymphocytes, findings consistent with TIN. She was given oral soda bicarbonate 1.8gm /day, alpha calcitriol 0.5 mcg daily and tablet enalapril 2.5 mg daily. She showed marked improvement in her symptoms and started gaining weight and walking. Her biochemical profile also improved with normalization of blood pH, bicarbonate and serum calcium levels. She was advised to take these medications regularly and was found to be symptom free on her last outpatient visit.

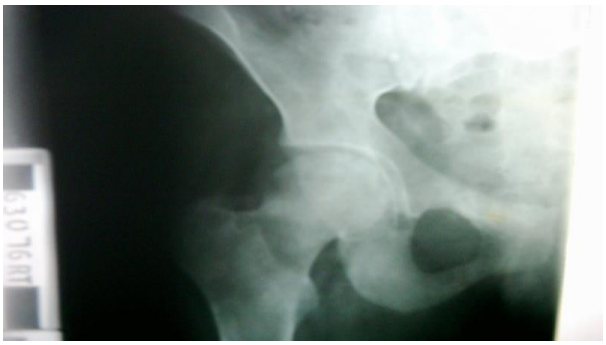

Fig.1: X-ray pelvis showing callus formation following pseudo fracture

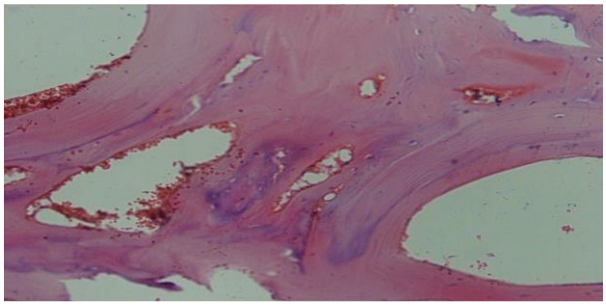

Fig. 2: Slide of bone biopsy showing osteomalacia

DISCUSSION

Bone pain, reduced bone density and pathological fractures in a relatively young patient require a thorough investigation. It is of paramount importance to differentiate between early onset osteoporosis and osteomalacia. The distinction between the two can be made most accurately by bone biopsy with double tetracycline labeling [1]. However, in clinical practice this test is rarely performed and diagnosis is usually made on the basis of history, physical findings, and laboratory results of serum calcium, phosphate, alkaline phosphatase, serum parathormone levels and radiological findings. In osteoporosis, all of these biochemical parameters are normal where as at least one of them is abnormal in osteomalacia. For adequate mineralization of bone, adequate extra cellular concentration of serum calcium, serum phosphates should be present with normal pH and normal bioactivity of alkaline phosphatase. There should be no inhibitors of calcification. Vitamin-D deficiency or its resistance may lead to osteomalacia [2]. This lady presented with generalized body aches and pains, low

calcium, raised alkaline phosphatase, raised PTH and radiological findings of osteopenia and pseudo fractures. These findings favored the diagnosis of osteomalacia, which was further confirmed on bone biopsy. Though the most common cause of osteomalacia is dietary deficiency and inadequate exposure to sunlight [3], but these factors were not operative in our patient and presence of proteinurea, impaired renal functions and hypokalemia pointed towards renal cause of her osteomalacia. Combination of osteomalacia, hypokalemia, hyperchloremic normal anion gap metabolic acidosis suggested renal tubular acidosis or some malabsorptive process such as celiac disease or inflammatory bowel disease. Since she did not has diarrhea, so RTA was high on the list. Chronic metabolic acidosis results in calcium loss from bone and hypercalciuria [4]. RTA should be suspected in patients with normal anion gap metabolic acidosis. The degree of acidosis is variable in type I and type II of RTA. Distal RTA (type I) causes osteomalacia through increased calcium loss [5]. In adults, distal RTA may result from autoimmune disorders such as Sjogren's syndrome, systemic lupus erythematosis, chronic active hepatitis, nephrocalcinosis secondary to idiopathic hypercalciuria, primary hyperparathyroidism, Wilson's disease, drugs like analgesics, lithium, renal diseases like renal transplant, pyeloneohritis and obstructive nephropathy. As her antinuclear antibodies, ENA and rheumatoid factors were negative, so Sjogren's syndrome and rheumatoid arthritis were excluded. Her proteinuria appear tobe due to TIN, that is known to occur with renal tubular defects usually distal and rarely with proximal [6]. As aminoglycosides and NSAID are known to cause renal tubular defects and TIN [7] and her problem started after the use of streptomycin, so we believe that this drug was possibly the cause of her TIN and RTA and subsequently osteomalacia. Correction of biochemical abnormalities and disappearance of symptoms with soda bicabonate and potassium supplements proved that she was in fact suffering from RTA.

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