

Case Report

Delayed fracture union in a case of vitamin D dependent rickets associated with pulmonary tuberculosis - a case report

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ABSTRACT

Rickets is a defect of bone mineralization caused by vitamin D deficiency, seen most significantly at growth plates that result in radiological bony abnormalities like metaphyseal flaring and cupping, physeal widening with focal and generalised osteomalacia. Here we present a rare case of 7 years old male, a case of vitamin D3 deficiency rickets in a known case of multi drug resistant pulmonary tuberculosis. The patient had suffered left proximal fibular fracture following trivial fall 1.5 month back and had delayed bony union leading to difficulty in walking and pain. The patient was treated with oral vitamin D supplementation. In vitamin D deficiency rickets, there is decreased bone mineralization leading to weak bones and delayed fracture healing in children. Low serum vitamin D levels also caused decreased immunity with increased susceptibility to respiratory infections like pulmonary tuberculosis. Appropriate treatment with injectable or oral vitamin D3 with adequate exposure of sunlight and proper nutrition is the best modality of treatment.

Keywords: Rickets, Vitamin D, Pulmonary tuberculosis, Delayed fracture healing

INTRODUCTION

Rickets is a defect of bone mineralization caused by vitamin D deficiency, seen most significantly at growth plates that result in radiological bony abnormalities like metaphyseal flaring and cupping, physeal widening with focal and generalised osteomalacia.¹

In rickets, there is failure of mineralization of preformed osteoid causing reduced or absent with associated growth plate deformity. It can lead to many lower limb deformities like bow legs, knock knees or windswept deformities. Radiological and biochemical rachitic changes have been reported to show improvement with both calcium and vitamin D supplementation.²

Vitamin D dependant rickets is most commonly seen between 6 months to 2 years of age. Normal vitamin D levels are measured by serum concentration of 25 hydroxy

vitamin D levels above 30 ng/ml. Vitamin D deficiency is defined as serum concentration of 25 hydroxy vitamin D less than 20 ng/ml.^{3,4}

Vitamin D regulates calcium homeostasis in human body by increasing intestinal calcium absorption, renal calcium reabsorption and bone resorption by osteoclasts.⁵

Nutritional rickets is common in children of Asian origin and those with dark skin. Dietary deficiency and avoidance of sunlight are recognized as most important factors in disease pathogenesis. Rachitic patients have increased complaints of respiratory signs and symptoms. They increased risk of contracting pneumonia and even more risk of dying from it when compared to non-rachitic infants.⁶

Vitamin D acts by binding to target cells. So, defect in receptor structure and low levels of vitamin D both result in impairment of host immunity to tubercle bacillus.⁷

Vit D plays an important role in modulating body's natural defences infection by promoting role of monocytes and macrophages. It suppresses MHC class 2, interferon gamma and interleukin 2 from CD4 helper T cells.⁸

Vitamin D deficiency is seen in 70% of fracture patients.⁵

CASE REPORT

A 7 years old male child brought to orthopaedic OPD by parents with complaint of pain in left knee following a trivial fall while playing 1.5 month back. Patient was a known case of pulmonary Kochs on CAT 1 AKT regimen later found out to have progressed to multi drug resistant TB. On examination there was mild pain and difficulty to walk but no local tenderness or swelling. No evidence of surrounding erythema or rise of temperature.

There was significant frontal bossing, rachitic rosary and pigeon chest features. There was mild swelling of bilateral wrist joints as seen Figure 1.



Figure 1 (A, B, C, D and E): Rickets features of swollen wrists, frontal bossing, rachitic rosary and pigeon chest seen.

On x-rays there was evidence of old left proximal fibular fracture as seen in Figure 2. On screening for rickets, x-rays of bilateral wrists and knee joints showed cupping, fraying and splaying of metaphysis as seen in Figure 2. Serum parathyroid, calcium and phosphate levels were normal. But there was significant decreased serum vitamin D3 levels.

Chest x-ray was suggestive of right upper and lower lobe consolidation with right para-hilar opacities as seen in Figure 3.

We started the child on STOSS regimen with vitamin D3 capsules 6000 IU daily for 12 weeks.

Patient was lost to follow-up due to COVID-19 lockdown.



Figure 2 (A, B, C and D): X-rays of cupping, fraying and splaying of metaphysis of bilateral wrists and knee with old left proximal fibular fracture showing delayed union.



Figure 3: Chest X-ray suggestive of right upper and lower lobe consolidation with right para-hilar opacities.

DISCUSSION

In rickets, there is chondrocyte apoptosis, impaired vascularization and mineralization of the cartilage matrix surrounding the apoptotic chondrocytes. There is disorganization of the growth plate due to accumulation of hypertrophic chondrocytes, which occurs as a result of delayed chondrocyte apoptosis, leads to a loss in their columnar arrangement.³

In vitamin D deficiency, there are high chances of fractures in rachitic long bones of physically active children due to failure of weight bearing. Factors like breast feeding, lack of sun exposure, clothing habits and low family income play important role in maintaining vitamin D levels.^{1,6}

Vitamin D owing to its anti-inflammatory action is a known immune modulator in pulmonary tuberculosis associated with cathelicidin mediated killing of mycobacteria. It causes resolution of inflammation by decreasing nuclear factor kappa light chain of b cells signalling pathways, matrix metalloproteinases expression and pro inflammatory cytokines and chemokines. Vitamin D supplementation along with anti-tubercular drugs regimen also has been found to increase sputum culture conversion rates of MDR TB and reduces relapse rates.⁸

Pulmonary tuberculosis is characterized by granuloma formation which is controlled bicellular immune system. Interferon gamma which mediates inflammatory reactions are increased in tubercular infections which in turn have positive correlation with bone fractures. The cytokine interferon gamma stimulates neopterin release and studies suggest increased levels of neopterin is associated with increased hip fracture risk. The dual effect of vitamin D being deficient in pulmonary tuberculosis and osteoporosis pateints makes it a confounding factor for association between pulmonary tuberculosis and delayed bone healing in fractures.⁹

This finding was more common in males than female owing to profound decrease in dehydroepiandrosterone and testosterone levels in pulmonary tuberculosis causing osteoporosis.⁹

Vitamin D can modulate the function of lymphocytes that produce antibodies and cytokines. There is reduced number of circulating T killer cells which are involved in getting rid of virus infected cells but there is also increased b cells in rachitic patients. Increased susceptibility to respiratory infections in rachitic children may be due to impaired handling of virus and impaired phagocytosis. There is reduced lung capacity with atelectasis and diffuse fibrosis causing cor pulmonale in children with severe rickets.⁶

Deficiency in vitamin D leads to decrease in calcium levels and these both contribute to reduction in bone mass and quality. This in turn leads to delay in fracture callus mineralization.⁵

Studies also suggest fall in serum vitamin D levels can cause activation of latent tuberculosis.⁷

Serum vitamin D levels have been found to be lower in pulmonary tuberculosis patients when compared to healthy individuals. Also, prolonged anti tubercular treatment is found to decrease serum vitamin D levels.¹⁰

Hence rachitic children in endemic countries should be screened for pulmonary tuberculosis and their serum vitamin-D should also be checked and supplemented due to increased chances of fractures with fragile bones. Adequate vitamin-D supplementation increases respiratory system immunity to fight against pulmonary tuberculosis with increased bone healing and mineralization.

The global consensus recommendations treatment of nutritional rickets states following infants less than 3 months age: 2000 IU/day for 12 weeks, with a maintenance dose of 400 IU, infants aged between 3-12 months: 2000 IU/day for 12 weeks or a single dose of 50 000 IU, with a maintenance dose of 400 IU, children aged between 1-12 years: 3000-6000 IU/day for 12 weeks or a single dose of 150 000 IU, with a maintenance dose of 600 IU, children older than 12 years: 6000 IU/day for 12 weeks or a single dose of 300 000 IU, with a maintenance dose of 600 IU.³

CONCLUSION

Here we present a rare case of multi drug resistant pulmonary tuberculosis with proximal fibular fracture with incidental decreased serum vitamin-D levels. In vitamin D deficiency rickets, there is decreased bone mineralization leading to weak bones and delayed fracture healing in children. Low serum vitamin D levels also caused decreased immunity with increased susceptibility to respiratory infections like pulmonary tuberculosis. Appropriate treatment with injectable or oral vitamin D3 with adequate exposure of sunlight and proper nutrition is the best modality of treatment.

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