*Case study*

**Vitamin D Deficiency and Sickle Bone Disease: A Case Report**

**Abstract:** Painful crises due to involvement of bone and joint are frequently reported finding in sickle cell disease. However, a generalised form of bone involvement termed as Sickle bone disease (SBD), is not well studied, especially in relation to the mechanism. Here is a case report of a patient who had Vitamin D deficiency as a contributing cause to sickle bone disease.

A young female with Sickle cell disease (SCD) presented with joint as well as bone pains, proximal muscle weakness and antalgic gait. Investigations were suggestive of severe vitamin D deficiency, hypophosphatemia and secondary hyperparathyroidism. She had clinical, biochemical and radiological features of oestomalcia and evidence of pathological bone fractures. Patient's response to vitamin D and calcium supplementation was observed.

**PURPOSE:** Associated vitamin D deficiency is a treatable condition. Supplementation with calcium and vitamin D can be part of prevention strategy in Sickle cell disease patients to avoid sickle bone disease.

**Case presentation:**

A 30-year-old female, presented with complaints of multiple joint pain and bony pain for one and a half years, starting from the right hip joint, later involving knee, ankle, elbow etc. However, small joints were not involved, and no complaint of morning stiffness was there.

**Key-words:**

- Sickle bone disease (SBD)
- Sickle cell disease (SCD)
- Vitamin D deficiency
- Osteomalacia
- Mineral bone disease

**Introduction:**

Sickle cell disease, a monogenetic disorder, is common worldwide. Generalized bone involvement is called Sickle bone disease, which is one of its chronic complications. Many theories are put forward for bone resorption due to vaso-occulsive crises leading to bone ischemia, accelerated pressure over haematopoiesis leading to proliferation of osteoclastic activity and associated Vitamin D deficiency (osteomalacia).[1] Vitamin D deficiency due to insufficient intake, inadequate sunlight exposure and malabsorption are the most widespread cause of osteomalacia[2]. It can also occur due to chronic liver, kidney and chronic haemolytic anemias.[3-5.] Here is a case report of a young female having sickle bone disease and osteomalacia.

**Case History:**

A 30-year-old female, presented with complaints of multiple joint pain and bony pain for one and a half years, starting from the right hip joint, later involving knee, ankle, elbow etc. However, small joints were not involved, and no complaint of morning stiffness was there. The patient was only able to walk with support. On examination, the patient had tenderness in the right posterior superior iliac spine and right lateral aspect of thigh. Multiple bony tenderness points were present with limping gait and proximal muscle weakness. The

Neurological examination was normal. Usg neck suggestive of no e/o parathyroid gland adenoma.

Osteomyelitis usually presents with pain, swelling and tenderness. Fever and raised inflammatory markers were normal in the case of our patient. No sign of bone in a bone formation and avascular necrosis was seen on x rays. Although the main cause of vitamin D deficiency is malabsorption syndrome. However, the patient's medical history and laboratory examination results were not suggestive of the same. Hypo-phosphatemia—a condition in which osteomalacia is caused by impaired phosphorus absorption and re-absorption—renal tubular acidosis. The urinary findings and Arterial blood gas analysis were not in support of renal tubular acidosis. Moreover, the medical history and laboratory examination results did not reveal any findings suggestive of Sjogren syndrome, multiple myeloma or nephrotic syndrome.

The patient was given injectable calcium for 3 days followed by Oral administration of 1500 milligrams of calcium and 60,000 IU of oral vitamin D per week were started for eight weeks. Nailing was done for subtrochanteric femur fracture. Patient was advised to have sun exposure and nutrition- rich diet. In the 3 month follow up, the complaints of patient of pain, muscle weakness and gait disturbance had been alleviated. Moreover, biochemical investigations were done on which adjusted calcium were- 8.8, vit d levels – 30 ng/ml. alkaline phosphatase, phosphorous and parathyroid hormone had improved.

Table 1- HPLC Report

| **HPLC report Concentration for sickle cell disease** | **F** | **A1c** | **A2** | **S- Window** |
|---|---|---|---|---|
| **Area %** | 16.0 | 4.1 | 1.5 | 66.7 |



Table2 - Markers for Bone Mineral Disease

| MARKERS FOR BONE MINERAL DISEASE | |
|---|---|
| Sr. Calcium levels | 8 mg% (9-11) |
| Sr. Phosphorus levels | 2.6 mg% (3.5-5) |
| Sr. Alkaline Phosphatase levels | 458 IU/L (48-147) |
| Vitamin D3 levels | 10.4 ng/ml (30-50) |
| Parathyroid Hormone levels | 718.7pg/ml (15-68) |
| Sr. Uric acid levels | 7.2 mg/dl (3-5.3) |
| Sr. Albumin | 2.6 g/dl (3.5-5.5) |
| Corrected calcium | 9.12 (8.5-10.2) |

TABLE:3- Biochemical Markers to Rule out Other Causes of Bone Mineral Disease.

| To rule out renal rickets | | To rule out inflammatory arthritis | |
|---|---|---|---|
| **Serum creatinine** | **0.6 mg/dl** | **ESR** | **15mm/hr** |
| **24-hour urinary protein** | **20 mg/ 24 hrs (25-140)** | **CRP** | **1.25 mg/L** |
| **24-hour urinary calcium** | **5.4 mg/ 24 hrs (25-300)** | **Rheumatoid factor** | **<10** |
| **USG KUB** | **B/L normal size kidney** | **LDH** | **255 u/l** |
| **Urine routine micro** | **Albumin- nil**<br>**Sugar-nil**<br>**RBC- nil** | **Sr. ferritin levels** | **109 mg/L** |
| **Electrolyte** | **141/4.3/103 mmol/L** | **HLAB27** | **negative** |
| **CBC** | **9.5/9800/3.4** | | |

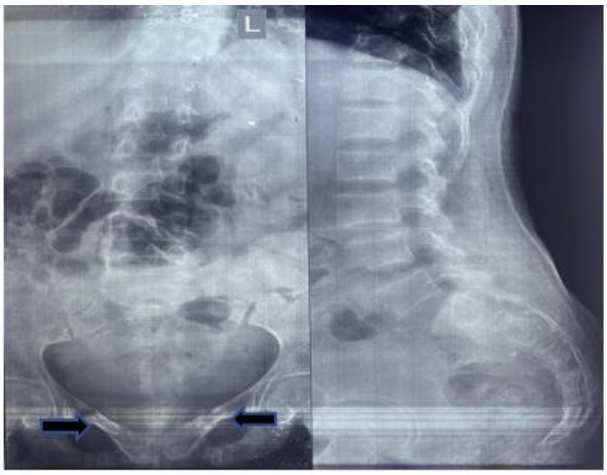

Figure 1A- A X-ray LS spine AP and LAT

[ Black arrow- Loser's zone]

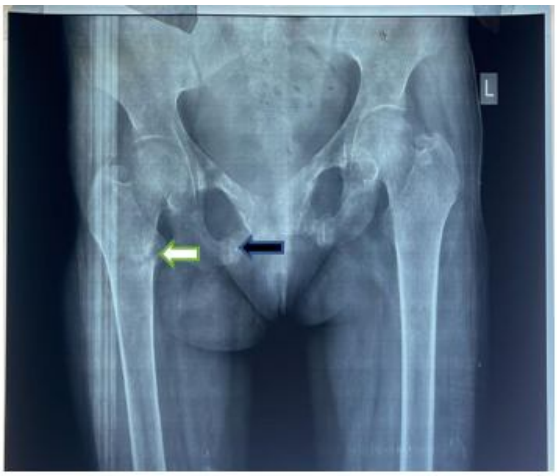

Figure1B- X-ray pelvis with both hip joint A

[white arrow- sub- trochanteric fracture]

**Discussion:**

Sickle cell disease (SCD) is an inherited disorder of haemoglobin (Hb) in which a mutation in the β- haemoglobin gene occurs. It leads to complications like acute chest syndrome, proliferative retinopathy, pulmonary hypertension, renal insufficiency, cerebral vascular accident and musculoskeletal complications. The bone involvement in SCD represents as acute manifestations, such as painful vaso-occlusive crisis or osteomyelitis, to more chronic complications, such as osteonecrosis, osteoporosis and osteopenia, impaired growth and chronic infections.[6] Poor intestinal absorption of calcium and vitamin D occur in SCD that stimulate PTH secretion that play role in renal conservation of calcium.[7]

Impaired blood flow due to microvascular occlusion by sickle erythrocyte leads to ischemia and was found to increase the apoptosis of osteoblasts and osteocytes leading to osteoporosis.[8] Blood loss accelerates haematopoiesis by stimulating osteogenic progenitor cells. Osteoporosis occurs due to proliferation of hematopoietic progenitor cells (osteoclasts) leading to bone resorption.[9]

Bone pain is generally evident in the lower spine, pelvis and lower extremities associated with fractures, and palpatory finding reveals severe tenderness. Pain can be accelerated by

activity and weight bearing. Fractures can typically arise without mild trauma or no trauma, including ribs, vertebrae and long bones. Proximal muscle weakness is characteristic and muscle loss may be accompanied by hypotonia.

Clinical evaluations such as gastrointestinal system diseases, sun exposure, dietary habits, and duration of initial symptoms (insidious or acute) may help to determine the aetiology of osteomalacia. Vitamin D deficiency causes secondary hyperparathyroidism by reducing the absorption of Ca and phosphate in the intestine.

The patient was diagnosed with mineral and bone disease- secondary to hyperparathyroidism with sickle cell disease. In SCD, there is accelerated pressure over haematopoiesis which leads to proliferation of osteoclastic activity. As a result, resorption of bone takes place. Although the patient presented with multiple joint pain which was unilateral and anaemia, which favours the diagnosis of vaso-occlusive crisis of sickle cell disease. Henceforth, one should always keep bone mineral disease as an underlying possibility in patients presenting with sickle cell crisis/disease differentiating from AVN of bones

Diagnosis of this patient was made on the basis of history and investigations (pathological, biochemical and radiological). Osteomalacia can be asymptomatic or radiologically may appear as osteopenia. It may also cause typical symptoms, such as extensive joint and bone pain, muscle weakness, and walking difficulty. Our patient had complained of multiple joint pain and limping gait with pathological fractures (No alleged history of trauma).

Vitamin D deficiency is a treatable condition. Associated Vitamin D deficiency may contribute to sickle bone disease which leads to fracture, pseudofractures and morbidity which happened in this young female patient. Vitamin D deficiency can lead to short stature in children, which can be prevented or corrected by supplementation.[10]

**Ethics -**Informed consent was taken from patient.

**Conclusion**

Vitamin D and calcium supplementation at a younger age may prevent or delay bone mineral disease. Further studies should be conducted regarding sufficient dose supplementation to prevent sickle bone disease in patients with sickle cell disease.

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