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Osteoporosis as a presenting symptom in a patient with small bowel Crohn's disease

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Abstract
This case report describes an uncommon presentation of Crohn's disease with osteoporosis in a 38 year old male from Mumbai. He had low back pain and easy fatigue for 3 months duration. Initial evaluation showed normal spine radiograph with no fractures and normal calcium & vitamin D_3 levels. Magnetic Resonance Imaging (MRI) of the spine showed features of osteoporosis (OP) with no evidence of disc prolapse or arthritis. Bone mineral density (BMD) evaluation confirmed the diagnosis of OP. He had mild iron deficiency anemia with occult blood loss in stool examination. Upper & lower gastrointestinal endoscopy did not reveal cause of gastrointestinal blood loss. A computed tomography (CT) scan of the abdomen showed jejunal wall thickening with absence of nodes or free fluid. Double balloon endoscopy (DBE) showed circumferential ulcers in the jejunum. Jejunal biopsy was suggestive of Crohn's disease (CD). He was treated with steroids, Azathioprine (AZA) and 5 aminocylic acid (ASA) drugs. His back pain reduced by 75% in one week & BMD showed improvement at 9 months. Osteoporosis is often observed in patients with CD due to mal-absorption of calcium, vitamin D_3 deficiency and steroid therapy. Crohn's disease presenting as osteoporosis & its marked improvement with steroid therapy are unusual features in our case.

Keywords: Presentation, azathioprine, improvement

Introduction
Osteoporosis occurs in 13-26% of patients with inflammatory bowel diseases (IBD) [1, 2]. The likely causes of osteoporosis in IBD include calcium & vitamin D_3 mal-absorption, steroid treatment, chronic inflammation and poor nutrition. Majority of patients with OP present with bone pains & a few with pathological fractures in advanced stages. Bone mineral densitometry value of less than -2.5 g/cm^2 is considered as a gold standard for the diagnosis of OP.
The spectrum of IBD includes ulcerative colitis (UC), crohn's disease (CD) and indeterminate colitis. The incidence of IBD and particularly CD is rising in India [3]. About 30% of patients with CD remain undiagnosed for long periods as they are often asymptomatic, have mild nonspecific abdominal symptoms & symptoms often confused with abdominal tuberculosis. Compared to the west extra intestinal manifestations (EIM) of IBD are less often observed in Indian patients with IBD. The commonest EIM of IBD is arthritis [4]. High blood levels of inflammatory cytokines like Interleukin 6 (IL-6) and tumor necrosis factor (TNF) are responsible for the majority of extra intestinal manifestations of IBD. Recent studies have shown that patients with high levels of inflammatory cytokines often suffer from bone loss [5].
Case report.
A 38 year old male, engineer by profession residing in western suburb of Mumbai presented with three months history of lower back pain. He had received pain killers and physiotherapy with no improvement in back pain. Radiograph of thoracolumbar spine showed no evidence of fractures or reduced intervertebral spaces. He had no history of long term steroid use & was a nonsmoker. He lived an active life. His body weight was 71 kgs with body mass index of 23. He had only mild tenderness over lower thoracic & lumber spine. Other systemic examination was normal. His investigations showed hemoglobin level of 11.2 g/l (13-14.5), positive stool occult blood, erythrocyte sedimentation rate (ESR) of 18 mm/h (1-15), C reactive protein level 24 mg/l (0-5), serum iron level of 110mcg/dl, transferrin saturation of 14% (15-50%), serum albumin level of 3.3 g/dl (4-4.5), serum 25-hydroxy vitamin D_3 of 28 ng/ml (30-40),

calcium of 9 mg/dl (8.5-10.2). His blood sugar levels, thyroid & kidney function test were normal. His human leukocyte antigen-B27 & IgA tissue trans glutaminase antibody results were negative.

Thoracolumbar spine radiograph showed no evidence of fractures or reduced intervertebral spaces. An MRI & limited CT of spine showed fatty marrow areas in T1W images representing bone loss and reduced bone density (Fig 1). BMD study showed marked reduction in T score: lumbar spine L1-L4 (-3.1), dual femur neck (-1.7), forearm (-3). An upper and lower gastrointestinal endoscopy failed to reveal a cause for low Hb and stool blood loss. A CT scan of abdomen with oral & intravenous contrast showed marked regular symmetrical segmental thickening of jejunum with mild mucosal enhancement, no nodes or free fluid (Fig 2). A Double Balloon Enteroscopic examination showed segmental ulcerations with no stigmata of recent bleed along the short axis of jejunum with mild luminal compromise (Fig 3). Multiple biopsies were performed from jejunal ulcers. Histology revealed marked distortion & crypt loss, plasma-lymphocytic infiltration, ulceration and non caseating granulomas suggestive of CD (Fig 4). Baseline stool calprotectin level was 230micrograms/mg (< 50). Interleukin 6 (IL) levels were 28pg/ml (1.4-1.6).

He received Prednisone 40mgs/day, Azathioprine (AZA) 50mgs/day and 5 ASA (Pentasa) 500 mgs three times a day for the first week. His pain reduced by 75% in one week. As he tolerated AZA, it's dose was increased to 125mgs/day and steroids were gradually tapered over next three months. At three months his stool showed no evidence of occult blood loss and calprotectin level reduced to 60micrograms/mg. He was advised to do regular exercises, take regular daily allowances of vitamin D_3 and calcium. At three months of therapy his IL-6 levels reduced to 6pg/ml. After nine months BMD study showed marked improvement with T score of -1.8 in spine. He was advised to repeat a DBE after one year but refused to undergo the test as he was asymptomatic. He is on regular follow up and is advised to take AZA & 5 ASA drugs.

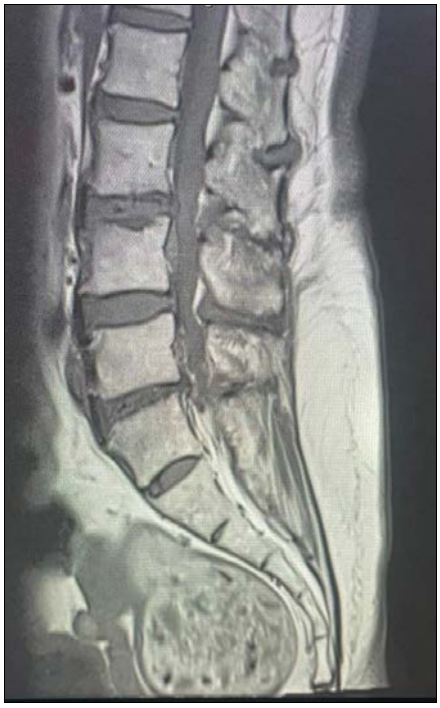

Fig 1: MRI of spine showing fatty marrow areas in T1W images representing bone loss and reduced bone density

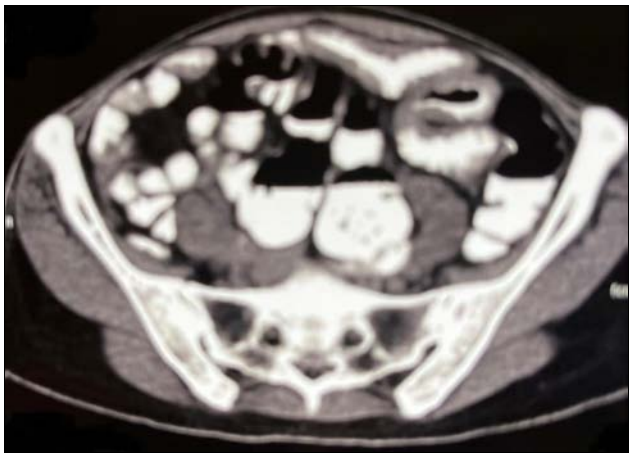

Fig 2: CT scan of abdomen with oral & intravenous contrast showing marked regular symmetrical segmental thickening of jejunum with mild mucosal enhancement, no nodes or free fluid

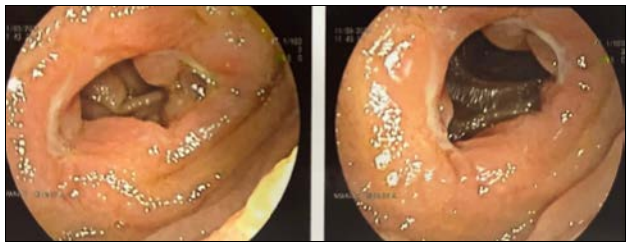

Fig 3: A Double Balloon Enteroscopic examination showing segmental ulcerations with no stigmata of recent bleed along the short axis of jejunum with mild luminal compromise

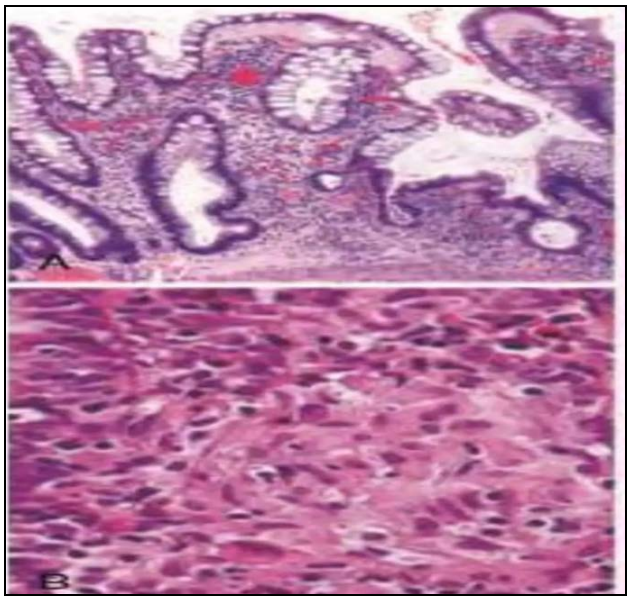

Fig 4: Histology showing marked distortion & crypt loss, plasma-lymphocytic infiltration, ulceration and non-caseating granulomas suggestive of CD

Discussion

Osteopenia and osteoporosis are often observed in the course of IBD due to poor nutrition, vitamin D_3 & calcium mal-absorption, steroid therapy, chronic inflammation, continued smoking or relative lack of exercises. Our patient presented with clinical features of osteoporosis before CD was detected. In the absence of smoking, steroid therapy, near normal calcium & vitamin D_3 the etiology of osteoporosis in our patient is likely to be inflammatory as his plasma IL-6 & stool calprotectin levels were elevated & he responded to steroid therapy.

Bone loss is an important extra intestinal manifestation of IBD. Its early detection can reduce morbidity related to bone pain, pathological fractures & hospitalization. Chronic inflammation is now considered an important driver for the development of bone loss in IBD patients. IL-6 & TNF alpha play an important role in mediating innate and adaptive immune responses. Many inflammatory cells like neutrophils, monocytes produce and respond to IL-6 resulting in amplification of inflammation. In our patient IL-6 levels were markedly elevated pre therapy & reduced with steroids suggesting down regulation of inflammatory response. This resulted in clinical improvement of OP. TNF alpha secreting cells are increased in the mucosa of inflamed intestine. Plasma TNF alpha levels often correlate with disease activity in IBD, more commonly in crohn's disease than ulcerative colitis. Anti TNF alpha therapy is recommended in IBD patients if they do not respond to steroids, have fistulizing CD or are intolerant to steroids and immunotherapy. We could not perform TNF alpha levels in our patient.

We conclude that chronic inflammation in patients with CD may lead to osteoporosis. In the absence of common causes of OP, clinicians should look for CD. Early recognition & suppression of inflammatory cytokines can reverse bone loss in CD. All patients with CD need to be supplemented with calcium, vitamin D_3 & need regular evaluation of bone health.

Conflict of Interest
Not available

Financial Support
Not available

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