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Case Series

Case series of orthopaedic complications associated with endocrine disorders presented at tertiary care center and review of literature

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ABSTRACT

Endocrine glands affecting skeletal system are parathyroid glands, adrenal glands, pituitary gland, thyroid and gonads. If any abnormality occurs in these glands, they cause structural and functional impairment of the skeletal system. Early diagnosis and treatment of these endocrine problems and ruling out musculoskeletal involvement helps to maintain skeletal integrity and prevent osteoporotic fractures and chronic bone pathologies. Here we present a case series of 4 patients who came to us with chronic bone pathologies or post-traumatic fractures associated with endocrine abnormalities; such as parathyroid adenoma (hyperparathyroidism), Cushing's syndrome and thyroid adenocarcinoma. One patient with osteoporotic and pathological fracture was managed operatively and sent for management of endocrine pathology and other three patients after evaluating cause for the bone pathology were referred for primary management of endocrine disease. Osteoclasts and osteoblasts of the bone are affected by the endocrine hormones, such as parathyroid hormone, thyroid, glucocorticoids and gonadotropins. Any abnormality in these hormones leads to alteration of bone mineral density. Hyperthyroidism, glucocorticoid excess, hyperparathyroidism, hypogonadism, and acromegaly decrease bone mineral density and aggravate the osteoporotic tendencies and leading to orthopaedic complications. As an orthopaedic practitioner we should be well aware of endocrine disorders affecting bones. Early diagnosis and treatment of these endocrine problems in older patients helps to maintain their skeletal integrity, prevent osteoporotic fracture and orthopaedic complications.

Keywords: Endocrine glands, Skeletal system, Osteoporosis

INTRODUCTION

Endocrine glands affecting skeletal system are parathyroid glands, adrenal glands, pituitary gland, thyroid and gonads.

Hyperthyroidism, glucocorticoid (GC) excess, hyperparathyroidism, hypogonadism, and acromegaly decrease bone mineral density and aggravate the osteoporotic tendencies of elderly individuals.

Important cause of morbidity and disability in patients with Cushing's syndrome is structural and functional impairment of the skeletal system.[1]

GC excess inhibits bone formation and calcium absorption from the gut, increases bone resorption, and alters the secretion of gonadotropin and growth hormones, cytokines and growth factors influencing bone.

Avascular necrosis, mainly of the femoral neck, and growth arrest in children are the most common skeletal disorders unrelated to osteoporosis encountered in patients with hypercortisolism.

Parathyroid adenomas are the most important cause of primary hyperparathyroidism (80-85%), causing alteration in calcium and phosphorus metabolism.[2]

Primary hyperparathyroidism causes excessive bone resorption with a decrease in bone mineral density.[3]

Thyroid hormones are essential for normal skeletal development and normal bone metabolism in adults but can have detrimental effects on bone structures in states of thyroid dysfunction.

Untreated severe hyperthyroidism influences the degree of bone mass and increases the probability of high bone turnover osteoporosis. Bone metastasis occurs in 4% of thyroid carcinomas.[9] After effective treatment of endocrinopathy, the bone attempts to return to the normal mineral density.[5] Early diagnosis and treatment of these endocrine problems in older patients helps to maintain their skeletal integrity and prevent osteoporotic fractures and improvement in bone pathologies.

CASE SERIES

Case 1

A 33-year-old male patient, resident of local vicinity presented to our tertiary care centre with complaints pain over bilateral hip (left>right) since 4 years aggravated since 8 months, pain was insidious in onset and gradually progressive in nature, with no history of (h/o) trauma. H/o high dose steroid (20 mg/day prednisolone) intake for 2 years. No h/o any comorbidities.

On general examination of the patient, we found round face with facial puffiness, reddish and florid face, pendulous abdomen with purple lines, weakness of muscle and hypertension. On local examination of bilateral hip joint- swelling and tenderness over bilateral hip joint and global restriction of the movements present. Routine investigations were normal with osteoporotic work up done with thyroid function tests (TFT), testosterone, parathyroid hormone (PTH), and calcium profile within a normal limit but raised cortisol level 35 mcg/dl was found. Plain radio-graphs were done, and were suggestive of B/L hip osteoarthritis (Figure 1). Magnetic resonance imaging (MRI) bilateral hip joints suggestive of avascular necrosis of the bilateral hip with osteoarthritic changes (Ficat and Arlet stage IV) (Figure 2).

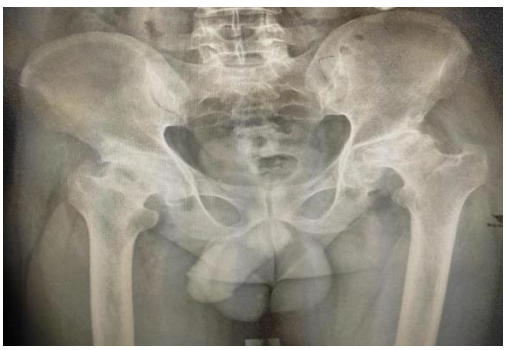

Figure 1: X-ray showing bilateral hip osteoarthritis in a patient of Cushing's syndrome.

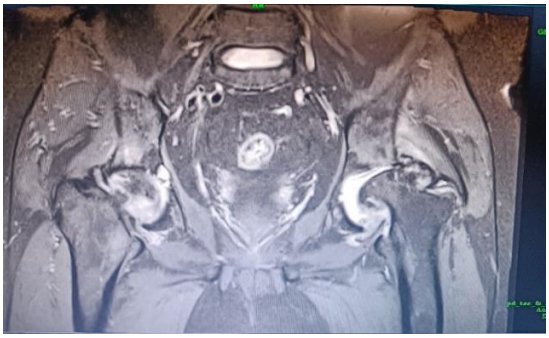

Figure 2: MRI coronal cut reading suggestive of bilateral hip avascular necrosis stage IV.

Dual-energy X-ray absorptiometry (DEXA) scan showed decrease in bone mineral density (BMD) s/o osteoporosis. Patient was diagnosed with Cushing's syndrome due to exogenous intake of corticosteroids for years with bilateral hip AVN and was referred to endocrinology for primary management of osteoporosis and syndrome.

Case 2

A 51-year-old female patient, resident of local vicinity presented to our tertiary care centre with complaints of difficulty, pain while walking and multiple joints pain of upper and lower limb since 8 months, pain was insidious in onset and gradually progressive in nature. There is no history of trauma. She was operated for parathyroid adenoma 1 year back. No h/o asthma, diabetes, hypertension, steroid intake, alcohol intake. On examination, no swelling was present. Severe tenderness, restricted and painful range of motion at hip, knee and ankle joints present. Also, on upper limb; moderate tenderness, restricted and painful range of motion at shoulder, elbow and wrist was present. Soft tissue tenderness over B/L upper with greater at lower limbs were present. Neurological examination was normal. Routine blood investigations were normal but specific blood test showed hypercalcemia, hypophosphatemia and raised hyper-parathyroid hormones. Plain radio-graphs were done, and were suggestive of right neck of femur osteoporotic fracture (Figure 3).

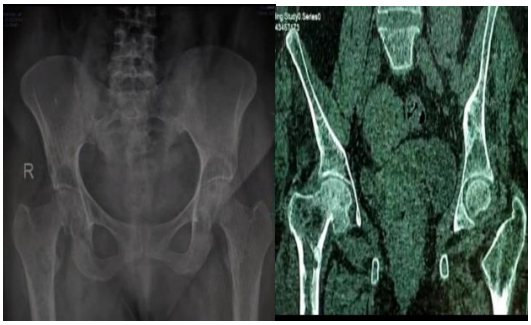

Figure 3: X-ray PBH and CT coronal cut showing incomplete right neck of femur old fracture with X-ray s/o bilateral hip osteoarthritic changes in a case of parathyroid adenoma.

MRI s/o incomplete fracture of right neck of femur and B/L hip avascular necrosis stage II (Figure 4).

DEXA scan showed decrease in BMD s/o osteoporosis.

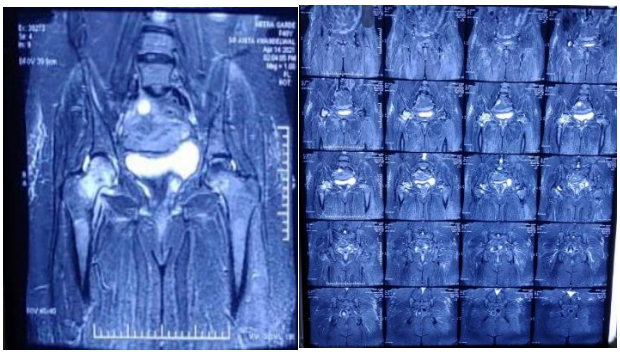

Figure 4: MRI Image showing bilateral hip avascular necrosis.

Patient was diagnosed with hyperparathyroidism which recurred, osteoporosis with bilateral hip AVN secondary to parathyroid adenoma and was referred for further primary management of parathyroid adenoma.

Case 3

45-year-old female patient, resident of local vicinity presented to our tertiary care centre with complaints of pain and swelling over left thigh since 1 month following alleged history of slip and fall (trivial trauma). There didn't have any history of head/chest injury nor ENT bleed. Medical history revealed patient is known case of follicular carcinoma of thyroid under treatment and is on thyrotropin (TSH)-suppressive therapy. No history of any comorbidities. Local examination of left thigh gave following findings- left lower limb shortened with tenderness around the middle 3rd of the thigh and painful range of motion around the knee joint; patient was primarily stabilised with thomas splint and skin traction; on admission all routine investigations done and thyroid profile shows mild hyperthyroidism. Plain radio-graphs were done, and were suggestive of left middle 3rd shaft of femur fracture with osteolytic lesion over distal end of femur.

Computed tomography (CT) guided biopsy of the lesion was done and sent for histopathology suggestive of metastasis of follicular carcinoma of thyroid. DEXA scan suggestive of osteoporosis. Patient was operated for shaft of femur fracture with distal femur nail. Then patient was referred for further management of the thyroid carcinoma and metastasis.

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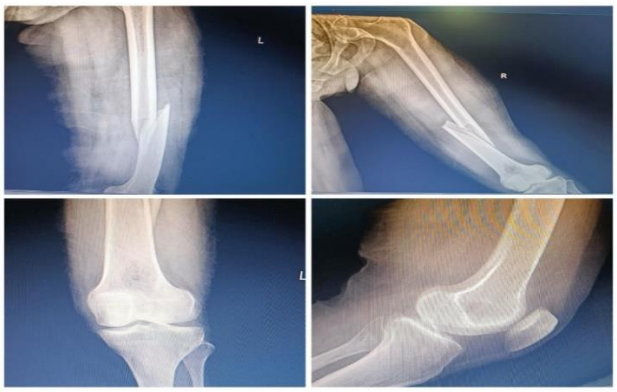

Figure 5: X-ray suggestive of left shaft of femur fracture with oval osteolytic lesion over distal femur in a case of follicular carcinoma of thyroid.

Local examination of left thigh gave following findings – left lower limb shortened with tenderness around the middle 3rd of the thigh and painful range of motion around the knee joint; patient was primarily stabilised with thomas splint and skin traction; on admission all routine investigations done and thyroid profile shows mild hyperthyroidism. Plain radio-graphs were done, and were suggestive of left middle 3rd shaft of femur fracture with osteolytic lesion over distal end of femur. Computed tomography (CT) guided biopsy of the lesion was done and sent for histopathology suggestive of metastasis of follicular carcinoma of thyroid. DEXA scan suggestive of osteoporosis. Patient was operated for shaft of femur fracture with distal femur nail. Then patient was referred for further management of the thyroid carcinoma and metastasis.

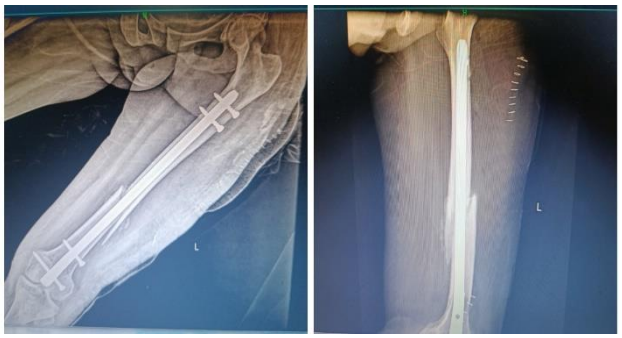

Figure 6: Post-operative X-rays.

Case 4

45-year-old male patient, resident of local vicinity presented to our tertiary care centre with complaints of multiple joint pain, bilateral pedal edema since 10 years, which was insidious in onset and gradually progressive.

No history of any trauma. H/o steroid intake (dexamethasone 40 mg/day) for 10 years with no other comorbidities.

On examination, patient had multiple small joints swelling and tenderness, bilateral lower limb pitting edema, multiple lesions over right foot, grade 2 bed sores (suggestive of immuno-compromised state), facial puffiness and abdominal distention. On osteoporotic work up, cortisol levels 42 mcg/dl and rest TFT, testosterone, PTH, calcium profile with in normal limit. Plain radiographs done suggestive of osteoporosis; DEXA scan suggestive of severe osteoporosis (Figure 7).

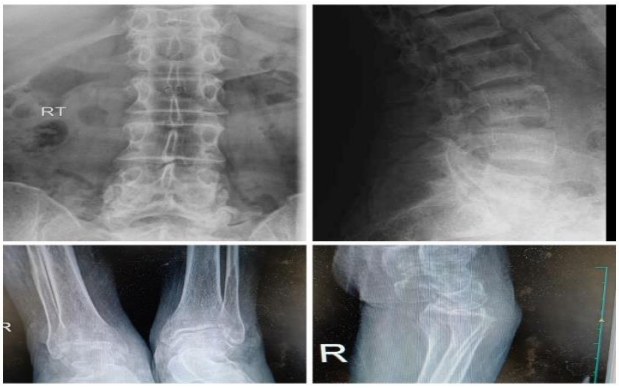

Figure 7: X-rays suggestive of osteoporosis and steroid induced arthropathy of ankle joint.

Patient was diagnosed with steroid induced arthropathy with osteoporosis, and referred to endocrinologist for weaning off steroids and management of osteoporosis.

DISCUSSION

Endocrine glands affecting skeletal system are parathyroid glands, adrenal glands, pituitary gland, thyroid and gonads, if any abnormality in these glands affect BMD.

Hyperthyroidism, glucocorticoid excess, hyperparathyroidism, hypogonadism, and acromegaly decrease BMD and aggravate the osteoporotic tendencies of elderly individuals.

Parathyroid adenomas are the most important cause of primary hyperparathyroidism (80-85%), causing alteration in calcium and phosphorus metabolism.[2] Primary hyperparathyroidism causes excessive bone resorption with a decrease in BMD.[3]

Hyperparathyroidism causes hypercalcemia and hypophosphatemia.

Eighty percent of patients are asymptomatic or complain only of atypical muscle pain. Multiple clinical symptoms may occur, including cardiovascular and neuropsychiatric disturbances, nephrolithiasis, nephrocalcinosis, constipation, peptic ulcer, and pancreatitis. Rheumatic symptoms observed in PHPT include chondrocalcinosis, diffuse bone pain, pseudo-gout, and gout.

Bone biopsy in hyperparathyroidism- increased resorption parameters with no loss of bone trabecular volume.

GC excess inhibits bone formation and calcium absorption from the gut, increases bone resorption, and alters the secretion of gonadotropin and growth hormones, cytokines and growth factors influencing bone.

BMD measurement at the lumbar spine should be performed as a screening test in all patients with Cushing's syndrome due to the preferential loss of trabecular bone induced by GCs.

Avascular necrosis, mainly of the femoral neck, and growth arrest in children are the most common skeletal disorders unrelated to osteoporosis encountered in patients with endogenous hypercortisolism. Osteonecrosis of the femoral head is most commonly encountered following exogenous GCs administration although cases following endogenous hypercortisolism are increasingly being recognized; occasionally both femurs and several other joints may be involved.

AVN is mediated by interosseous hypertension followed by intramedullary venous stasis, edema, necrosis, fibrosis, and infarction that finally leads to collapse of the femoral head.[4]

Thyroid hormones are essential for normal skeletal development and normal bone metabolism in adults but can have detrimental effects on bone structures in states of thyroid dysfunction. Untreated severe hyperthyroidism influences the degree of bone mass and increases the probability of high bone turnover osteoporosis.

Subclinical hyperthyroidism, defined as low TSH and free hormones within the reference range, is a subtler disease, often asymptomatic, and the diagnosis is incidentally made during screening exams. However more recent data suggest that this clinical condition may affect bone metabolism resulting in decreased BMD and increased risk of fracture, particularly in postmenopausal women.[6]

Cortical bone is affected more than trabecular bone, and postmenopausal women are at a greater risk than premenopausal women. The initiation of levothyroxine treatment in hypothyroid women results in a reduction in cortical bone width to levels seen in euthyroid controls after 6-12 months.[7]

Osteoporosis and fractures are important comorbidities in patients with differentiated thyroid cancer. The main determinant of skeletal fragility in differential thyroid cancer (DTC) is the TSH-suppressive therapy, which is commonly recommended to prevent disease's recurrence, especially in patients with structural incomplete response after thyroid surgery and radio-iodine therapy. TSH-

suppressive therapy can stimulate bone resorption with consequent bone loss, deterioration of bone microstructure and high risk of fragility fractures. The skeletal effects of TSH-suppressive therapy may be amplified when thyroid cancer cells localize to the skeleton inducing alterations in bone remodelling, impairment of bone structure and further increase in risk of fractures.[8]

Bone metastasis occurs in 4% of thyroid carcinomas.[9] Bone metastases are more frequent in follicular and medullary thyroid cancers, requiring closer bone surveillance in patients with this histology.

Young hypogonadal women also often develop osteoporosis, and estrogen deficiency has been associated with both trabecular and cortical bone loss.[10] Osteoporosis occurs less commonly in men but can result in significant morbidity when present.

Men with idiopathic hypogonadotropic hypogonadism, who are hypogonadal due to an isolated deficiency of hypothalamic gonadotropin-releasing hormone (GnRH) but have otherwise normal pituitary function, provide a valuable clinical model in which to assess the impact of profound, isolated, gonadal steroid deficiency on bone density in men.[10]

Testosterone deficiency is a major risk factor for spinal compression fractures in men, and men with hypogonadism associated with either hyperprolactinemia or anorexia nervosa.[11]

After effective treatment of endocrinopathy, the bone attempts to return to the normal mineral density. Early diagnosis and treatment of these endocrine problems in older patients helps to maintain their skeletal integrity and prevent osteoporotic fractures and any other complications.

CONCLUSION

Osteoclasts and osteoblasts of the bone affected by the endocrine hormones, such as PTH, thyroid, GCs and gonadotropins, any abnormality in these hormones leads to alteration of BMD. Hyperthyroidism, glucocorticoid excess, hyperparathyroidism, hypogonadism, and acromegaly decrease bone mineral density and aggravate the osteoporotic tendencies and leading to orthopaedic complications. As orthopaedic practitioner we should be well aware of endocrine disorders affecting bones. Early diagnosis and treatment of these endocrine problems in older patients helps to maintain their skeletal integrity, prevent osteoporotic fracture and orthopaedic complications.

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