Original Article

Treatment of Fractures in 15 cases of Osteitis Fibrosa Cystica - Hyperparathyroidism: A Case Series

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Objective: To study retrospectively the results of treatment of cases of pathological fractures presenting with osteitis fibrosa cystica due to hyperparathyroidism.

Material & Methods: Records of cases of hyperparathyroidism treated for pathological fractures in the past seven years were reviewed to assess success of treatment by various modalities. All patients had been investigated for vitamin D deficiency, parathyroid levels, serum calcium & phosphate levels along with renal function tests. All X-rays were restudied for evidence of osteitis fibrosa cystica.

Results: Thirteen cases healed uneventfully, one died of unrelated reasons and one failure led to non union. All patients had received oral calcium supplements and injectable vitamin D for three months at least. There were no complications of this treatment regimen.

Conclusion: Pathological fractures due to bone weakness caused by hyperparathyroidism can be treated by various treatment modalities supplemented by oral calcium and injectable vitamin D.

Keywords: Osteitis fibrosa cystica, hyperparathyroidism, Pathological fractures

Introduction

The incidence of primary hyperparathyroidism is 1 per 1,000 people (0.1%) while there are 25-30 new cases/100,000 people per year in the United States.[1,2] Its prevalence has been estimated to be 3 in 1000 in the general population and as high as 21 in 1000 in postmenopausal women.[3] ICD classifies it as E21.1.[7] The signs and symptoms of primary hyperparathyroidism are those of hypercalcemia. They are classically summarized by the mnemonic "stones, bones, abdominal groans and psychiatric moans." "Stones" refers to kidney stones, nephrocalcinosis, and diabetes insipidus (polyuria and polydipsia). These can ultimately lead to renal failure. "Bones" refers to bone-related complications like arthritis, osteoporosis, osteomalacia, osteopenia and osteitis fibrosa cystica, which results in pain and sometimes pathological fractures. The cortices may become thin and there may be cystic cavities in the bones filled with hemosiderin laden giant cells commonly known as Brown Tumors.[15] The incidence of skeletal brown tumors in CRF ranges from 1.5 to 13%.[15] Changes interpreted as those of osteitis fibrosa cystica have been described by Denninger[1] in the skeleton of a prehistoric American Indian excavated in Illinois.[14] The descriptive title actually used in 1891 by von Recklinghausen was 'von Recklinghausen's disease of bone' or osteitis fibrosa cystica.[14] With the development of newer diagnostic aids and better medical services very few patients go on to have osteitis fibrosa cystica, commonest presentation being that of a patient with end stage renal failure (ESRF) undergoing renal dialysis and some following renal transplants. In 1935 Albright, Aub and Bauer[46] reported the findings in 17 cases studied at the Massachusetts General Hospital. For the first time they emphasized that the renal manifestations of hyperparathyroidism may be the first and only symptoms.[14] Now it is seen as a primary presentation in under-served populations. "Abdominal groans" refers to gastrointestinal symptoms of constipation, indigestion, nausea and vomiting. Hypercalcemia which is the commonest reason for the patient to seek medical advice can lead to peptic ulcers and acute pancreatitis. The peptic ulcers can be an effect of increased gastric acid secretion by hypercalcemia but may also be part of a multiple endocrine neoplasia type 1 syndrome of both hyperparathyroid neoplasia and a gastrinoma.[4] "Psychiatric moans" refers to effects on the central nervous system. Symptoms include lethargy, fatigue, depression, memory loss, psychosis, ataxia, delirium, and coma. Some patents may develop left ventricular hypertrophy and have an increased all-cause mortality.[5,6] Note that hyperparathyroidism preferentially affects the cortical bone at the radius (distal third). Many of these patients present with pathological features. The mainstay of diagnosis is the Parathyroid immunoassay. Once elevated Parathyroid hormone has been confirmed, the goal of diagnosis is to determine whether the hyperparathyroidism is primary or secondary in origin by obtaining a serum

calcium level. Quartary and quintary are rare conditions that may be observed after surgical removal of primary hyperparathyroidism. Surgical removal may have led to renal damage that now again induces a form of secondary (quartary) hyperparathyroidism that may itself result in gland autonomy (quintary hyperparathyroidism).[4] Alternatively quartary hyperparathyroidism may result from hungry bone syndrome after parathyroidectomy.[5] The clinical picture in all these subtypes for an orthopedic surgeon remains essentially the same, he faces a very paper thin fractured bone needing treatment. Frequently the dilemma is between operative and conservative management. The goals of prevention and treatment of Brown tumors include normalizing blood levels of calcium and phosphate with phosphate binders, calcium and 1,25 dihydroxy-vitamin D. Some cases have been successfully treated with high doses of vitamin D, control of alkaline phosphatase levels in serum or oral calcitriol.[15,16,17,18] Though the bones look very osteopenic, the pathology does not seem to interfere with healing process. Our series summarizes the retrospective analysis of cases treated in the past at various centers.

Objective

To study retrospectively the results of treatment of cases of pathological fractures presenting with osteitis fibrosa cystica due to hyperparathyroidism.

Material & Methods

It is a retrospective analysis of cases of hyperparathyroidism treated for long bone fractures in three different units in the last seven years (2004-2011). All have been treated and discharged from treatment upon completion of required follow-up. Existing medical records were analyzed for presence of complete documentary proof of hyperparathyroidism and varieties thereof. All the cases with incomplete records were excluded. A tabulated chart was developed which is being presented for review. Only cases with complete S/Calcium, S/Phosphate, Alkaline Phosphatase, PTH levels and serum albumin and renal function tests were included. Total serum calcium and albumin levels or ionized calcium levels should have been measured. Hypercalcemia should be documented on more than one occasion before a diagnostic workup is undertaken. Testing of the intact parathyroid hormone level is the core of the diagnosis. An elevated intact parathyroid hormone level with an elevated ionized serum calcium level is diagnostic of primary hyperparathyroidism. A 24-hour urine calcium measurement is necessary to rule out Familial Hypercalcemia (it was not done in most of the cases hence it was ignored). Secondary hyperparathyroidism (SHPT) develops early in chronic kidney disease before dialysis is initiated. Most patients with end-stage renal disease (ESRD) have elevated parathyroid hormone and secondary hyperparathyroidism of variable severity exists. Vitamin D deficiency is common and is underdiagnosed. Hence only records where vitamin D serum levels were available were included. All patients had been given injections of 300,000 IU of vitamin D intramuscularly as bolus dose of vitamin D2 thrice monthly or 600,000 IU (15 milligrams) of vitamin D had been given each month for three months. Patients with secondary hyperparathyroidism usually have a low-normal calcium and elevated parathyroid hormone. The phosphate level may vary based on the etiology, showing high values in renal insufficiency and low values in vitamin D deficiency states. All patients had been advised to use calcium supplements orally as chewable tablets 1 gram per day. These were continued even after vitamin D supplements were withheld. A raised serum level for the vitamin was an indication to withhold the drug after the Alkaline phosphatase levels returned to normal.

Results

In all, only fifteen cases fulfilled the inclusion criteria because of incomplete records. All the selected cases were studied and the data available was tabulated. Majority of the cases were females (male to female ratio was 4:1). The average age of the cases was 29.6 years (range17-55). Regardless of the treatment method adopted for the fractures all patients completed a uniform calcium and vitamin D supplementation regimen. No parathyroidectomy was done in this group (the cases with such interventions were excluded). Those with renal failure continued with their hemodialysis programs as per routine. The parathyroid hormone was found consistently elevated in all; 184.06 pg/dl (range104-311). Low vitamin D levels were seen in most 11.09 ng/ml (range5-16.5). Vitamin D levels were consistently lower than normal in all cases. Thirteen cases of fractures healed well regardless of the treatment modality adopted. One case went into non-union and had to be operated. One case died of hepatic failure due to concomitant hepatitis C

Table-1: Varieties of hyperparathyroidism

Serum Parathyroid Hormone	Serum calcium	Likely type
High	High	Primary hyperparathyroidism
High	Low or normal	Secondary hyperparathyroidism
High	High	Tertiary hyperparathyroidism (H/O CRF or sec. hyperparathyroidism)

Table-2: Patient data

	Age	Sex	PTH Levels 10-65pg/ml	S/Cal 85-10.5mg/dl	S/Ph 2.4-4.1mg/dl	Alk/Ph 20-140IU/L	Vit-D >30ng/ml	CRF Chronic RF	Fracture	Treatment	Result
	35	F	104 P	11.4	4.9	542	12	Y	# Neck of humerus	U-slab	Healed
	45	F	155 P	12.1	3	296	8	Y	Bil # shaft femora	ORIF with ILN	Healed
	16	F	165 S	8.1	3.4	950	10	N	Bil NOF iz	Preventive activity modification	Healed
	22	M	143 S	9.2	4	548	9	Y	SC # Femur	PC K Wires plus POP	Healed
	47	F	256 S	10	3.2	634	5	Y	# SO Humerus	U-slab	Healed
	55	M	163 S	7.9	2.5	835	17	Y	PT # Femur	ORIF DHS	Healed
	29	F	200 P	12.5	3.7	1200	5.65	N	Rib #s, #d radiaus, IZ nOR	POP cast radius	Healed
	32	M	230 S	11.9	5.2	567	11.7	Y	# SOF	ORIF ILN	Died
	30	F	198 S	8.2	3.3	640	9.20	Y	# Tibia	ORIF	Healed
	23	F	311 S	10	2.4	700	6.8	N	# Radial Ulna	POP Cast	Healed
	17	F	209 S	8.1	4	698	12	N	# Humerus	TENS	Healed
	33	F	220 P	9.2	4	548	9	Y	SC# Femur	PC Wires Plus POP	Healed
	40	M	213 P	10	3.2	634	5	Y	# Tibia	POP cast	NU
	21	F	194 S	8	3.3	800	21	N	# NOF	Can. Screw	Healed
Av.	29.6	4:1	184.06	9.98	3.34	256	11.09				
Range	17-55		104-311	7.9-12.4	2.4-5.2	296-1200	5-165	Yes=8 No=7			H=13 NU=1 D=1
Male =3 Female=12			Primary=5 Secondary-10								

infection. No complications with simple therapeutic regimen was noted.

Discussion

Osteomalacia associated with hyperparathyroidism is caused by the high parathyroid hormone secreted by overactive parathyroid gland(s). Excess parathyroid hormone (PTH) acts indirectly on osteoclasts as they lack a PTH receptor. Instead, PTH stimulates osteoblasts, which in turn increase their expression of RANKL. RANKL (a member of the tumor necrosis factor [TNF] cytokine family which is a ligand for osteoprotegerin and functions as a key factor for osteoclast differentiation and activation) is then able to bind osteoclasts which stimulates their activation which ultimately leads to the removal of calcium from

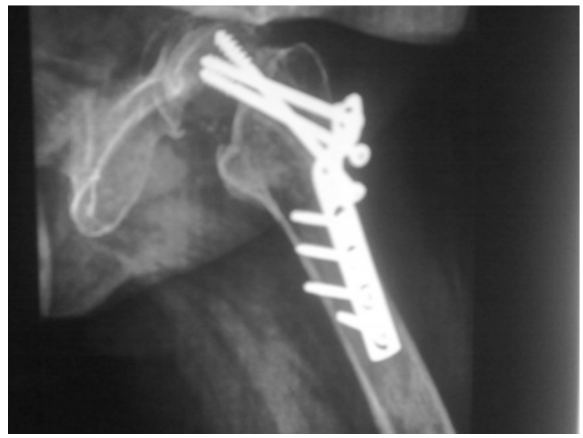

Fig-1: A case of implant failure after fixation for fracture neck of femur.

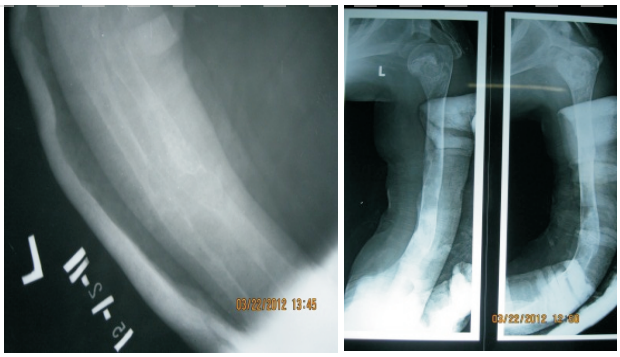

Fig-2: Conservatively treated healing fractures.

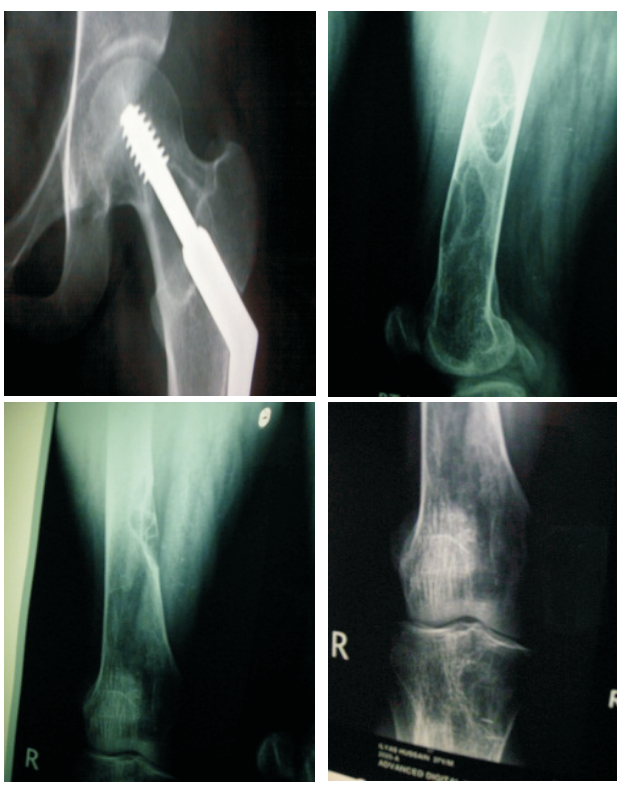

Fig-3: Brown Tumors

the bones.[8,9] Thus, the high calcium in the blood comes partly from the bones as well as from increased renal reabsorption. Removing the offending parathyroid gland will restore normal bone density over several years with restoration of trabecular bone but not cortical bone. Reports indicate that non-union in these fractures is rare and that healing proceeds uneventfully after excision of the offending adenoma if needed.[17,18,19] Bone histology returns to normal within 5 or 6 weeks of treatment. Concomitant vitamin D deficiency can lead to delays in healing. Some authors report only partial correction of bone loss after surgery, such correction occurring only in the first year.[17] The original pathology apart from the dilemma facing the orthopedic surgeon remains mono-faceted. The bone is too weak to hold implants like plate held in place with screws or to tolerate the intra-medullary implants which may split the cylindrical bone on introduction. A twofold reduction in bone density gives rise to a fourfold decline in ultimate compressive strength, a loss which may be the most important factor in fixation failure in osteoporotic bone.[10] Screw holding power also diminishes as cortical thickness decreases. Similar principles apply to the wires used in circular external fixators; and when an intra-medullary nail is used to stabilize a fracture at the distal end of the femur it is exposed to large loads and risks breaking.[10,11] The patients are generally suffering from muscular weakness decreasing their ability to avoid weight bearing over the injured limb walking with supports. Most surgeons prefer intra medullary implants in the presence of fragility fractures. Short intra medullary nails have developed considerably over the last ten years. Hip fractures present a special mention as this area concentrates a lot of bio-mechanical stress even when the patient is confined to his bed. Continuously newer implants are being tested namely the Gamma nail, intra medullary hip screw (IMHS), proximal femoral nail (PFN), Holland nail & Targon nail.[10,11] Comparisons of these implants against the sliding hip screw have been made in frequently published trails.[12] In summary, the nails are associated with an increased risk of fracture healing complications (7.5% versus 3.6%) and an increased re-operation rate (5.6% versus 3.5%).[13] Each implant has its own differences and local complications in such fractures depending upon its design.[11,12,13] Since our series does not include many cases of similar fracture patterns hence an inference suggestive of best treatment method for each bone cannot be made conclusively. However it would be prudent to suggest that control of hypercalcemia and secondary hyper parathyroidism with vitamin D supplementation backed by a prolonged calcium oral supplement-ation does tend to reverse the osteopenic effects of osteitis fibrotica cystica and promotes bone healing. We believe that these fractures take longer to heal and are prone to malunion unless splinted anatomically till union.

Conclusion

Calcium & vitamin D supplementation does tend to help fracture healing in cases of osteitis fibrotica cystica. The main mechanism at work seems to be control of secondary hyperparathyroidism.

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