Right tibia brown tumor revealing primary hiper parathyroidism : a case report

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Abstract
Primary hyperparathyroidism is a systemic endocrine disorder due to parathyroid adenoma accounts for 80 % of cases. This condition is rare and only 2-5% patients have multiple bone brown tumor lesions. Hyperparathyroidism has significant effects on bone remodelling through the action of parathyroid hormone on the musculo skletal system. Brown tumor as result from primary hyperthyroidism is a localized bone cyst and may cause swelling, pathological fracture, and bone pain in the skletal system. Here we would like to present a 30-year-old woman patient with pain on her right tibia that not alleviated by taking a rest. On right tibia radiological examination we found permeative lytic lesion on the metaphysis and diaphysis region with well define margin, septated, with chondroid matrix and expansile lesion to the postero medial cortex of right tibia. Comprehensive medical examination was done to explore the cause of this condition till the underlying disease was treated and we started to administered biphosphanate injection as chemotherapy to treat the skeletal lesion from this patient. The purpose of this case report was to evaluate the effectiveness bisphosphonate as a chemotherapy for brown tumor on the right tibia after the underlying disease for the primary hyperthyroidism treated by hemiparathyroidectomy and hormonal theraphy. After the hyperparathyroidism was confirm due to primary cause of hyperparathyroid adenoma, this patient was performed hemi parathyroidectomy. Parathyroid hormone was controlled by hormonal theraphy and after the value was almost reach normal, we start to administered bisphosphonate injection for 6 months with single dose of biphosphonate injection every month. Radiological examination before and after bisphosphonate administered then was compared to evaluate the radiological changes for this patient. The patient have a good functional outcome after bisphosphonate administered. Bone density with localized pain was observed. There was no adverse effect after bisphosphonate injection with increasing of bone density on the lesion, localized pain also decreases. Complete and comprehensive treatment for brown tumor followed by biphosphonate administered as chemotherapy combined with hormonal theraphy, resulting better outcome for this patient. Educate and make the patient understand that this condition need time to exclude any related condition which mimicking its. When the underlying disease treated, chemotherapy is able to perform. This condition need hospital with complete facilities and professionals health experts. Long term observation also needed to evaluate and maintain the result after bisphosphonate administered will give patient good functional outcome.

Keywords: Brown tumor, primary hyperthyroidism, giant cell tumor, endocrine system.

1. Introduction

Hyperparathyroidism is mainly divided into three types: primary, secondary, and tertiary hyperparathyroidism. This condition appears with excessive secretion of parathytoid hormone (PTH) caused by excessive hyperplasia, neoplasia, and carcinogenesis of parathyroid. About 75 – 80% of cases of hyperparathyroidism are diagnosed when routine assay shows hypercalcemia. Due to parathyroid hormone hyper secretion, several consequences occur, such as excess calcium reabsorption from kidneys, phosphaturia, increased vitamin D synthesis, and bone resorption. Clinically, most patients are asymptomatic or show nonspecific symptoms such as fatique, mild depression, or cognitive impairment.[1,2,3,5]

Catabolic effects parathyroid hormone defends against a decrease in serum calcium by increasing bone resorption more than formation, para thyroid hormone appears to have discrete effects on trabecular and cortical bone compartments. Brown tumor is a localized bone cyst and in histological perception it is a benign lesion which compose of fibrous stroma associated with multinucleated giant cells, fibroblast embedded in areas of hemorhage and hemosiderin deposits. Lesion on bone caused by rapid osteoclastic activity due to hyperparathyroidism resulting in a locally destructive phenomenon. In regions where bone loss is rapid, hemorhage, hemosiderin deposition, and vascularized fibrous tissue replace the normal bone contents, resulting in a redish brown appearance. Common site of brown tumor are the ribs, clavicle, tibia, femur, and pelvic girdle.[3,4]

The aim of this case report is to evaluate clinical outcome and determine the efficacy of the use of bisphosphonate as chemotherapy which have been used successfully for many years to reduce the skeletal complications associated with benign and malignant bone disease that are characterized by enhanced osteoclastic bone resorption. Biphosphonate are simple chemical compounds that are based on a phosphorous – carbon – phosphorus template. There are three main groups of biphosphonates: (i) the first generation compounds, such as elondronate and etidronate, (ii) the second generation bisphosphonate such as pamidronate, alendronate, and ibandronate, (iii) the third generation N-Biphosphonate are characterized by a heterocyclic subsituent, containing one nitrogen atom in a pyridyl ring or two nitrogen atom in an imidazole ring.[8,9,10]

All bisphosphonate appear to induce the apoptosis of osteoclasts by the activation of caspase-3-like protease. Their dominant effect in early and rapid inhibition of osteoclast function resulting in reduced bone resorption, rather than through a decrease in cell viability number. Evidence from invitro and animals models confirms that N-biphosphonate also inhibit osteoclastogenesis and the recruitment of osteoclast progenitors into bone.8,9,10

The advantage of using bisphosphonate are ideal bone targeting agents due to their selective affinity for pathological calcifications in highly metabolic region in bone tissue such as bone metastases, it also inhibit tumor growth and prevent metastatic bone progression.8,9,10The purpose of our study is to describe our experience treating brown tumor with biphosphonate administered after the primary hyperparathyroidism treated.

2. Case Report

A 30-years old patient came to our polyclinic. She felt pain and swelling on her right middle tibia region. The pain was increased by time and didn't subside when she was rest. No history of trauma and others comorbid disease were found in history taking. For the last 3 months she aknowledge felt more fatique than usual with increasing of heart rate. The right leg seems more swelling compare to the left leg, no wound or ulcer were found. Her right leg on the midle region looks shiny compare to the left side and no venectasy was found. Tenderness was found on the right middle tibia region and peripheral pulses were palpable at popliteal artery, dorsalis pedis artery, tibialis anterior artery, tibialis posterior artery, all fingers saturation are 99 %. (Fig 1).

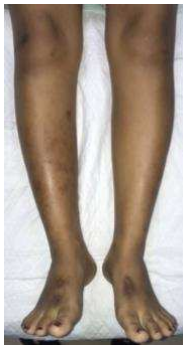


Fig 1. Clinical presentation

We send this patient for radiological and laboratory examination. Initial laboratory test showed no abnormality (complete blood test, liver function, renal function, electrolyte, protein electrophoresis serum). The radiological examination on her right tibia showed permeative lytic lesion on the metaphysis and diaphysis region with well define

margin, septated, chondroid matrix and expansile lesion to the postero medial cortex of right tibia (Fig 2), on her left cruris x ray we also found lytic lesion on medial distal tibia in metaphysis and diaphysis region, well define margin, lobulated, with chondroid matrix, no destruction on tibia cortex. From thorax x ray showed normal appearance with no metastatic lesion in lungs (Fig4). Pelvic x ray also showed normal appearance with no other lesions on lower lumbal, pelvic bone, and proximal femur (Fig5).

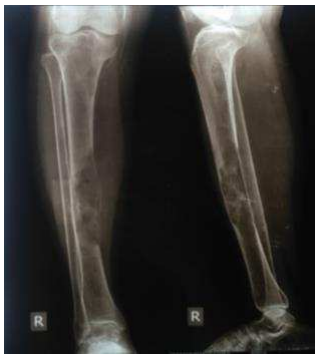


Fig 2. Right Cruris x ray AP and Lateral view

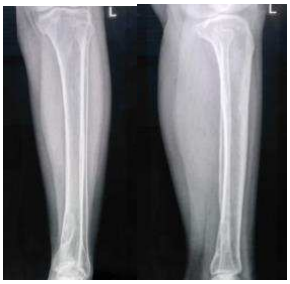


Fig 3. Left cruris x ray AP and Lateral view

Schaedle x ray also showed in normal appearance with no other bony lesion on the skull (Fig6). Thoracal and lumbar spine x ray also showed no other bony lesion (Fig 7&8).

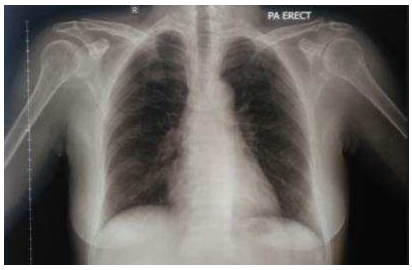


Fig 4. Thorax x ray

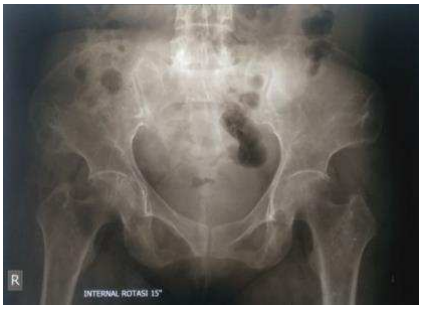


Fig 5. Pelvic x ray

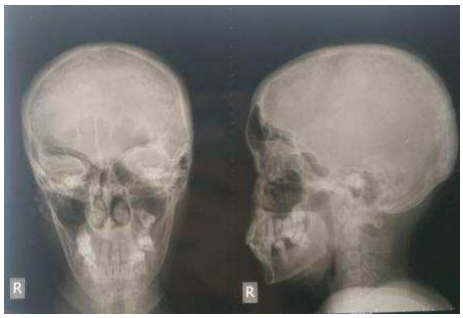


Fig 6. Schaedle x ray AP and Lateral view

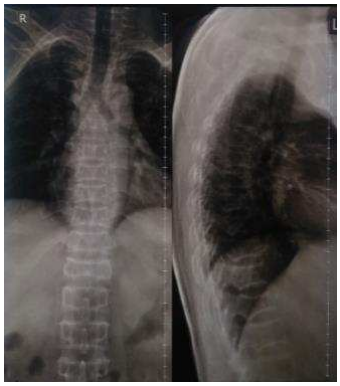


Fig 7. Thoracal x ray AP and Lateral view

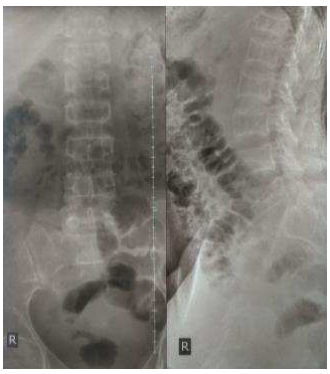
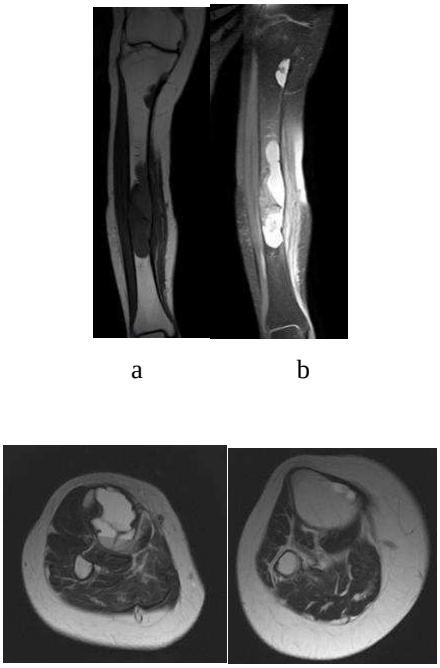


Fig 8. Lumbal x ray AP and Lateral view

We also send the patient to perform right cruris MRI and showed lesion involved to ventral midline cortex in the proximal epimetaphysis with intermediate intensity in T1 image, iso-hyperintense in T2 image, with size about 0,8 x 1,4 x 1,0 cm, well define margin, multi septated with clear border. Lesion also involved the ventral cortex of tibia on proximal medial diaphysis, with intermediate signal in T1 image, iso hyperintense in T2 image, size is about 0,8 x 1,6 x2,7 cm,well define margin, multi septated with clear border, neuro vascular bundle was normal (Fig 9).

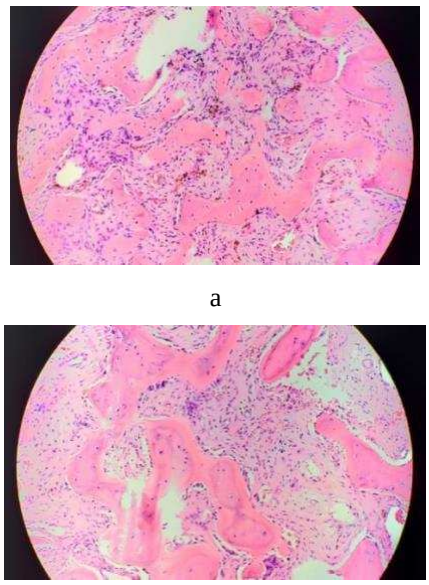


a b

c d

Fig 9. Right cruris MRI

For histopathologis examination, we performed core biopsy and from this examination we found multi nucleated giant cells between proliferation of fibrous tissue and fibroblast. Proliferative bone trabeculae found with hemosiderin pigment deposite. There is no sign of malignancy (Fig 10).

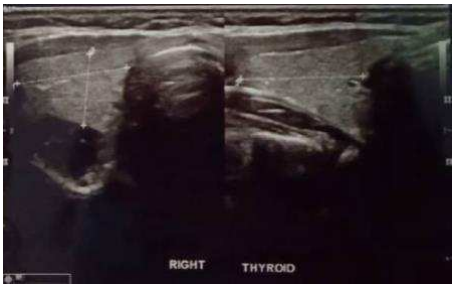


a

b

Fig 10. Histopathology

We consult the patient to Oncology division and they performed laboratory test, thyroid ultrasonography, and parathyroid scan.



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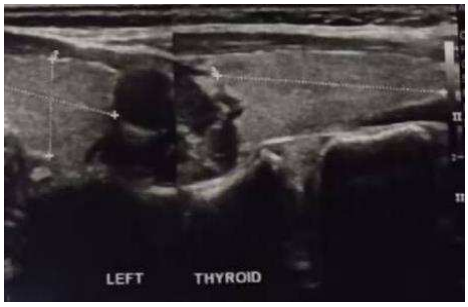
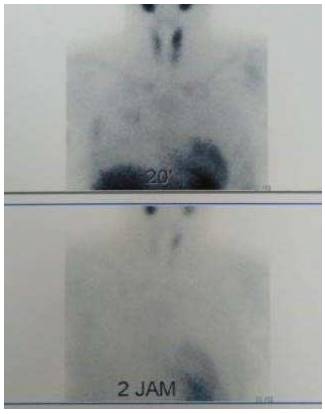


b

Fig11. Thyroid ultrasonogram



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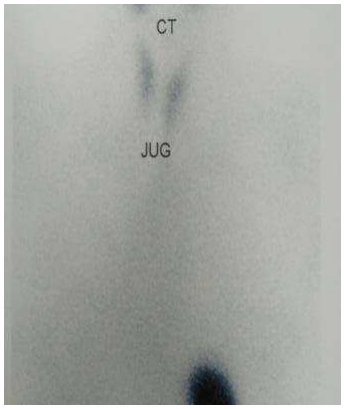

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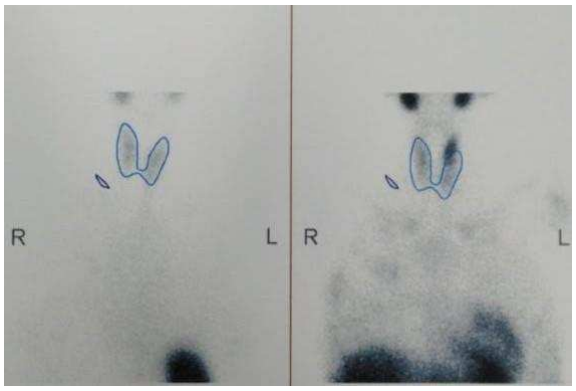


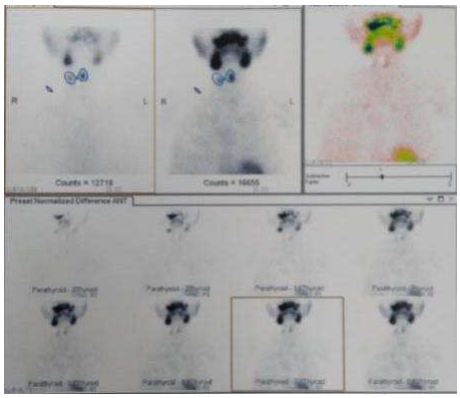
c

Fig 12. Parathroid scintigraphy

Laboratory test from oncology divison revealed that excessive blood parathyroid hormone increases in 1.249 pg/ml (15 – 65 pg/ml), TSH 107,318 uU/ml (0,35 – 4,94 uU/ml), FT4 0,81 ng/dl (0,70 – 1,48 ng/dl), unorganic phosphor 2,22 mg/dl (2,5 – 5,0 mg/dl), calcium ion 1,42 mmol/L (1,12 – 1,32 mmol/L). Thyroid ultrasonogram showed enlargement parathyroid gland, there was no focal lesion with lymphadenopathy (Fig 9). Parathyroid scan with double tracer using Tc-99 showed enlargement of both parathyroid lobe with normal distribution and radioactive catching above the normal state. In subtraction scanning showed radioactive catching activity on left superior lobe of thyroid gland. There was also increasing radioactive catching on neck of mediastinum on the left superior lobe of thyroid gland. In dual phase showed that radioactive catching activity was in stagnant condition in 120 minutes period on the left superior lobe of thyroid gland. This imaging was appropriate for parathyroid adenoma with diffuse nodose struma (Fig 10).

Oncologic division then planned the patient to perform hemithyroidectomy and from endocrinologist division provide chemoteraphy for this patient. After the hemiparathyroidectomy performed, the sample was sent to evaluate the histopatological confirmation. From this examination we found in histological parathyroid gland sample were groups of tumor cells with thin fibrous septae. Tumor cells forming trabecular pattern, with oval and polygonal cells form, large of nuclei, prominent. Mitosis was found and clear of cytoplasm, and with congestion and dilatation of blood vessels. From thyroid gland sample, the histological showed that most of thyroid gland formed by macro and micro

follicle with a layer cuboid epithelial, lumen was filled with colloid mass Stroma formed by fibrous tissue with vascular congestion. From histopathological examination we conclude that the patient condition was an atypical parathyroid adenoma.



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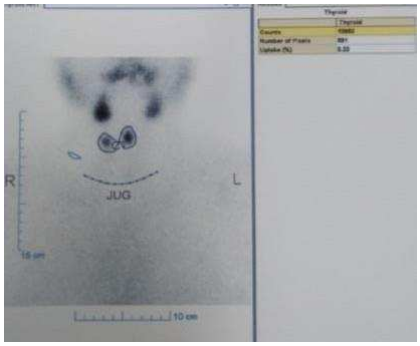

b

Fig 13. Parathyroid scintigraphy

After post operation wound care, we then reschedule the patient to performed the second parathyroid scintigraphy. A month after the surgery, this examination showed in subtraction scanning thyroid gland was remain functional with radioactive catching about 0,22% (0,5 – 5 %). In subtraction procedure radioactive catching activity was not found. Laboratory test then performed with normal electrolyte result, FT4 0,82 ng/dl (0,7 – 1,48 ng/dl), PTH intact 97,63 pg/ml (15 – 65 pg/ml), TSH 6,61uU/ml (0,35 – 4,94 uU/ml), thyroglobulin 0,95 ng/ml (1,4 – 78 ng/ml), and from this condition we started to administered the bisphosphonate that planned for 6 times for a month each.

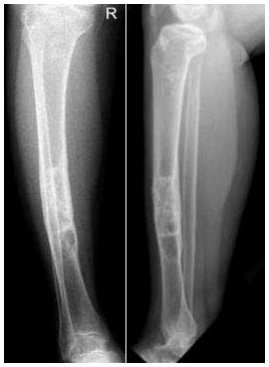

Fig 14. Left cruris x ray AP and Lateral view

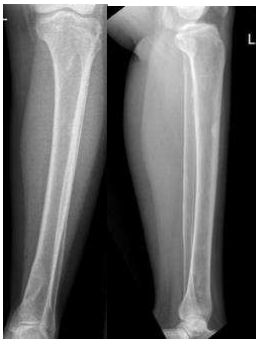

Fig 15. Right cruris x ray AP and Lateral view

On the right tibia, litic lesion was decrease if we compared it with right tibia x ray by the patient came to polyclinic. The lesion density is increase and form by sclerotic lesion which means osteoclastic activity already inhibit, the margin is still able to differentiate clearly (Fig 12). On the left tibia, there is also increasing the density from the lesion at the distal part and also form a sclerotic lesion. The margin is also still able to differentiate by surrounding normal tibia bone. The patient also claim that the pain was subsided significantly.

3. Results

The Patient have a good result with good functional outcome after bisphosphonate administered. Bone density with localized pain was observed. There was no adverse effect after bisphosphonate injection with increasing of bone density on the lesion, localized pain also decreases.

4. Discussion

The frequency of bone disease has been reported to be around 10 – 15%. Brown tumor is a rare aspect of manifestation (2-3%) and its exceptionally revealing the disease. Brown tumor, also known as osteitis fibrosa cystica has three stage progression. First of all, elevated PTH secretion stimulates osteoclast to absorb bone while collagen fibers form in bone marrow. In the second phase is the stage of fibrotic osteitis, trabecular bone is absorbed and bone marrow is replaced by loosened fibrosis, hemosiderin containing macrophages, microfracture hemorhage area and reactive woven bone. As hyperparathyroidism and hemorhage continues, cystic degeneration eventually occurs, leading to the final stage of disease (fibrous cystic osteitis). Cyst are result of intra bone hemorhage and tissue degeneration. They are filled with a large number of osteoclast, macrophages, and fibroblast that engulfed with hemosiderin. Hemorhage, hemosiderin, and excessive blood vessels lead to brown appearance, so it called brown tumor.[1,2,3,4,5,6,7]

The tumor may be asymptomatic or cause pain and fracture. On radiograph, they are seen as lytic foci with tortuous contour and margins that are usually well defined, without sclerosis. Primary hyperparathyroidism is characterized by the hyper functioning of parathyroid glands. Female and male ratio is 5:2. Most of this condition have single parathyroid adenomas (85%), 15 % have multiple gland involved (Hyperplasia or multiple adenomas), and carcinomas are rare (<1-2%). Serum calcium correlate significantly with weights of parathyroid glands. [5,6,11]

This case ilustrate brown tumor due to primary hyperparathyroidism with lower extremity manifestation. Improved laboratory test and radiological method, it diagnosed early and asymptomatically. Only 2% of all cases occur below

the age of 30 years. The usual sites of this lesions are the ribs, clavicles, pelvic girdle, and facial bones, and the presentation may be a pathological fracture. The lower limb is rarely affected.[11]

The use of bisphosphonate as a chemotherapy to treat brown tumor based on bisphosphonate prevent skeletal morbidity and relief bone pain. When compared to other cancer therapies, the frequency and severity of adverse events related to bisphosphonate therapy are generally mild and infrequent, renal toxicity is unusual, usually predictable and reversible, and serious bisphosphonate induce renal complication are rare (<0,5%).[8,9,10]

In our case report, the good result happened in the 30 years old woman with brown tumor due to primary hyperparathyroidism accompanied by multiple bony lesions on her lower leg that treat the bony lesion by administering bisphosphonate for 6 months. Single dose of bisphosphonate was injected to this patient every month. Before we started the chemotherapy with biphosphonate, the underlying disease of primary hyperparathyroidism due to adenoma hyperparathyroid was treat by hemiparathyroidectomy. Comprehensive study was also performed to determine the cause of this primary hyperparathyroidism. When the underlying disease already known, we treat it early so we can start the admission of bihosphonate as a chemotherapy before any serious bony complication due to the bony lesion appears.

5. Conclusion

We observed this patient for 1 year, from early she came to our polyclinic until she finished administered by bisphosphonate chemotherapy. The pandemic state due to corona virus was also made this patient not as fast before the pandemic state to confirm the underlying cause of her hyperparathyroidism. The multiple bony lession on her lower leg can be treated with bisphosphonate injection after comprehensive health care was done to find the underlying disease and treat it first before starting the bisphosphonate administered. We are aware this is a short-term study and require further evaluation and more inputs.

6. References

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