Fibrous Dysplasia Associated with Primary Hyperparathyroidism Absent of McCune-Albright Syndrome: Tc-99m MIBI and Tc-99m MDP Findings

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국문초록

섬유성 골이형성증은 비정상적인 섬유성 골조직으로 대체되며 느리게 진행하는 골병변이다. 섬유성 골이형성증과 부갑상선기능항진증은 흔하게 관찰되는 질환이나 McCune-Albright 증후군 없이 일차성 부갑상선기능항진증에 동반된 섬유성 골 이형성증은 거의 보고된바가 없다. Tc-99m MDP 골스캔이 섬유성 골이형성증의 진단에 유용하다고 알려져 있으나, Tc-99m MIBI 영상은 아직 보고된 바가 없다. 저자들은 McCune-Albright 증후군이 없이 부갑상선기능항진증에 동반된 섬유성 골 이형성증의 Tc-99m MIBI 스캔과 Tc-99m MDP 골스캔의 영상을 비교하였다. Tc-99m MDP 골스캔상 병변 부위에서 증가된 섭취 소견을 보였으며, Tc-99m MIBI 조기영상에서도 동일한 위치에서 섭취증가가 관찰되었다. 2시간 지연 Tc-99m MIBI 영상에서는 Tc-99m MIBI의 섭취가 배출되는 소견을 보였다. 섬유성 골이형성증 병변에서 Tc-99m MIBI 스캔이 유용할 것이라고 생각하며, 섬유성 골이형성증 병변에서 Tc-99m MIBI의 섭취를 증가시키는 인자에 대한 더 많은 연구가 필요할 것으로 생각한다.

Key Words : Tc-99m MIBI, Tc-99m MDP, fibrous dysplasia, hyperparathyroidism, McCune-Albright syndrome

INTRODUCTION

Fibrous dysplasia is a chronic disorder of the skeleton that causes expansion of one or more bones due to abnormal development of the fibrous, or connective tissue within the bone. The abnormality will cause uneven growth, brittleness and deformity in affected bones. Some patients have only one bone affected, whereas other patients have numerous bones affected. While any bone can be affected by fibrous dysplasia, the most common sites of the disease are the femur, tibia, ribs, skull, facial bones, humerus, and pelvis.

Some patients with fibrous dysplasia can present with hormonal disturbances such as early puberty, hyperthyroidism, excessive secretion of several pituitary hormones, and high blood calcium from parathyroid hormone. The combination of fibrous dysplasia, hormonal disturbances, and skin pigmentation is called McCune-Albright syndrome.[1] Isolated presentation of fibrous dysplasia or hyperparathyroidism is a common finding. However, fibrous dysplasia associated with primary hyperparathyroidism without McCune-Albright syndrome has been rarely reported before.[2-4]

Tc-99m methoxylisobutylisonitrile (MIBI) is a tracer that is widely used as a myocardial perfusion imaging. After being reported to accumulate in tumors, Tc-99m MIBI has been widely used in tumor studies and is known to be useful in the detection of various primary tumors, metastases, and recurrent tumors.[5-7]

The magnetic resonance imaging, plain radiography, and computed tomography had been used as a tool for diagnosing

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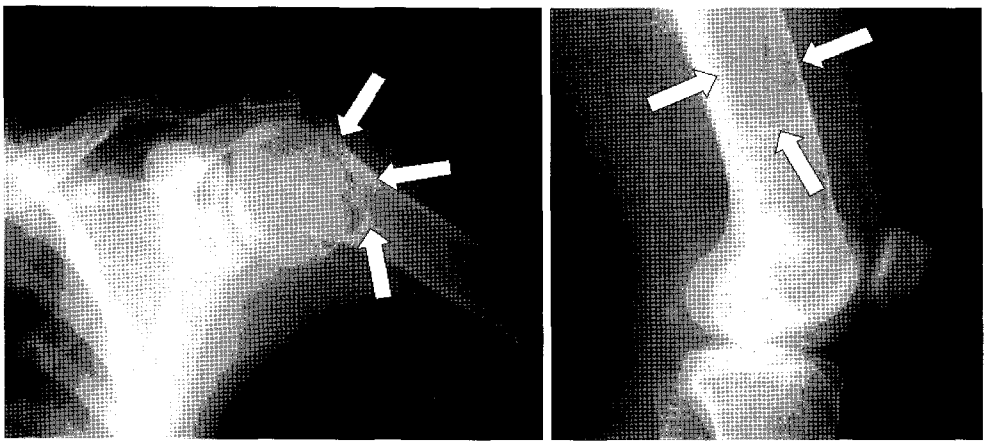

Fig 1. Anteroposterior radiographies of left shoulder and left femur showed large irregular lucencies with neck fracture in left humerus (A) and the cystic and gound-glass-like density in the left distal femur (B) (arrows).

fibrous dysplasia.[8-11] Also, Tc-99m methylene diphosphonate (MDP) bone scan was reported to be useful for the diagnosis of fibrous dysplasia.[12-16] However, the scintigraphic appearances of fibrous dysplasia using Tc-99m MIBI are not well documented. Also, no other study of fibrous dysplasia associated with primary hyperparathyroidism without McCune-Albright syndrome has used Tc-99m MIBI and has compared Tc-99m MDP bone scan.

In the current report, we describe Tc-99m MIBI scan findings in a patient with fibrous dysplasia associated with primary hyperparathyroidism without McCune-Albright syndrome and compared with Tc-99m MDP findings. Also, we review the literatures.

CASE REPORT

A 21-year-old man was hospitalized for left shoulder pain caused by fall down and tingling sensation on both hands. In the past, he had repeated pathologic fractures and had received 3 times of extracorporeal shock wave lithotripy (ESWL) for repeated right renal stones. Plain radiographies of left shoulder and left distal femur showed left humerus neck fracture and the cystic and gound-glass-like density in the left distal femur (Fig. 1).

To evaluate the underlying cause of repeated fractures, bone scan after injection of 925 MBq (25 mCi) Tc-99m MDP was performed. The bone scan showed multiple increased uptakes on both humeri, ribs, left femur, and left pubic bone resembling multiple bone metastases (Fig. 2).

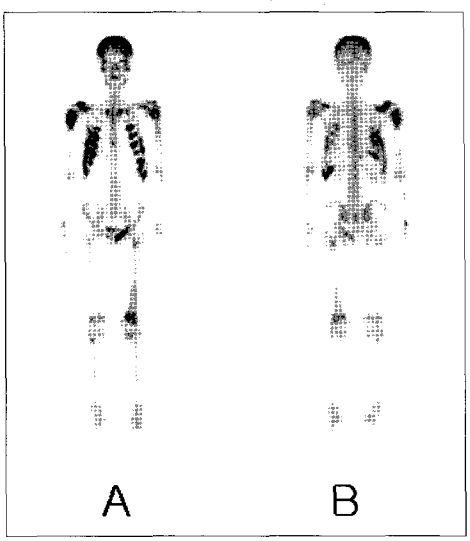

Fig 2. Anterior (A) and posterior (B) Tc-99m MDP bone scan showed multiple increased uptakes on both humeri, ribs, left femur, and left pubic bone mimicking multiple bone metastases.

Blood analyses at admission revealed total calcium 13 mg/dl, phosphorus 1.2 mg/dl, ionized calcium 2.68 mEg/L, intact PTH 1304 pg/ml, and ALP 4869 mg/dl. Physical examination showed chvosteck sign. The BMD showed severe osteoporosis (T-scores: -2.87 L1, -2.61 L2, -3 L3, -3.54 L4). The diagnosis of primary hyperparathyroidism was made. We performed Tc-99m MIBI double phase parathyroid scan 10 minutes and 2 hours after injection of 925 MBq (25 mCi) Tc-99m MIBI to localize the parathyroid lesion. The early and delayed planar anterior and SPECT images were acquired. A large-field-of-view dual detector gamma camera (Vertex; ADAC, Milpitas, CA, USA) and a computer system (Pegasys, ADAC) equipped with low energy, high resolution collimators were used. The energy discriminator was centered on 140 keV photopeak of Tc-99m with a symmetric 20% window.

The gamma camera rotated through 180 degrees in a circular

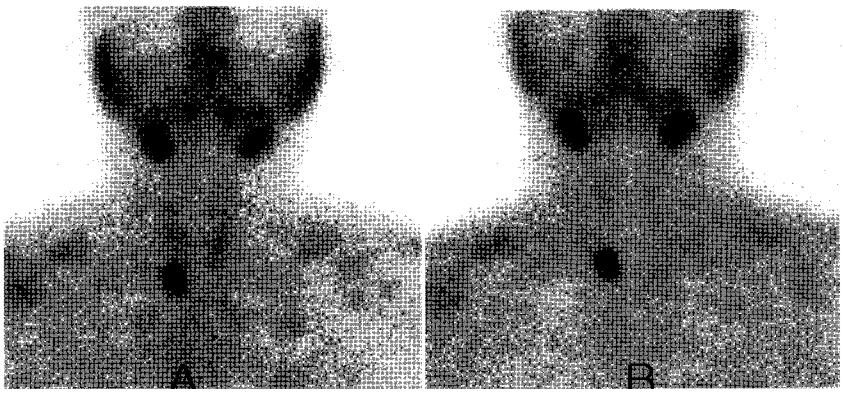

Fig 3. Double phase Tc-99m MIBI parathyroid scan. Early (A) and delayed (B) Tc-99m MIBI scan showed increased uptake on right anterior lower neck compatible with right parathyroid adenoma

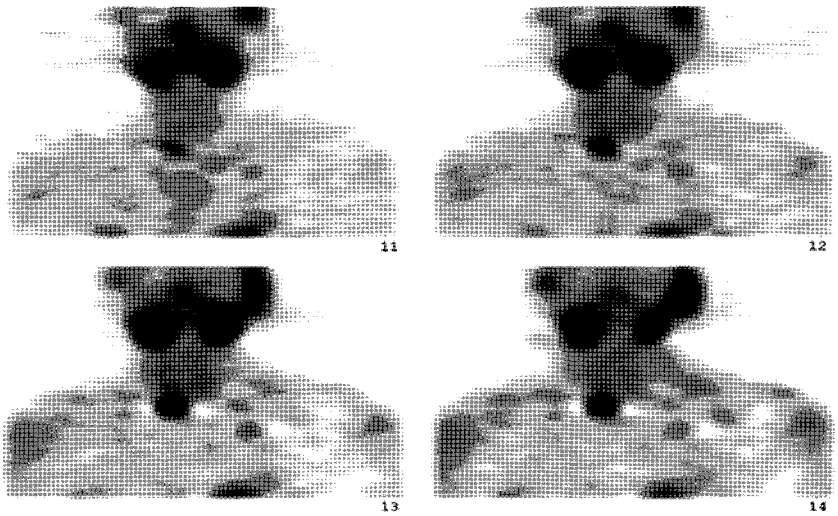

Fig 4. Coronal SPECT images also revealed increased MIBI (arrows) uptake on right lower anterior neck.

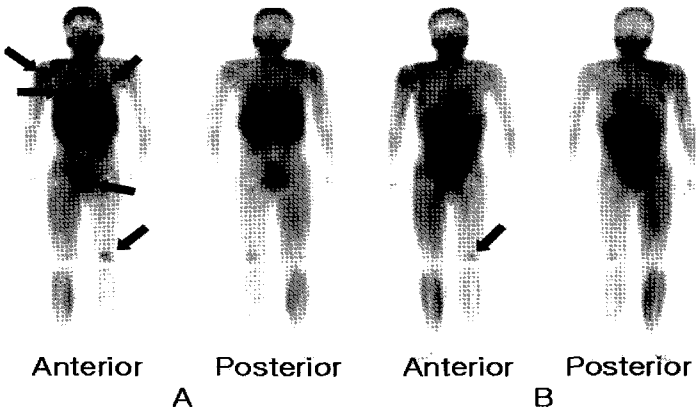

Fig 5. Double phase Tc-99m MIBI whole body scan. Early (A) image showed increased uptakes on the same lesions noted on Tc-99m MDP bone scan. However, delayed image (B) showed remarkable washout of MIBI from the lesions.

Fig 6. (HE stain, x40) Photomicrograph showed variable-sized bony spicules surrounded by fibromatous stroma.

orbit in 32 steps of 20 seconds. SPECT images were reconstructed according to the filtered backprojection method using a Butter-worth filter. Early and delayed Tc-99m MIBI scan showed increased uptake in the right anterior lower neck (Fig. 3). The coronal SPECT images also revealed increased uptake on right anterior lower neck (Fig. 4).

Surgery was performed and the pathologic diagnosis was right parathyroid adenoma. To rule out the presence of underlying brown tumors caused by hyperparathyroidism, double phase whole body Tc-99m MIBI scans were also acquired. Early Tc-99m MIBI whole body scan showed increased uptake on the same lesions noted on Tc-99m MDP bone scan (Fig. 5). However, 2 hours delayed Tc-99m MIBI image showed remarkable washout of MIBI from the lesions which showed increased uptake at early image. For definitive diagnosis and treatment, the patient underwent left humerus curettage and bone graft. Also, surgical specimens were obtained from left femur and rib. The histopathologic examination of surgical specimens revealed fibrous dysplasia (Fig. 6). After parathyroid adenoma removal, the patient's symptoms improved and he was discharged.

DISCUSSION

Fibrous dysplasia is a benign, noninherited skeletal developmental disorder of unknown origin in which osteoblasts fail to undergo normal morphologic differentiation and maturation.[17] It may be confined to a single focus (monostotic) or multiple foci (polyostotic). The well known example of the association of fibrous dysplasia and primary hyperparathyroidism is the McCune-Albright syndrome. This syndrome is characterized by precocious sexual development, fibrous dysplasia and many endocrinological abnormalities such as goiter, hyperthyroidism, primary hyperparathyroidism, acromegaly, Cushing's syndrome, and hyperprolactinemia.[18]

Fraser et al.[19] reported first evidence suggesting that parathyroid hormone related protein (PTHrP) may contribute to the etiology of fibrous dysplasia in McCune-Albright syndrome. However, Hammami et al.[2] reported a patient with primary hyperparathyroidism associated with polyostotic fibrous dysplasia without McCune-Albright syndrome. Their patient's genomic DNA sample did not show any abnormalities. They concluded that the association of hyperparathyoidism and fibrous dysplasia may not represent a variant of the McCune-Albright syndrome. Although, we did not examined this mutations and PTHrP in our patient, he showed normal sexual development, no cafe au lait skin pigmentation and could be excluded the presence of McCune-Albright syndrome.

In the present case, we could not detect any endocrinological abnormalities except for primary hyperparathyroidism. Except for McCune-Albright syndrome, concomitance of primary hyperparathyroidism and fibrous dysplasia had been reported in 6 patients with no acceptable theory to explain the association of these two clinical conditions.[20] Our patient is a rare case of fibrous dysplasia associated with primary hyperparathyroidism without McCune-Albright syndrome.

Various imaging modalities such as plain radiography, computed tomography, MRI, and conventional Tc-99m MDP bone scan had been used for the diagnosis of fibrous dysplasia. It is well known that fibrous dysplasia is commonly associated with intense uptake on conventional bone scan with Tc-99m MDP.[12-16] The increased vascularity of lesions in fibrous dysplasia as demonstrated by early perfusion bone imaging has been postulated as the cause of abnormally high intensity of those lesions.[16] However, Han et al.[21] reported a case of fibrous dysplasia which showed barely increased uptake on bone scan. According to their assumption, patient age and bone infarction occur in areas of fibrous dysplasia may contribute barely increased uptake on Tc-99m dicarboxypropandiphosphonate (DPD) bone scan. Also, they concluded that clinicians should be cautious in interpreting bone scans of radiographically indicated fibrous dysplasia.

Besides to Tc-99m MDP, gallium-67 citrate,[22] In-111 pentetreotide,[23] and In-111 leukocyte scan[24] also showed increased uptake on fibrous dysplasia. According to Chen et al.,[23] increased pentetreotide uptake on fibrous dysplasia may be due to specific binding of pentetreotide to vascular beds and possibility of somatostatin receptors expression by the fibrous dysplastic cell themselves.

However, no other study of fibrous dysplasia associated with primary hyperparathyroidism without McCune-Albright syndrome had used Tc-99m MIBI and compared Tc-99m MDP bone scan. Tc-99m MDP bone scan showed intense increased uptake on both humeri, ribs, left femur, and left pubic bone resembling multiple bony metastases. Double phase Tc-99m MIBI whole body scan was done to rule out the presence of brown tumors according to previous report.[25] The early Tc-99m MIBI whole body scan showed increased uptake on the same lesions noted on Tc-99m MDP bone scan. However, 2 hours delayed Tc-99m MIBI image showed remarkable washout of MIBI.

Using double phase Tc-99m MIBI scan in breast cancer patients, Fujii et al.[26] reported that the retention index of MIBI is closely related to chemosensitivity to anthracyclines. Also, Yoon et al.[27] reported the washout of MIBI was correlated with p-glycoprotein expression in patients with untreated breast cancer. However, the quantitative indices such as lesion to non-lesion ratios and washout rate of MIBI in patients with fibrous dysplasia could be prognostic predictors should be analyzed after long-term follow up study. The significance of increased MIBI uptake in fibrous

dysplasia is unclear. In part, it may be due to increased delivery of radiopharmaceutical to these lesions, which can be highly vascularized in areas.[16]

It is likely that many factors are simultaneously involved in MIBI uptake, including biochemical characteristics of MIBI, the degree of local blood flow, transcapillary exchange, interstitial transport, and the negative intracellular charge of both mitochondria and cell membranes. Also, MIBI is a transport substrate recognized by the multidrug resistant p-glycoprotein. To identify the mechanism of MIBI uptake in fibrous dysplasia, further studies on the correlation between Tc-99m MIBI scan and the expression of p-glycoprotein in fibrous dysplasia are needed.

In conclusion, Tc-99m MDP bone scan as well as Tc-99m MIBI scan may be useful for the detection of fibrous dysplasia. Also, factors responsible for the uptake of MIBI by fibrous dysplasia will need to be studied further.

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