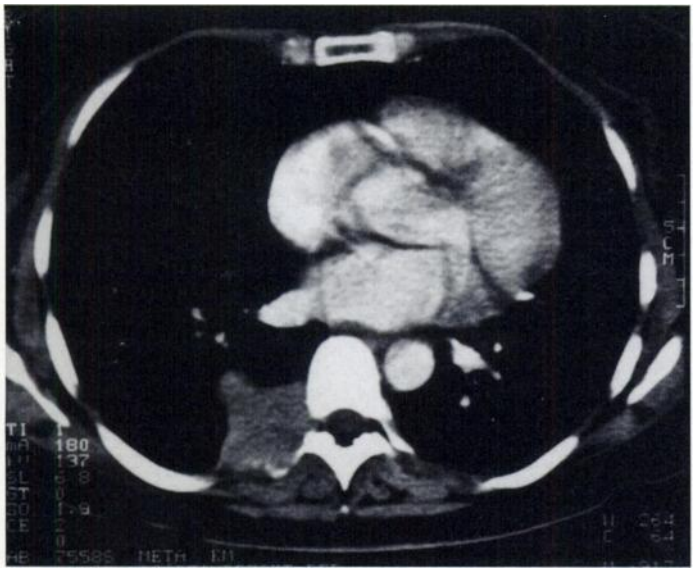

FIGURE 3. Transmission CT confirmed the scintigraphically detected lesion in the posterior mediastinum.

with some ^{131}I positive metastases, ^{201}Tl or other nonspecific tracers can detect additional ^{131}I negative lesions (*16,17*).

CONCLUSION

We report a patient with metastasizing papillary thyroid carcinoma oxyphilic subtype, in whom neither ^{131}I whole-body scan nor measurement of serum Tg was able to indicate metastatic disease. The lack of ^{131}I accumulation in differentiated thyroid carcinoma with oxyphilic subtype is well known (*18,19*). However, the additional absence of Tg expression, as demonstrated in this case, is a rare phenomenon. For patients with oxyphilic subtype and negative Tg expression, ^{201}Tl or other nonspecific tracers may be the only tool to detect metastatic disease. Therefore, ^{201}Tl whole-body scans or other nonspecific radionuclides should be used consistently in the postoperative follow-up, especially in patients with oxyphilic subtype of differentiated thyroid carcinoma and negative immunohistochemical Tg expression.

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Visualization of Fibrous Dysplasia During Somatostatin Receptor Scintigraphy

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Somatostatin receptor scintigraphy was performed on a patient with McCune-Albright syndrome and acromegaly. No evidence of pituitary disease was found, but uptake of ^{111}In-pentetreotide was noted in areas of fibrous dysplasia. This uptake was not changed after 6 mo of octreotide therapy. The patient's bone disease also remained stable. The possible implications of these findings are discussed.

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Somatostatin receptor scintigraphy with ^{111}In-pentetreotide (OctreoScan®), a labeled form of the somatostatin analog octreotide, is used primarily in localizing neuroendocrine tumors. Sensitivities of >90% have been reported for gastrinomas, paragangliomas and carcinoid tumors (*1*) and of 70%–75%

for growth hormone (GH)-secreting pituitary adenomas (*2,3*). Specific binding also occurs in inflammation (leukocytes) (*4*), myxedema (fibroblasts) (*5*) and veins (*6,7*). We report a case of ^{111}In-pentetreotide uptake by areas of fibrous dysplasia in a patient with McCune-Albright syndrome and acromegaly.

CASE REPORT

The patient was an 11-yr-old girl with McCune-Albright syndrome manifested by café-au-lait spots, precocious puberty, goiter and subclinical hyperthyroidism and polyostotic fibrous dysplasia. She had progressive bone disease primarily involving the skull and extremities and required bilateral hip osteotomies with placement of femoral rods by age 7. Radiographic evidence of rickets also was noted and she was treated with calcitriol and phosphate supplements. At age 10, acromegaly was diagnosed with a coarsening of facial features and elevated levels of GH, insulin-like growth factor (IGF)-Type I and IGF-binding protein-Type 3 (*8*). Magnetic resonance imaging with gadolinium enhancement showed no pituitary or hypothalamic abnormalities.

Before initiating therapy with the somatostatin analog octreotide (Sandostatin®), the patient was imaged with ^{111}In-pentetreotide (4 mCi), and 4-hr whole-body images using a double-headed gamma camera and medium-energy collimators were obtained. SPECT images of the skull also were obtained at 4- and 24-hr. No intracranial abnormalities were noted, however, multiple areas of abnormally increased bone uptake were observed (Fig. 1).

After 6 mo of treatment with Sandostatin (100 μg tid), GH, IGF-Type I and IGF-binding protein-Type 3 levels had returned to normal. Indices of bone turnover (serum alkaline phosphatase, urinary hydroxyproline, urinary pyridinium cross-links), which had been fluctuating before therapy, continued to do so. Repeat ^{111}In-pentetreotide imaging performed 1 wk after discontinuation of Sandostatin was unchanged, and again revealed multiple areas of increased bone uptake. These were later correlated with lesions observed on a bone scan (14 mCi ^{99m}Tc-MDP) performed to assess extent of bone disease (Fig. 2).

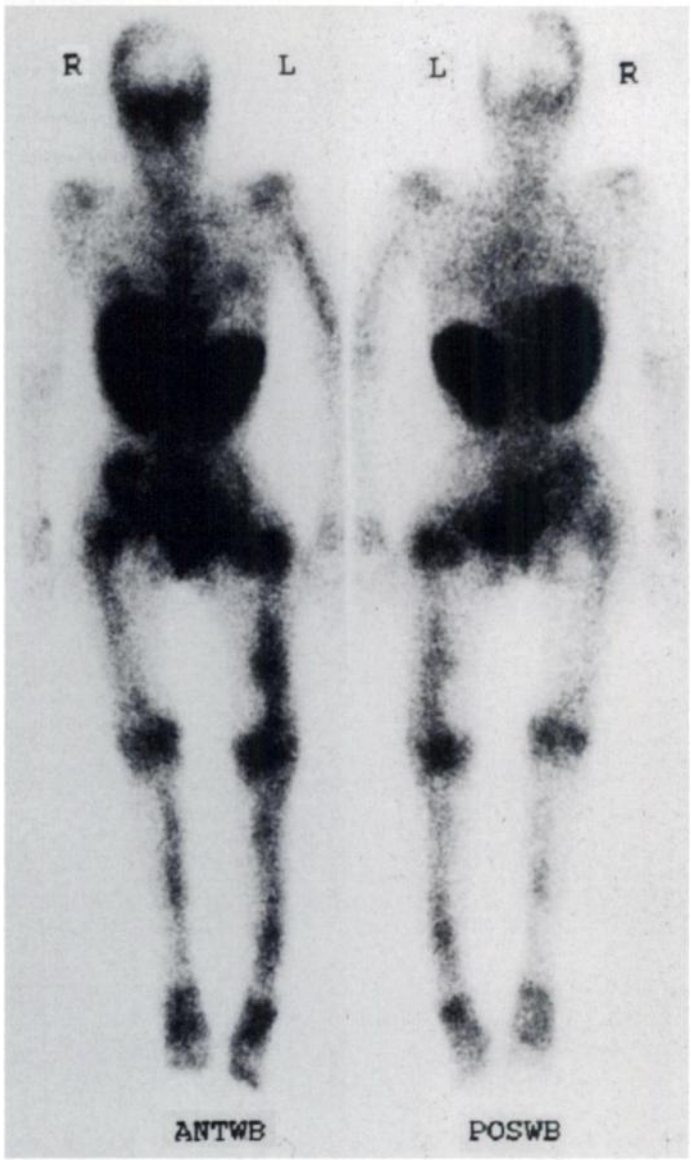

FIGURE 1. Pretreatment Octreoscan shows abnormal increased bone uptake, particularly in the skull, left humerus, left femur and right hemipelvis. Lesser increased uptake is seen in the right proximal femur and both tibias. These findings correspond to areas of fibrous dysplasia on bone scan (Fig. 2). Follow-up Octreoscan after 6 mo of therapy with Sandostatin was unchanged.

DISCUSSION

McCune-Albright syndrome, which is characterized by polyostotic fibrous dysplasia, café-au-lait spots, precocious puberty and other associated endocrinopathies such as thyroid disease and acromegaly, is thought to result from the presence of activating somatic mutations in the alpha subunit of the G_s protein (G_s α). These mutations result in increased G_s protein activity and overproduction of cyclic AMP and are thought to underlie all the varied endocrine and organ disorders observed in McCune-Albright patients including bone lesions (*9,10*).

Somatostatin receptor scintigraphy has a sensitivity of 70%–75% for detecting GH-secreting pituitary adenomas (*2,3*). However, whereas 80%–90% of patients with acromegaly have radiographic evidence of pituitary adenoma, approximately 50% of McCune-Albright patients with acromegaly do not (*11*). Thus, the negative pituitary findings with ^{111}In-pentetreotide and MRI in our patient are not suprising.

Garcia et al. (*12*) reported increased uptake of pentetreotide in the frontal bone of an adult male acromegalic patient with hyperprolactinemia and polyostotic fibrous dysplasia of the skull and right lower extremity. However, they did not specify if this finding corresponded to the area of known involvement with fibrous dysplasia in the skull. No abnormal uptake was described in the right lower extremity as the rest of the study was described as normal. In another report, Gessl et al. (*13*) observed pituitary uptake of ^{111}In-pentetreotide in a patient with atypical McCune-Albright syndrome (fibrous dysplasia and a pituitary adenoma but without the G_s α mutation). Uptake in the patient's fibrous dysplasia was not described. In contrast, abnormal uptake of pentetreotide was present in all major sites of known fibrous dysplasia in our patient, although several smaller lesions such as those in ribs were not appreciated.

The significance of increased uptake of ^{111}In-pentetreotide in fibrous dysplasia is unclear. In part, it may be due to increased delivery of the radiopharmaceutical to these lesions, which can be highly vascularized in areas (*14*). In addition, specific binding of pentetreotide to vascular beds may be occurring as described in tumors (*6*) and in the synovium of patients with active rheumatoid arthritis (*7*).

There is the possibility that somatostatin receptors are expressed by the fibrous dysplastic cells themselves. Dysplastic lesions are thought to derive from osteoblastic precursors that have been developmentally arrested by the activating G_s α mutation (*10*). Somatostatin receptors have been found in osteoblastic precursors in neonatal rat bones (*15*), and they have been implicated in regulating bone development (*16*). Inanir et

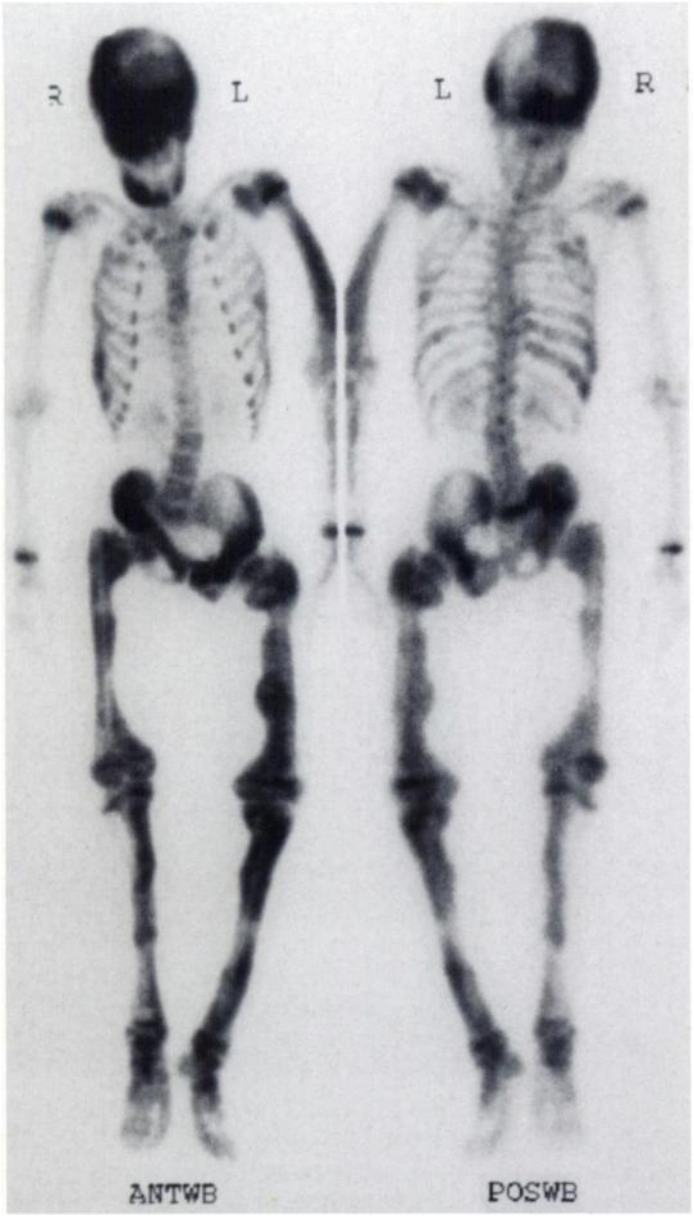

FIGURE 2. Bone scan showing multiple areas of increased uptake consistent with fibrous dysplasia. Major findings correlate with those seen on Octreoscan. The bone scan reveals additional areas of bony disease that are not seen on the Octreoscan.

al. (*17*) observed that ^{111}In-pentetreotide uptake in benign and malignant bone tumors, which could be decreased after a course of cold octreotide therapy, also suggests the presence of specific somatostatin receptors in those lesions.

If there are somatostatin receptors in fibrous dysplasia as suggested by ^{111}In-pentetreotide scanning in our patient, might there be a role for somatostatin in the pathogenesis or treatment of this disease? Somatostatin is known to act through G protein-coupled receptors and, in many organ systems, modulates function negatively by inhibiting adenylyl cyclase and decreasing production of cylic adenosine monophosphate (*18*). It inhibits both proliferation and differentiation of bone/cartilage precursor cells (*16*), and has shown some effectiveness in the treatment of osteosarcoma-bearing mice (*19*) and rats bearing chondrosarcoma (*20,21*). Somatostatin analogs may nullify the effects of the G_s α mutation and halt or reverse the progress of bone disease in McCune-Albright syndrome. However, there have been no reports documenting either positive or negative responses of fibrous dysplasia to octreotide therapy. In our patient, no changes were noted in her bone disease after 6 mo of Sandostatin, and her laboratory indices of bone metabolism continued to fluctuate as they had before therapy. We were not able to document any definite effect of Sandostatin on our patient's fibrous dysplasia. Further investigation is needed to clarify somatostatin's role, if any, in this and other bone diseases.

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