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# Adrenal Glands Imaging with Indium-111-DTPA-D-Phe<sup>1</sup>-Octreotide Following ACTH Therapy

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Somatostatin receptors have been identified in a variety of neuroendocrine tumors and activated leukocytes. A high density of somatostatin receptors is also present in most intestinal intramural veins of patients with inflammatory bowel disease. We present a case of a 25-yr-old female with severe Crohn's disease unresponsive to medical therapy, including adrenocorticotrophic hormone (ACTH) administration. The patient underwent <sup>111</sup>In-DTPA octreotide scintigraphy to evaluate the potential role of somatostatin receptor imaging in inflammatory bowel disease. Despite the lack of significant somatostatin receptors in the affected bowel, an unexpected prominent activity of <sup>111</sup>In-DTPA octreotide was noted in the adrenal glands on the SPECT images, presumably resulting from excessive stimulation by ACTH. The expression of somatostatin receptors in the stimulated adrenals may be used to image other adrenal pathologies and could potentially indicate response to therapy.

**Key Words:** somatostatin receptors; adrenocorticotrophic hormone; Crohn's disease

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**S**omatostatin is a small regulatory peptide that exerts an inhibitory effect on a broad spectrum of physiologic functions. The somatostatin analog octreotide labeled with <sup>111</sup>In-DTPA-D-Phe<sup>1</sup> is used to localize a wide variety of neuroendocrine and non-neuroendocrine tumors that possess a high number of

somatostatin receptors (1-5). In addition, tracer uptake in granulomas and inflammatory foci in autoimmune diseases was successfully imaged (6).

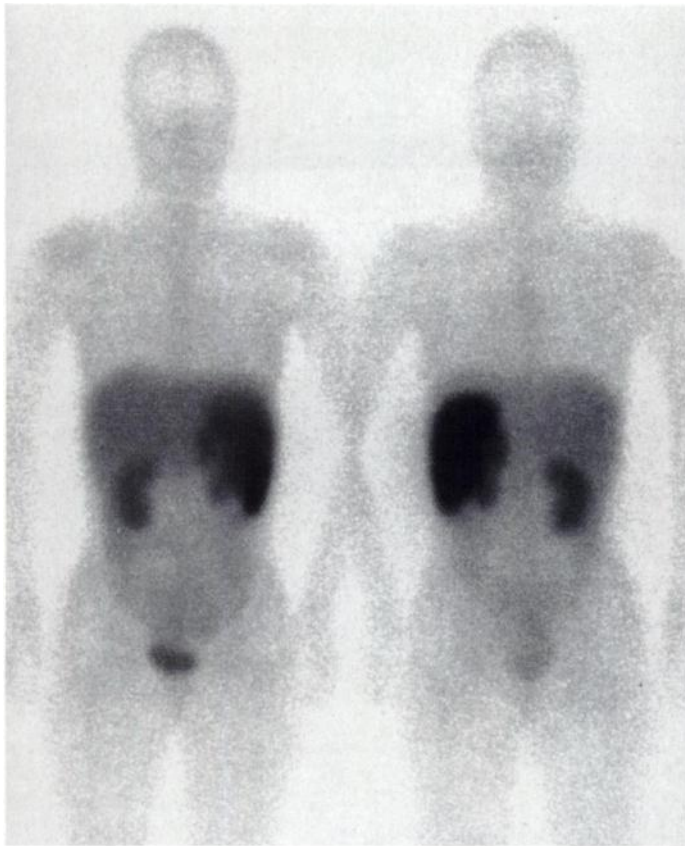
The known expression of somatostatin receptors in inflammatory cells was used in our patient to evaluate a potential role for octreotide scintigraphy in inflammatory bowel disease. A nonphysiologic stimulation by external adrenocorticotrophic hormone (ACTH) in this patient revealed an unexpectedly high receptor expression in the adrenal glands.

## CASE REPORT

A 25-yr-old woman with a history of Crohn's disease since 1981 underwent ileal resection in 1987 after developing a fistula to the bladder. In 1990, she had recurrent loose bowel movements, rectal pain, tightness and bleeding. Sigmoidoscopy revealed active Crohn's disease of the rectum and left colon. The patient was intolerant to steroids (developing psychosis) and was treated with cyclosporine, klotrix (potassium chloride) and ACTH 40 U intravenously every day. She underwent a secondary ileocollectomy and ileosigmoid anastomosis. However, the patient did not respond well to surgery. A <sup>111</sup>In-DTPA octreotide scan was performed to evaluate the potential role of somatostatin receptor imaging and determine the extent of residual inflammatory bowel disease. The patient was injected with 4 mCi <sup>111</sup>In-DTPA octreotide, followed by anterior and posterior whole-body images at 4 and 24 hr postinjection and a SPECT study of the abdomen. The planar images were unremarkable except for a large spleen (Fig. 1). The

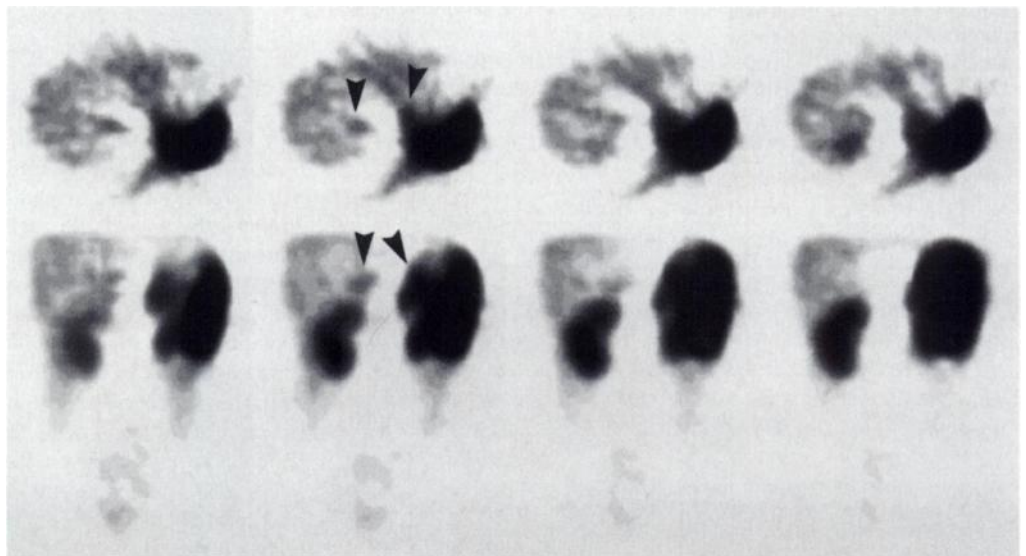
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**FIGURE 1.** Whole-body anterior (left) and posterior (right) planar images at 24 hr after injection of  $^{111}\text{In}$ -octreotide show a large spleen but no significant activity in the bowel.

SPECT study of the abdomen showed increased activity in both adrenal glands, more on the left than the right (Fig. 2). Despite the negative scintigraphic evidence of abnormal bowel activity, the patient deteriorated clinically and eventually underwent abdominoperineal resection in June 1995. The pathological examination revealed severe, active Crohn's ileitis and distal proctitis. After surgery the patient had prompt relief of her symptoms.



**FIGURE 2.** SPECT study of the abdomen with representative transaxial slices (upper row) and coronal slices (lower row) showing uptake of  $^{111}\text{In}$ -octreotide in both adrenal glands (small arrowheads).

## DISCUSSION

Somatostatin is a small cyclic peptide consisting of 14 amino acids that exerts an inhibitory effect on different organ systems in the body (7,8). The natural peptide has a short half-life in the circulation of less than 3 min, and its withdrawal causes a rebound hypersecretion of hormones. Consequently, the original molecule was modified to synthesize octreotide, consisting of eight amino acids with better pharmacokinetic properties. Various endocrine and nonendocrine tumors that contain a high number of somatostatin receptors were localized by octreotide scintigraphy (2,4). It was suggested that  $^{111}\text{In}$ -DTPA octreotide scintigraphy may be a predictor of response to palliative treatment with unlabeled octreotide. Additionally, granulomas and tissues affected by autoimmune processes can also be visualized, presumably due to the expression of somatostatin receptors in macrophages and granuloma cells (6).

In the human gastrointestinal tract, somatostatin receptors are expressed in the gastrointestinal mucosa, the peripheral nervous system and gut-associated lymphoid tissue (9). Somatostatin receptors were detected in intestinal samples of patients with Crohn's disease and ulcerative colitis, demonstrating high receptor density in most intestinal intramural veins, but not in arteries (10). The receptors remain undetectable in the veins of noninflamed control intestine. In addition, patients with ulcerative colitis were found to have a higher 24-hr amplitude, a higher average level and a sustained peak level of plasma somatostatin (11). These findings suggest a regulatory role for this peptide in the pathophysiology of inflammatory bowel disease. In contrast, our patient did not demonstrate scintigraphic evidence of increased somatostatin receptor levels in the bowel despite clinical disease and pathological evidence of florid ileitis and proctitis. A search of the literature has failed to reveal studies that suggest down-regulation of somatostatin receptors in the bowel after endogenous secretion or exogenous administration of ACTH. The affected bowel in our patient was not tested for somatostatin receptors *in vitro*.

ACTH is produced by corticotroph cells in the anterior pituitary gland and controls the release of cortisol from the adrenal cortex. Many of the patients with inflammatory bowel disease are treated with ACTH to stimulate endogenous secretion of steroids. Increased production of cortisol from the adrenal cortex may also result from hypersecretion of pituitary ACTH (Cushing's disease) or from primary adrenal

tumors. The most widely used radiopharmaceutical for imaging of the adrenal cortex is  $^{131}\text{I}$  6-beta-iodomethyl-norcholesterol (NP59), which delivers a high radiation dose, requires blocking of the thyroid gland and has a limited resolution in addition to the considerable delay from injection to imaging.

## CONCLUSION

Imaging of the adrenal cortex with  $^{111}\text{In}$ -DTPA octreotide using a SPECT technique has a good resolution, and it may potentially differentiate bilateral adrenal hyperplasia secondary to over-secretion of ACTH and increased cortisol levels secondary to primary adrenal tumors. Although octreotide scintigraphy is occasionally used to image pheochromocytomas and neuroblastomas that originate in the adrenal medulla, imaging of the adrenal cortex has not been described previously, including the large series by Krenning et al. (2) with more than 1000 patients. Follow-up scintigraphy may also be used as an indicator of the response to therapy. Further research is necessary to evaluate this issue.

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# Technetium-99m-MDP Patterns in Patients with Painful Shoulder Lesions

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There is no consensus on the optimum mode of imaging in patients with painful shoulder lesions. There is a particular paucity of scintigraphic data. As a result, the strengths and weaknesses of scintigraphy cannot be adequately compared to other imaging techniques used in shoulder imaging. This study evaluated whether specific patterns of scintigraphic abnormality could be detected in patients with painful shoulders seen in rheumatological practice using  $^{99\text{m}}\text{Tc}$ -methylene diphosphonate (MDP). **Methods:** Scintigraphic abnormalities were recorded in consecutive patients presenting to a rheumatology clinic with unilateral shoulder pain. Patients were subdivided according to patterns of clinical abnormality consistent with a working diagnosis of a lesion located in the subacromial region, adhesive capsulitis (frozen shoulder) or a lesion likely to be located in the glenohumeral joint. Patterns of radiopharmaceutical distribution in different regions of the shoulder were evaluated in the light of clinical data and the results of shoulder radiographs. **Results:** Technetium-99m-MDP scans were abnormal in 19 of 24 (79%) patients, and radiographs were abnormal in 8 of 24 (33%) patients. Distinct patterns of  $^{99\text{m}}\text{Tc}$ -MDP image abnormality were identified: an increase in  $^{99\text{m}}\text{Tc}$ -MDP uptake in the coracoid, acromion and medial humeral head on anterior planar images, together with an absence of posterior planar image abnormality, frequently occurred in association with a working diagnosis of a lesion located in the subacromial region. Posterior planar  $^{99\text{m}}\text{Tc}$ -MDP image abnormalities always occurred in patients with clinical features consistent with a diagnosis of adhesive capsulitis. There was an 85% agreement between two observers' scores when  $^{99\text{m}}\text{Tc}$ -MDP distribution in specific shoulder regions was graded. **Conclusion:** Distinct patterns of  $^{99\text{m}}\text{Tc}$ -MDP distribution may be associated with clinically-distinct

patterns of abnormality in patients with painful shoulder lesions. Further studies to elucidate a role for  $^{99\text{m}}\text{Tc}$ -MDP scintigraphy in this patient group are warranted.

**Key Words:** shoulder lesions; bone scan; technetium-99m-methylene diphosphonate

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Localizing the site of painful shoulder lesions can often be difficult due to the interdependent movement of several functional articulations that make up the shoulder joint. Clinical diagnosis frequently relies on the presence of a characteristic but complex pattern of examination findings (1). In addition, there is no consensus on the best imaging technique for identifying any specific shoulder lesion, or of the optimum imaging modality where the diagnosis is unclear (2). Available imaging methods include radiographs, arthrography (3), arthrotomography (4), CT arthrography (5,6), MRI (7) and ultrasound (8,9). The potential use of [ $^{99\text{m}}\text{Tc}$ ]pertechnetate scintigraphy for understanding the painful shoulder was recognized 20 yr ago (10). An association between  $^{99\text{m}}\text{Tc}$ -methylene diphosphonate (MDP) scintigraphic abnormalities and clinically diagnosed frozen shoulder (adhesive capsulitis) subsequently has been recognized (11). There are few if any studies, however, assessing the merits of scintigraphy, either alone or combined with other imaging modalities, in evaluating patients with shoulder pain.

We performed shoulder scintigraphy on consecutive patients presenting to a rheumatology clinic with shoulder pain. Our objective was to identify and evaluate whether specific  $^{99\text{m}}\text{Tc}$ -MDP scintigraphic abnormalities could be associated with

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