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Prostate Cancer Abdominal Metastases Detected with Indium-111 Capromab Pendetide

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To provide appropriate therapy for prostate cancer, accurate staging of the patient's disease is essential. Determination of tumor size, location, periprostatic extension and metastatic disease in the skeleton and soft tissue are needed to stage properly. Current diagnostic modalities may lead to understaging in 40%–70% of prostate cancer. Detection of metastatic disease, both at the time of initial diagnosis and in patients with suspected local recurrence, can significantly alter the type of therapy given. Clinical studies using the ^{111}In radiolabeled immunoconjugate, MAb 7E11-C5.3-GYK-DTPA (capromab pendetide), have shown the superiority of radioimmunoscintigraphy over other diagnostic modalities in the detection of both primary and metastatic prostate cancer. Radioimmunoscintigraphy with capromab pendetide depends on expression of tumor-associated antigen rather than lesion size. Earlier detection of extraprostatic invasion and metastases by means of radioimmunoscintigraphy provides valuable information for treatment decisions. A case of metastatic prostate cancer in the abdomen of a patient without local disease, in which the extent of disease was confirmed at autopsy after sudden cardiac arrest, is presented.

Key Words: prostate cancer; indium-111; capromab pendetide; radioimmunoscintigraphy

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CASE REPORT

A 50-yr-old man was found on routine physical examination to have an elevated prostate-specific antigen (PSA) level (20.3 ng/ml) and an enlarged prostate by digital rectal examination. After biopsy, the initial diagnosis was moderately-to-poorly differentiated prostatic carcinoma involving both lobes. His past medical history was otherwise unremarkable and he was not taking any medication. CT of the abdomen and pelvis and a radionuclide bone scan revealed no evidence of metastatic disease. A radical prostatectomy was performed, and histopathologic examination showed a solitary micrometastasis in a left obturator lymph node. Moderately differentiated (Gleason 6) adenocarcinoma was found in both prostatic lobes. Local margins were free of tumor including urethral and bladder margins (Stage 4, T3, N1, M0). Postoperatively, the patient did well clinically and his postoperative 1-mo PSA level was < 0.5 ng/ml. However, 5 mo after surgery, the PSA had increased to 1.4 ng/ml and at 8 mo it had risen to 2.4 ng/ml. Needle biopsy of the prostatic bed was negative. Radionuclide bone scan disclosed no evidence of skeletal metastatic disease.

The patient was enrolled in a clinical study involving radioimmunoscintigraphy with ^{111}In capromab pendetide. This recently FDA-approved radiopharmaceutical is composed of the antibody, 7E11.C5, which recognizes PSMA or prostate-specific membrane antigen (*1*). At this time, his PSA level was 6.1 ng/ml and peroxidase-antiperoxidase (PAP) level was 0.3 U/liter. No other lab values were abnormal. The patient denied bone pain, weight loss and urologic symptoms. An MRI of the abdomen and pelvis showed no evidence of lymphadenopathy. The patient received 203.5 MBq (5.5 mCi) ^{111}In capromab pendetide and whole-body and SPECT images were completed 4 days later. Uptake was noted in the upper abdomen at the level of the upper pole of the left kidney (Figs. 1 and 2). A second finding was an increased uptake at the aortic bifurcation (Figs. 2 and 3).

Based on these results, the patient was started on hormonal therapy. Four days later, he died at home of sudden cardiac arrest. At autopsy, no grossly residual tumor was identified in the pelvic cavity. Several enlarged periaortic lymph nodes were found in the upper left abdomen corresponding to positive uptake on the nuclear medicine images. Metastatic prostate cancer was identified in two of these, as well as in two of four nodes at the level of the aortic bifurcation. A solitary 1-cm nodule with central necrosis that was shown to be a benign adenoma was identified in the lower pole of the left kidney.

Samples of the tumor-positive periaortic and aortic-bifurcation lymph nodes were sent for PSMA and PSA expression determination along with a portion of the left kidney mass. Two lymph nodes from the aortic bifurcation area showed approximately 70% of the cells positive for PSMA with moderate (2+) to strong (3+) staining intensity. All tumor cells also were PSA (+) and displayed strong (3+) stain intensity. A third lymph node from the same area was negative for both tumor and PSMA and PSA staining. Two lymph nodes from the periaortic area showed 90% of the tumor cells positive for PSMA with moderate (2+) to strong (3+) staining intensity. A small foci of tumor in a third lymph node also stained positive for PSMA. All three nodes stained 100% for PSA with a strong (3+) staining intensity. As expected, the adenoma of the left kidney was nonreactive.

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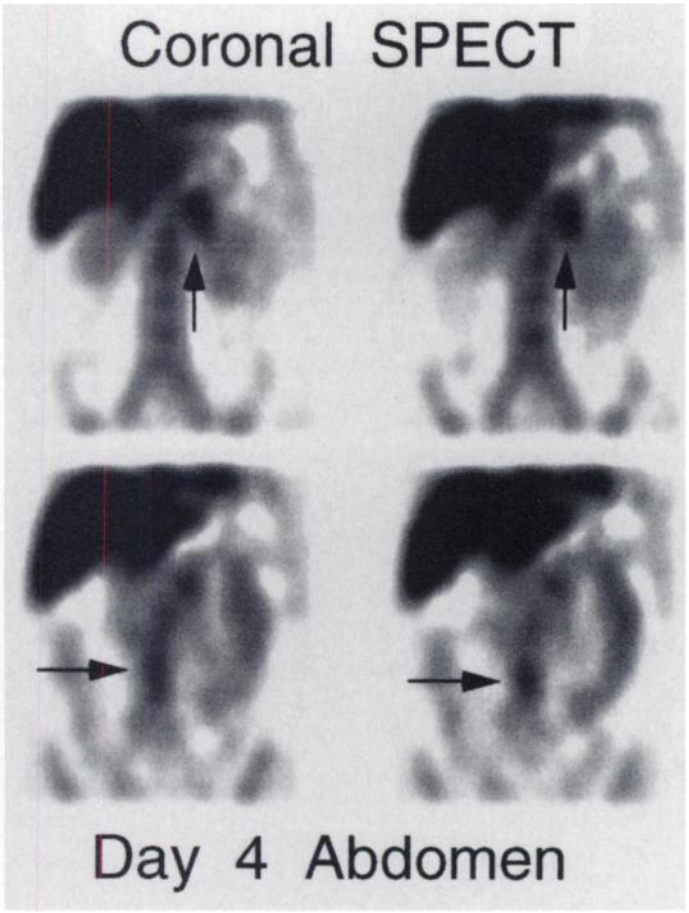

FIGURE 1. Day 4 coronal SPECT images of the abdomen. Arrows in the two lower images point to localization in lymph nodes near the aortic bifurcation. Arrows in the upper two images point to uptake in lymph nodes in the periaortic area just left of midline.

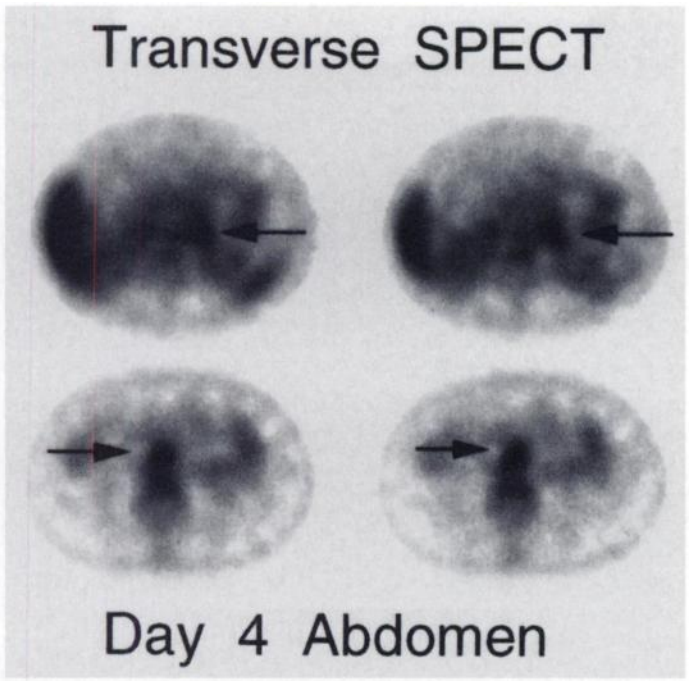

FIGURE 2. Day 4 transverse SPECT images of the abdomen. Uptake in lymph nodes near the aortic bifurcation is indicated with arrows in the two lower images. Uptake in periaortic lymph nodes on the left side of the patient is indicated by arrows in the upper two images.

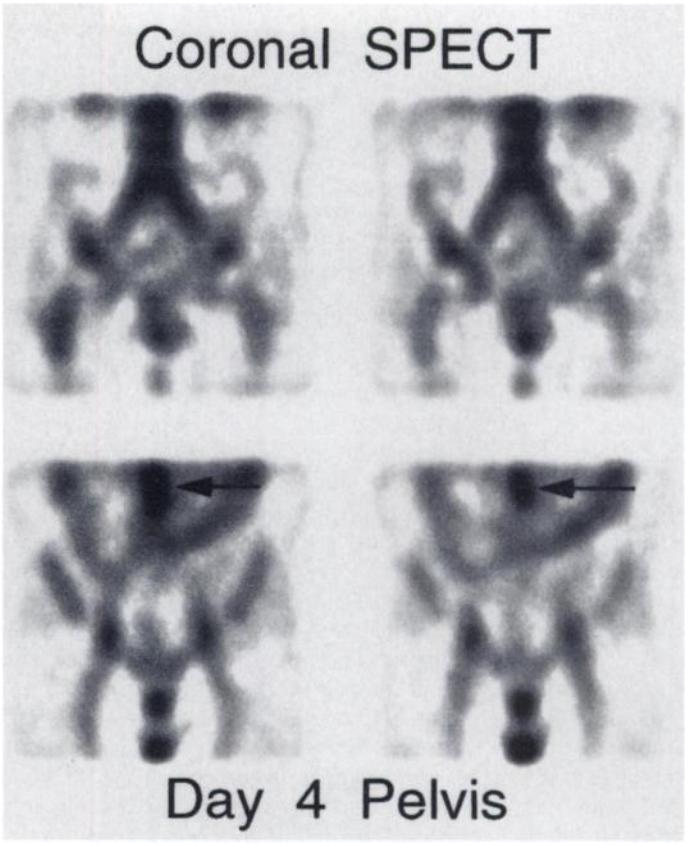

FIGURE 3. Day 4 coronal SPECT images of the pelvis. Arrows in the two lower images point to localization in lymph nodes near the aortic bifurcation.

DISCUSSION

Adenocarcinoma of the prostate is the most common solid tumor in adult men with more than 300,000 new cases and more than 40,000 deaths attributed to this malignancy in 1996 (*2*). Once the diagnosis of adenocarcinoma has been made through biopsy, guided by transrectal ultrasound, clinical staging of the disease must be completed.

Accurate staging is the dominant factor in selecting the appropriate therapeutic modality. Therefore, staging is critical to enhanced patient management and cost-effective treatment. Physical examination, CT and/or MRI of the abdomen and pelvis, radionuclide bone scans and biochemical markers, such as PSA and PAP, are used in combination to determine if the disease has spread beyond the prostate or has recurred after therapy.

Imaging modalities such as CT and MRI frequently lead to clinical understaging of prostate cancer with neither modality being sufficiently accurate to determine the extent of disease within the prostate (*3–5*). Both have limited use in the detection of direct extraprostatic extension and reportedly only 18%–45% sensitivity in the detection of lymph node metastases (*6,7*).

Digital rectal examination is the first diagnostic test used to determine if there has been local recurrence after radical prostatectomy (*6*). The detection of thickened tissue or mass lesions suggests recurrence. Digital rectal examination cannot distinguish between tumor and scar tissue resulting from original surgery. In fact, the patient reported by us had a smooth, flat rectal fossa consistent with scar tissue. Furthermore, digital rectal examination only provides evidence for local recurrence, not metastatic disease. Transrectal biopsy of the surgical site is another procedure used to evaluate local recurrence. Although in the present case report, only two locations were biopsied in the prostatic fossa, the negative biopsy was supported by the

capromab pendetide imaging and confirmed by the autopsy finding.

Pelvic lymphadenectomy can accurately stage pelvic lymph node spread of the disease (*8*). However, presence or absence of pelvic lymph node disease does not unequivocally predict malignancy since greater than 50% of pelvic node negative patients may still have aortic lymph node metastases (*9*). The patient described in this case report had involvement of a left obturator lymph node at the time of pelvic lymphadenectomy and radical prostatectomy. In addition, there was extensive capsular penetration with the tumor invading the pericapsular fat. These findings, along with the short time interval from surgery to the appearance of rising serum PSA levels, are indicators of tumor dissemination (*6*). Unfortunately, conventional imaging modalities failed to detect the extensive nature of our patient's disease preoperatively or the presence of distant spread postoperatively. Using conventional methods, the typical dilemma for treatment was presented with this patient: treatment based on a rising serum PSA value with no radiographic confirmation of disease.

Choosing the appropriate treatment of postprostatectomy biochemical failure is difficult and controversial because of the lack of diagnostic modalities that can accurately identify where local or regional recurrence exists. Patients have the choice of watchful waiting, radiotherapy or hormonal therapy. But it is impossible to make the best decision without knowing where the cancer is located. For example, irradiation of the prostatic bed with curative intent has only shown modest durable response. Initial responses of 67%–80%, as measured by decreases in the serum PSA value, remain low or undetectable in only 26%–43% at 18–30 mo postirradiation (*10–12*).

Our studies with ^{111}In capromab pendetide have shown that approximately 60% of patients with an increasing serum PSA level postprostatectomy have evidence of distant metastases as was demonstrated and histologically confirmed in the patient presented here (*13*). Obviously, patients with disease outside the prostate bed will fail local adjuvant irradiation.

The recently FDA-approved ^{111}In capromab pendetide is an IgG1 murine monoclonal antibody conjugated with the chelator GYK-DTPA to form an immunoconjugate that can be readily labeled using high purity ^{111}In-chloride. This antibody reacts with a prostate specific membrane glycoprotein expressed by benign and malignant prostatic epithelial cells but not with secretory glycoproteins such as PSA or PAP (*14*). This helps explain the findings in clinical studies of the failure to correlate ^{111}In capromab pendetide imaging results with serum tumor markers with lesions being reported in patients with both high and low tumor marker levels (*13,15,16*). A major advantage of ^{111}In capromab pendetide imaging is the ability to evaluate the entire body for metastases. Detection of occult metastases can have a major effect on clinical staging in patients with both primary and recurrent disease (*13*).

CONCLUSION

Several reports have shown ^{111}In capromab pendetide can detect soft-tissue recurrences of prostate cancer in the prostatic fossa and in extraprostatic including distant metastases (*13,16–18*). These studies also suggest the clinical use of ^{111}In capromab pendetide imaging. The study can assist in determining the extent of disease in patients who demonstrate biochemical failure after definitive primary therapy. CT and MRI often fail to differentiate between tumor lesions and benign anatomic changes and are not as specific as the antigen-antibody uptake system used for cancer detection with ^{111}In capromab pendetide. In addition, CT and MRI cannot detect small tumor nodules in the absence of lymphadenopathy (*19–21*). Imaging with ^{111}In capromab pendetide provides a more accurate presurgical staging in patients at high risk for local spread of the disease as well as a method for earlier detection of recurrences.

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