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RADIOIMMUNOGUIDED SURGERY USING INDIUM-111 CAPROMAB PENDETIDE (ProstaScint) TO DIAGNOSE SUPRACLAVICULAR METASTASIS FROM PROSTATE CANCER

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ABSTRACT

A 59-year-old man presented with a Gleason score of 4 + 4 = 8 prostate cancer and with multiple bilateral pelvic nodes involved at open pelvic lymph node dissection. On indium-111 capromab pendetide (ProstaScint) scan, there was increased tracer deposition in the prostate, the mesenteric nodes, the right pulmonary hilum, and the left supraclavicular fossa. The ProstaScint injection was repeated, and the gamma probe was used to localize tissue that accumulated radiotracer. Two nodes were excised, one that exhibited increased uptake and one that did not. The radioactive lymph node contained metastatic prostate cancer. No malignancy was found in the second node. UROLOGY **56:** 669xii–669xiv, 2000. © 2000, Elsevier Science Inc.

The goal of assessment in the patient newly diagnosed with adenocarcinoma of the prostate is the determination of the extent of spread of the disease. By combining the use of indium-111 capromab pendetide (ProstaScint) (Cytogen, Princeton, NJ) with the use of the Navigator Gamma Guidance System (NGGS; Auto Suture, Norwalk, Conn), it was possible to facilitate the pathologic diagnosis of a left supraclavicular metastasis in a newly presenting prostate cancer patient.

CASE REPORT

A 59-year-old man presented with a prostate-specific antigen (PSA) level that rose from 1.5 to 7.4 ng/mL in 1 year. Biopsy of the prostate was positive for involvement with a Gleason score 4 + 4 = 8 adenocarcinoma in 7 of 7 sampled cores. On nodal sampling prior to prostatectomy, multiple bilateral pelvic nodes macroscopically involved with metastatic prostate carcinoma were found. The patient requested pelvic radiotherapy, and a ProstaScint scan was obtained to assess the patient's suitability. Following the intravenous administration of 5 mCi of ProstaScint, SPECT imaging was performed on day 0, on day 4, when planar images of the chest, abdomen, and pelvis were also performed, and again on day 5. There was increased tracer deposition seen on days 4 and 5 within the left mid-abdomen. Rounded foci of increased tracer deposition were aligned in a curvilinear pattern, extending from the periaortic region to a level medial to the spleen (Fig. 1). No abnormal uptake was demonstrated in this region on day 0, and there was no change in the pattern seen between days 4 and 5. No increased uptake was seen within the periaortic nodal chain. Tracer accumulation occurred within the prostate bed consistent with the patient's known prostate malignancy. There was increased focal tracer deposition in the medial left supraclavicular region as well as punctate accumulation in the right mid-lung lateral to the hilum, suggestive of metastatic disease (Fig. 2). Subsequent computer tomographic images failed to reveal any abnormalities.

Rather than perform a blind biopsy to confirm metastatic disease, it was elected to repeat the ProstaScint administration. Imaging was repeated on day 4, and the previously described pattern of radiotracer accumulation was again seen. By using the NGGS (Fig. 3), an open biopsy was performed in the operating room under local anesthesia. A mildly enlarged lymph node located in the medial portion of the left supraclavicular fossa had accu-

R. S. Anderson owns stock in the manufacturer of the product mentioned in this article.

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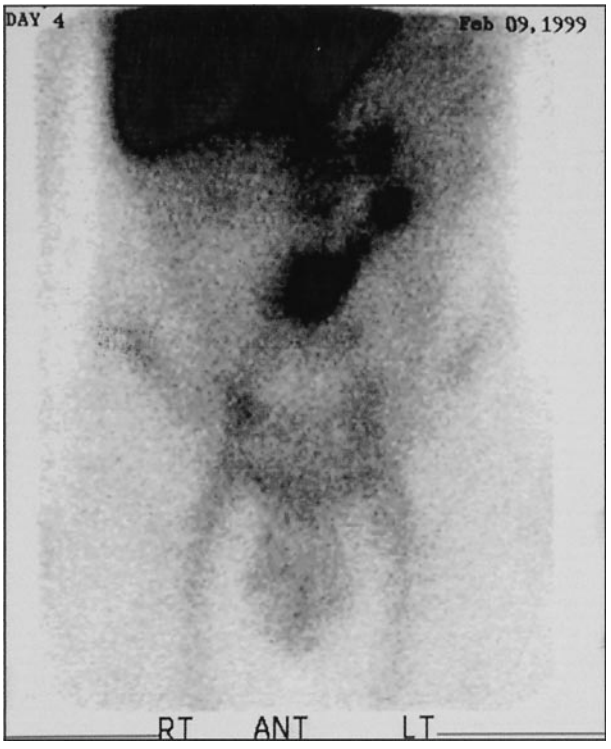

FIGURE 1. *Abnormal uptake of ProstaScint within multiple mesenteric lymph nodes in a patient with carcinoma of the prostate.*

FIGURE 2. *Suspicious deposition of ProstaScint within a single left supraclavicular lymph node.*

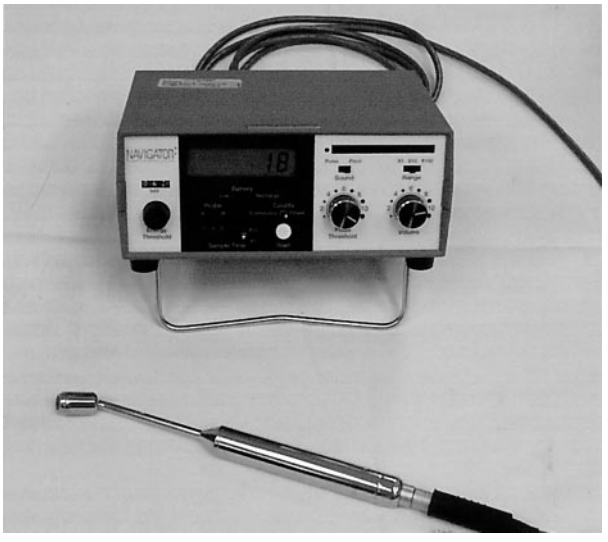

FIGURE 3. *The Navigator Gamma Guidance System produced by the Auto Suture Company, Norwalk, Conn.*

mulated radiotracer and was excised. A second node, similar in size and appearance, that did not accumulate tracer was also excised. The radioactive tissue contained a 1.7 × 1.5 × 1.2 cm lymph node. The lymph node was noted to have malignancy present in the peripheral sinuses compatible with a prostatic origin. The ProstaScint negative tissue contained a 0.9 × 0.7 × 0.6-cm lymph node that showed no evidence of metastatic malignancy. Special stains were performed by Bostwick Laboratories (Richmond, Va) and revealed the metastatic tumor to be only minimally immunoreactive for PSA with less than 5% of cells staining positive. Virtually every cell was strongly immunoreactive with prostatic acid phosphatase (PAP), and 80% of cells demonstrated immunoreactivity to prostate-specific membrane antigen (PSMA). The patient was placed on total hormonal ablative therapy.

COMMENT

With the demonstration of pelvic metastasis at staging lymphadenectomy, the purpose of further evaluation was to determine whether or not metastatic disease existed beyond the pelvis. Pelvic radiotherapy, with a boost delivered to known disease, may cure cases in which disease is limited to the pelvis. Pilepich *et al.*[1] in their analysis of 448 patients randomized in RTOG 75-06 observed no significant difference in survival in patients with Stage C cancer between those patients with positive nodes and those with uninvolved nodes when treated to adequate irradiation volumes. To assess the effect of positive nodes in various locations, Bagshaw *et al.*,[2] in a review of radiotherapy patients, reported disease-free survival of 86% for those patients with negative nodes, 71% for those with positive pelvic lymph nodes, and 30% for those with positive periaortic

nodes. The treatment of positive pelvic lymph nodes, however, remains a controversial issue.

To evaluate metastatic spread, a ProstaScint scan was performed in the manner previously described. ProstaScint is the immunoconjugate, indium-111 capromab pendetide. It is the immunoglobulin G1 class murine monoclonal antibody 711-C5.3 directed against a prostatic epithelial glycoprotein, PSMA. PSMA is a membrane-bound antigen that is distinctly separate from secretory antigens, such as PSA and PAP.[3] Quantitative expression of PSMA is higher in prostate carcinoma than in normal tissues and greater yet in metastatic deposits.[4] Capromab pendetide is linked to the radioisotope indium-111 that decays to produce photons of two energies useful for detection, with mean energies of 171.3 and 245.4 keV.[5] Manyak *et al*.[6] used ProstaScint prior to pelvic lymph node dissection to evaluate 152 prostate cancer patients felt to be at high risk for pelvic nodal metastasis. Positive pelvic lymph nodes were found in 64 patients; 40 had been detected by the scan, yielding a sensitivity of 62%. Of the 88 patients found to be node negative, 63 had negative preoperative scans, with a specificity of 72%.

The initial scan in this patient was suspicious for metastatic spread, but the pattern was atypical. Periaortic nodes were not seen to accumulate radiotracer. However, a pattern consistent with mesenteric involvement was seen, as well as localized accumulation of radiotracer in the left medial supraclavicular fossa and the right pulmonary hilum. In a review of 753 cases in which prostate cancer was found at autopsy, Saitoh *et al*.[7] analyzed the distribution of metastasis according to whether nodal involvement was seen in the pelvic nodes, the periaortic nodes, both, or neither. In a cohort of 63 patients found to have pelvic nodal involvement without evidence of periaortic involvement, 7 (11%) were found to have spread to the cervical or supraclavicular nodes, 13 (21%) had involvement of the pulmonary hilar nodes, and 2 (3%) exhibited mesenteric spread.

To pursue pathologic confirmation of metastatic disease, the supraclavicular area was chosen because it could be easily biopsied under local anesthesia. Radioimmunoguided surgery (RIGS) is a technique described by Martin *et al*.[8] and used primarily in colorectal cancer, but it has been tried in breast,[9] lung,[10] and prostate[11] cancers as well. ProstaScint was thought to be the best agent to guide the nodal sampling. It has been found to have very low human anti-mouse antibody titers following administration. In repeat administrations, 93% of the studies demonstrated normal tissue distribution of the immunoconjugate. Adverse reactions were reported in 4% of single-dose administrations and in 5% of repeat administrations.[12] The patient was brought back on day 4 after injection, and, on rescanning, the pattern of uptake was unchanged. The area of uptake in the left supraclavicular fossa was tattooed on the skin surface. In the operating room, an incision was made in the left supraclavicular fossa, and the NGGS was used to locate radioactive tissue. The probe has an energy detection window of 90 to 511 keV. This range encompasses both of the major photons released in the decay of indium-111.

RIGS involves the intravenous injection of a biologically specific agent to systemically target lymphatic and visceral tissues expressing the target antigen. Whether ProstaScint-guided RIGS can be used to enhance sampling accuracy remains to be tested, but it is deserving of further investigation. The demonstration of PSMA-positive metastatic disease outside the abdomen indicates that this technique may prove useful in confirming disease beyond the pelvic and periaortic lymph nodes.

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