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Autopsy of a Cadaver Containing Strontium-89-Chloride

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An autopsy was performed on a patient who died after receiving ^{89}Sr-chloride for treatment of bone pain from metastatic prostate carcinoma. Coordination between nuclear medicine physicians, radiation safety division personnel and pathologists resulted in minimal radiation exposure and the acquisition of dosimetry data.

Key Words: strontium-89-chloride; metastatic carcinoma; autopsy; biodistribution studies

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Strontium-89-chloride has proven efficacy in the treatment of bone pain associated with metastatic prostate (*1,2*) and metastatic breast carcinoma (*1–3*). Patients who receive ^{89}Sr therapy have advanced metastatic disease, and many are markedly debilitated. Although ^{89}Sr-chloride is generally reserved for patients who have a life expectancy of at least a few months, occasional deaths may occur soon after treatment.

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CASE REPORT

An 83-yr-old man with Stage C prostate carcinoma and pain associated with widespread bony metastases [confirmed by bone scan (Fig. 1)] was referred to the nuclear medicine division for ^{89}Sr-chloride therapy. The patient had no other known significant medical problems. He was treated with 162.1 MBq (4.38 mCi) ^{89}Sr-chloride [$T_{1/2}$], 50.5 days, beta Emax 1.463 MeV(100%)], intravenously, given over 2 min. Because of difficulty adequately managing the patient's pain at home, prior arrangements had been made for the patient's admission to the hospital after administration of strontium. The patient was therefore admitted to the hospital, in stable condition, after his discharge from the nuclear medicine clinic. He died approximately 4 days later.

The body was not moved until the radiation safety staff arrived and performed appropriate safety surveys with a thin window "pancake" Geiger-Mueller detector to determine levels of contamination. The body was then tagged, wrapped in bed linens, transported to the morgue using universal precautions and autopsied.

Two pathologists and a technologist conducted the autopsy 1 day after the patient's death (i.e., 5 days after ^{89}Sr treatment). Before proceeding, each member of the pathology staff donned two pairs of standard latex surgical gloves, a standard polyester surgical

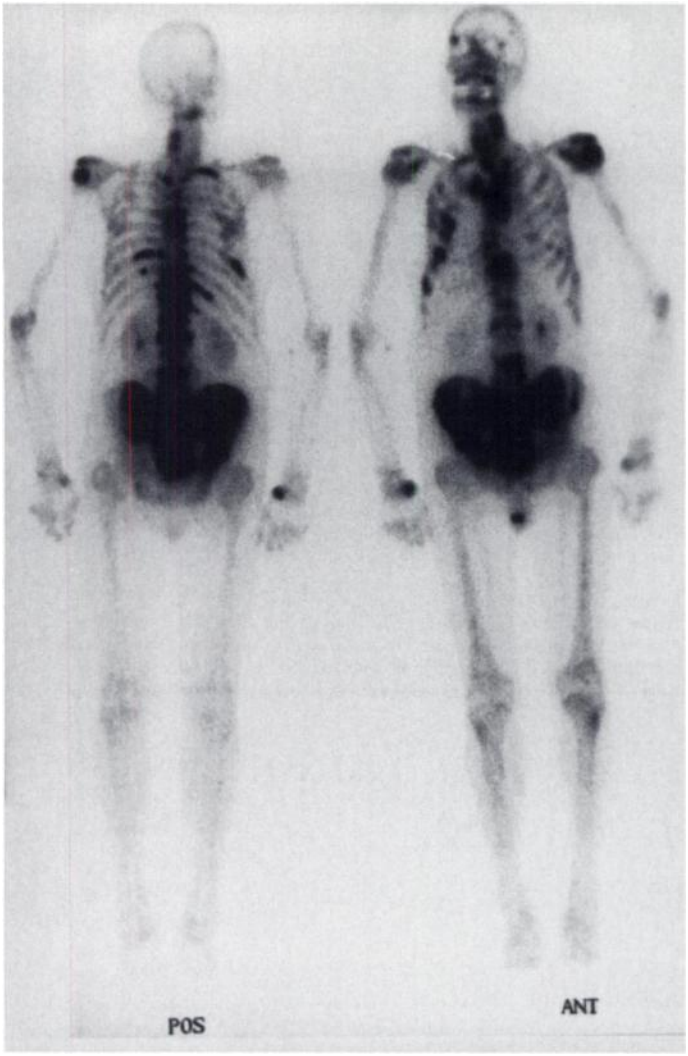

FIGURE 1. Whole-body bone scan performed 3 hr after the intravenous administration of ^{99m}Tc-MDP.

gown, a waterproof apron (worn over the surgical gown), a surgical mask, a plastic face shield and paper shoe coverings. Additionally, Pathologist 1 wore a cut-resistant nylon mesh glove on her left hand, and Pathologist 2 wore one of these gloves on each hand. Each of the people performing the autopsy was also issued a whole-body dosimeter (consisting of four TLD chips and filters) designed to record skin exposures and deep dose equivalent, which each wore on his or her surgical gown collar (under the above-noted multiple layers of clothing). Each member of the pathology staff also wore a TLD finger ring on each hand under the gloves. A standard GM detector with a thin window was used to make measurements of the patient and his organs, the autopsy equipment and the background.

DISCUSSION

Our detector system, the ANPDR-27 (a standard GM detector with an open, thin, mica end window) provided readings in mr/hr. Although these mr/hr measurements were useful for comparing the relative amount of activity at various locations (assuming beta radiation from or close to the surface of the organ or material being measured is representative of the concentration), measurements of actual activity concentration would also be of interest. We therefore calibrated our detector to allow conversion of a mr/hr reading to an activity concentration in μCi/cc. This was done by preparing a 3000-ml dilute solution of ^{89}Sr Cl (0.049 μCi/cc) in water and obtaining

TABLE 1
Activity and Concentration Measurements

Location or organ	5-cm measurement distance	
	mr/hr	μCi/cc
5 cm below xiphoid (omentum in place)	0.40	0.02
5 cm below xiphoid (omentum removed)	0.35	0.02
at umbilicus (omentum in place)	0.12	0.01
at umbilicus (omentum removed)	0.42	0.05
Lumbar spine metastasis (organs removed)	1.90	0.21
Right lung	0.48	0.05
Left lung	0.41	0.02
Heart	0.20	0.03
Liver	0.30	0.02
Spleen	0.16	0.02
Right kidney	0.20	0.02
Left kidney	0.22	0.02
Bladder	0.30	0.03
Small bowel	0.35	0.40
Large bowel	0.36	0.04
Stool	2.30	0.26
Supraorbital skull	0.80	0.09

readings with the GM detector at 5 cm from the surface of the solution through a plastic container. We assumed the cumulative bremsstrahlung effect of plastic and water are similar to tissue. This dilution was chosen empirically to give detector readings in the same range as those recorded from the cadaver. A 1-mr/hr reading was obtained from this solution. This number was then used to obtain a crude approximation of the ^{89}Sr concentration in each of the organs and areas measured. During the autopsy, which lasted approximately 2 hr, measurements were made at various locations above the surface of the body and inside the body cavity. Additionally, a measurement was taken at 5 cm above the surface of each organ, after the organ was removed and isolated. The results of these measurements are provided in Table 1. The data indicate that ^{89}Sr is fairly evenly distributed throughout the soft tissue organs of the body. The bone and stool displayed significantly higher activity concentrations than did the soft-tissue organs. The large metastatic deposit in the lumbar spine was found to have a concentration of ^{89}Sr over twice that of normal bone in the skull. This latter observation correlates well with observations made by Breen et al. (*7*) concerning the ratio of ^{89}Sr concentration in metastatic lesions compared with normal bone. The relatively large fecal concentration was also anticipated in light of the fact that approximately one-third of the ^{89}Sr clearance occurs via the bowel (*8*).

Personnel whole-body (skin and deep) and hand exposures (measured in rem) received during the autopsy were "0.000" for all autopsy participants. This can be explained by analysis of ^{89}Sr biodistribution. Total retention of ^{89}Sr after 4 days is estimated to be approximately 50%, with approximately 1% being in the extracellular fluids. Except for that in the extracellular fluids, the ^{89}Sr is assumed to be bound to bone. If the unbound ^{89}Sr is fairly evenly distributed, we would not have expected measurements of the radioisotope in the various organs to differ significantly; and this is what was observed. Based on these same estimates and assumptions, approximately 200 μCi were expected to be distributed outside of the bone, giving a concentration of approximately 0.07 μCi/cc. This is in fair agreement with the concentrations determined from our crude analysis (i.e., 0.02–0.05 μCi/cc). Because the beta radiation cannot, for the most part, penetrate more than 0.8 cm

in tissue, exposure to the staff would be from activity located within the first 0.8 cm of the body and would represent a potential exposure hazard only to their hands. Assuming 25% of the 200 μCi of activity is distributed within the first 0.8 cm of the peritoneal wall, and the hands remain in the cavity for a total of 1 hr (a significant overestimation), an exposure of 0.05 mCi-hr would result. Using this information and data from *NCRP Handbook No. 37* (*4*) for radiation dosimetry for ^{32}P {assuming that ^{89}Sr is roughly equivalent to ^{32}P [T1/2–14.3 days, beta Emax 1.7 MeV (100%)]} in terms of dosimetry (when in fact, the beta energy in ^{89}Sr is less) and that the pathology staff wore two sets of autopsy gloves, the calculated dose to the hands would be 15 mrem, and the whole-body dose would be significantly less. Fifteen millirem is below the minimum detection level for the dosimeters worn by the pathology staff, and thus the readings of "0.000" are expected.

CONCLUSION

We have documented that an autopsy can be safely performed on a patient who dies within a short interval after receiving a standard dose of ^{89}Sr-chloride. Additionally, our measurements have corroborated previously published kinetic and biodistribution data concerning ^{89}Sr-chloride.

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Effect of Hyperglycemia on In Vitro Tumor Uptake of Tritiated FDG, Thymidine, L-Methionine and L-Leucine

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We have previously demonstrated in vitro and in vivo that tumor uptake of FDG is markedly diminished by acute hyperglycemia. This in vitro study was designed to determine if tumor uptake of PET tracers (FDG, thymidine, L-methionine and L-leucine) is affected by acute or chronic hyperglycemia. **Methods:** Human ovarian adenocarcinoma (HTB 77 IP3) cells were grown in media containing 100 or 300 mg/dl of glucose. At 7, 20, 38, 51 and 72 days after initial culture, uptake of ^{3}H-labeled FDG, thymidine, L-methionine and L-leucine into the cells was determined in the presence of 100 or 300 mg/dl of glucose. **Results:** With acute hyperglycemia (300 mg/dl of glucose), the percent decreases in uptake of FDG, thymidine, methionine and leucine were 76.7%, 22.4%, 7.4% and 11.1%, respectively, as compared to assay at 100 mg/dl of glucose (mean day 51 and day 72 data). Significant decreases were observed in FDG and thymidine uptake with acute hyperglycemia ($p < 0.0005$). When cells grown at 300 mg/dl of glucose for 51 and 72 days were assayed at 100 mg/dl of glucose, the mean percent decreases in uptake of these tracers were 10.4%, 7.8%, 8.0% and 16.8%, respectively, as compared to cells grown and assayed at 100 mg/dl of glucose. No significant decrease was observed in tumor uptake of these tracers, except for leucine ($p < 0.05$). **Conclusion:** These human adenocarcinoma cells do not significantly change FDG uptake with chronic hyperglycemia while acute hyperglycemia markedly reduces uptake of FDG and thymidine. Neither methionine nor leucine uptake is significantly affected by acute hyperglycemia. To optimally evaluate tumor biology by PET, the fasting state seems necessary for FDG and thymidine studies, while methionine or leucine appears more suitable for hyperglycemic patients.

Key Words: fluorodeoxyglucose; nucleotide and amino acid uptake; hyperglycemia; cancer cell line; PET tumor tracers

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Previous in vitro and in vivo studies have demonstrated the feasibility of using positron-emitter labeled 2-fluoro-2-deoxy-D-glucose (FDG) (*1-10*). Thymidine and amino acids such as L-methionine and L-leucine are used to detect malignant lesions, which allow accurate staging of cancers and monitor therapeutic effects. We have previously reported that tumor FDG uptake is markedly diminished by acute hyperglycemia in vitro and in vivo because of direct competition between FDG and D-glucose for tumor uptake (*11,12*). In human studies, FDG-PET images obtained in either the fasting state or the glucose-loaded state have demonstrated that tumor FDG uptake is decreased, and thus the PET image quality is impaired when plasma glucose levels are increased (*13,14*). These results suggest that patients should fast before FDG-PET studies and their plasma glucose concentration needs to be considered when assessing tumor glucose metabolism (*15*).

Since many patients are diabetic and some diabetic patients also have cancers, it is important to determine if chronic exposure of cancer cells to hyperglycemia may influence glucose metabolism. In addition, little is known about the effect of acute or chronic hyperglycemia on tumor uptake of non-

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