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Skeletal Muscle Uptake of Fluorine-18-FDG: Effect of Oral Diazepam

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We have observed a pattern of symmetrically increased uptake of [^{18}F]fluorodeoxyglucose (FDG) in the neck and thoracic paravertebral regions of several patients referred for whole-body PET. The distribution is suggestive of uptake in contracting skeletal muscle in tense patients. **Methods:** To test this hypothesis, six successive patients who exhibited this pattern of uptake underwent rescanning using an identical imaging protocol but with oral diazepam before injection of FDG. **Results:** The increased neck and paravertebral uptake was significantly reduced or abolished with diazepam, confirming the supposition that this increased neck and paravertebral uptake represents a normal variant of muscle uptake. **Conclusion:** Oral diazepam given before the uptake period can be helpful in such patients to exclude the masking of potential abnormalities by this characteristic pattern of FDG uptake.

Key Words: fluorine-18-fluorodeoxyglucose; muscles; glucose metabolism; diazepam

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Whole-body [^{18}F]-fluorodeoxyglucose (FDG) PET is used in oncology to stage patients at initial presentation and to assess tumor recurrence and the effects of therapy (*1–3*). We have observed a distinctive pattern of symmetrical uptake of FDG in the neck and thoracic paravertebral region of several patients referred for whole-body imaging. The distribution is suggestive of uptake in contracting skeletal muscle in tense patients, but can be of sufficient intensity to mask true potential sites of disease, particularly in the cervical and supraclavicular regions. To test our hypothesis that this uptake was physiological, we rescanned six patients who exhibited this pattern of FDG uptake after administration of oral diazepam.

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MATERIALS AND METHODS

Patients

Consecutive patients referred for whole-body scans between March 1994 and April 1995 who exhibited symmetrical FDG uptake in the neck or paravertebral region were recalled within 6 wk of their initial scan for repeat imaging. Referring clinicians were advised that repeat scans were required to assess whether the uptake represented pathological lymph node involvement or normal muscle activity. The patients did not receive any treatment in the interval between scans. The indications for initial scanning in five patients restudied were to assess the effects of chemotherapy. Two patients were thought to be clinically free of disease (one with a synovial sarcoma treated with surgery and chemotherapy; one with symptomatic improvement after chemotherapy for an infiltrative brachial plexopathy due to breast carcinoma). Three patients with Hodgkin's disease underwent rescanning because specific sites of clinical concern were thought to represent active disease (one with persistent induration in the right supraclavicular fossa; one with persistently enlarged axillary lymph nodes; one with a residual mediastinal mass on CT). Another patient with neurofibromatosis underwent scanning at the routine follow-up visit after surgical excision of a midthoracic sarcoma 12 mo earlier.

Imaging

The preparation and imaging protocol for both studies were identical, but on the second occasion each patient received 5–10

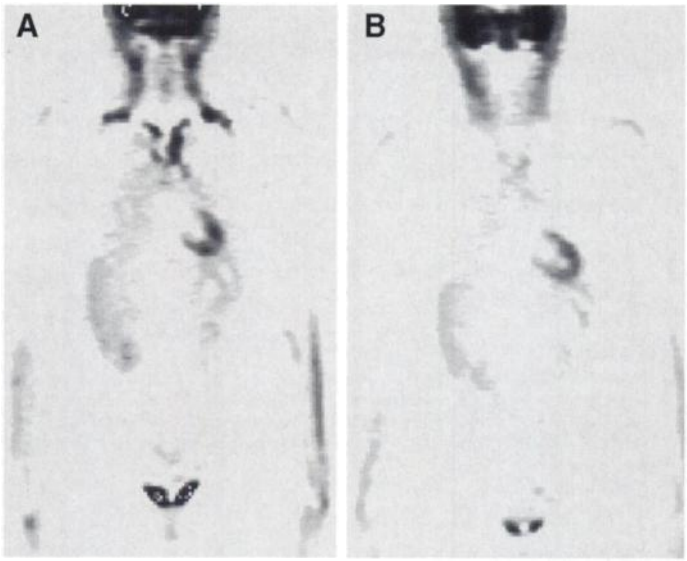

FIGURE 1. (A) Intense "physiological" uptake of FDG in the strap muscles of the neck and sternocleidomastoid masks potential sites for disease spread in this patient with synovial sarcoma. (B) The same patient underwent rescanning 4 wk later. After administration of 5 mg oral diazepam 30 min before injection of FDG, neck uptake is no longer visible.

mg of oral diazepam 30–60 min before intravenous administration of FDG. Patients were asked to fast for 6 hr, and venous blood glucose levels were measured using a glucose test strip immediately before injection.

All studies were acquired on a whole-body PET scanner which produces 31 slices over a 10.6-cm axial field of view, with an intrinsic resolution of 6 mm transaxially and 4.5 mm axially centrally. Whole-body images were obtained 30 min after injection by acquiring 10 consecutive 5-min images from the patient's head to below the pelvis. The complete sets of 310 image planes were reconstructed and smoothed in the axial direction to obtain a single three-dimensional dataset with a spatial resolution of 12 mm.

RESULTS

During the period of the study, a total of 336 whole-body scans were performed. Six women (age 24–42 yr; mean age 34 yr) were restudied after administration of diazepam. None of the patients were diabetic and all had blood glucose levels less than 5.0 mmole/liter before each scan. There was no significant change in blood glucose levels between scans (mean change, 0.6 mmole/liter; maximum change, 1.5 mmole/liter). The time interval between scans ranged from 8 days to 6 wk. All patients had marked symmetrical uptake of FDG in the neck on initial scanning. Five patients also demonstrated associated bilateral thoracic paravertebral uptake. Repeat scans after oral doses of diazepam significantly reduced or abolished uptake in these areas in all patients (Fig. 1 and 2). Quantitative analysis was possible in one patient who had local emission views acquired over the brachial plexus. The standardized uptake value (SUV) of the area of increased uptake of FDG within muscle in the supraclavicular fossa was 6.1 on the initial scan. The SUV for an analogous area of the same dimensions on the scan after diazepam administration was 1.3.

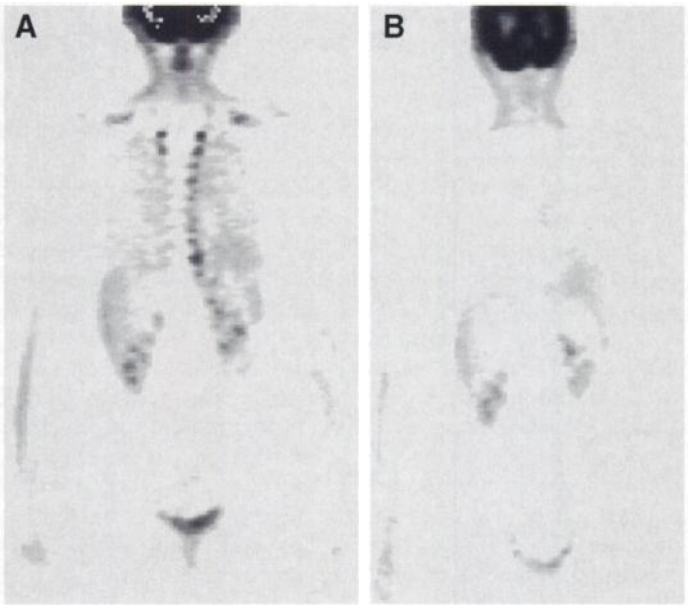

FIGURE 2. (A) Paravertebral uptake of FDG is associated with the pattern of increased neck uptake in the same patient as in Figure 1. (B) Paravertebral uptake is also abolished after administration of diazepam.

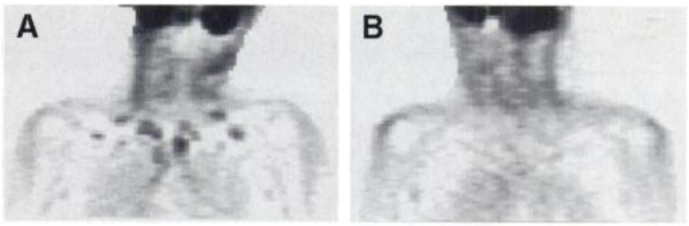

FIGURE 3. (A) Foci of increased uptake of FDG in the region of the neck and mediastinum, reported as representing malignancy. (B) Repeat scan 13 days later shows complete resolution of supposed "malignant" uptake.

In two patients, administration of diazepam enabled clinicians to confidentially exclude disease in sites of clinical suspicion (right supraclavicular fossa and brachial plexus). In three patients, potential sites for disease spread were clearly seen to have normal FDG uptake only on repeat scanning. In one patient, two experienced clinicians independently reported the presence of focal uptake, thought to represent malignant disease in the region of the superior mediastinum, in addition to what was recognized as physiological muscle uptake in the supraclavicular fossae. Repeat scanning 13 days later showed resolution of the supraclavicular uptake and the supposed "mediastinal" uptake, confirming that both were due to physiological uptake of FDG (Fig. 3).

DISCUSSION

The enhanced uptake of glucose into muscle during exercise is well recognized (*4*). Uptake of FDG in skeletal muscle is increased in vivo when muscle is electrically stimulated to undergo isometric contraction. This method has been used to study the kinetics of glucose metabolism in skeletal muscle (*5*). The mechanisms for the increased uptake are not entirely clear but appear to be distinct from those concerned with the regulation of glucose metabolism by insulin. Increased blood flow and the translocation (from intracellular pool to sarcolemmal membrane) and activation of protein carriers, such as GLUT1 and GLUT4, in response to calcium released from the sarcoplasmic reticulum during exercise may be responsible (*4*).

The characteristic pattern of symmetrically increased FDG uptake in the neck that we observed was associated with bilateral paravertebral thoracic uptake in a majority of the patients scanned. The distribution corresponds to the origins and insertions of the sternocleidomastoid and the strap muscles of the neck and the superficial muscles of the back (trapezius and rhomboids). Diazepam was chosen for repeat scanning because of its antianxiolytic and muscle-relaxant effects. That diazepam abolished the high FDG uptake in these areas suggests that the hypothesis that it is caused by voluntary muscle

contraction in tense patients is correct. Oral diazepam appears to offer a simple solution to the diagnostic confusion that can arise between enhanced physiological muscle uptake of FDG and malignant uptake. It is conceivable that patients presenting for restudy are less anxious about the scan procedure and might show reduced muscle uptake for this reason. The potential risk of rescanning without diazepam is that muscle uptake might persist, and a further scan would be required, incurring additional radiation (effective dose equivalent 9.5 mSv per study). We did not consider it justified to rescan the young patients included in the present study without diazepam.

Interestingly, two of the patients who demonstrated enhanced muscle uptake had done so only on their second visit to the PET center. The patients were aware on this occasion that the scan findings would directly influence whether future chemotherapy was required, and it may be that this anxiety was manifested by the increased muscle uptake rather than anxiety about the procedure itself. In these patients, rescanning without the use of diazepam would have been unlikely to help.

CONCLUSION

It is important to recognize that this characteristic pattern of muscle uptake is physiological and, if necessary, to repeat scanning where sites of potential pathology may be obscured. The interpretation of scan results may be significantly altered if the reporting clinician is not aware that this pattern of uptake represents a normal variant, and in one case in our series this might have led to the erroneous diagnosis of malignant disease. For whole-body studies, we have now adopted the policy of administering all injections with the patient in a supine position, with the neck supported by a pillow in an attempt to reduce muscle tension. Scans are repeated, if warranted, after the simple procedure of oral administration of 5–10 mg of diazepam.

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SPECT Imaging of Dopamine Transporters in Human Brain with Iodine-123-Fluoroalkyl Analogs of β-CIT

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Iodine-123-2β-carbomethoxy-3β-(4-iodophenyl)tropane (β-CIT) is a useful SPECT tracer for imaging the dopamine transporter. Its slow kinetics, however, necessitate imaging on the day after the injection. Two N-ω-fluoroalkyl analogs of β-CIT, the fluoropropyl and fluoroethyl compounds (β-CIT-FP and β-CIT-FE, respectively), characterized by faster kinetics in baboons, were tested in humans as potential tracers for the dopamine transporter. Four healthy volunteers were injected with [^{123}I]-β-CIT-FP and another four were injected with [^{123}I]β-CIT-FE. SPECT data were acquired for 1149 ± 590 min and 240 ± 30 min, respectively. Both tracers demonstrated high brain uptake (6.37% ± 0.37% and 7.8% ± 1.5% of the injected dose, respectively). Activity concentrated with time in the striatal area, reaching a peak within 30 min, with little or no washout for [^{123}I]β-CIT-FP and a faster washout for [^{123}I]β-CIT-FE (14.7% ± 6.9%). Occipital and midbrain activity showed similar patterns, displaying a peak within 15 min and rapid washout, followed by stable levels at approximately 100 min for both tracers. The ratio of peak specific striatal-to-peak specific midbrain activity was 9.1 ± 1.8 for [^{123}I]β-CIT-FP and 7.7 ± 0.7 for [^{123}I]β-CIT-FE, showing high in vivo selectivity for the dopamine transporter. These preliminary results suggest that both compounds could be used as SPECT (labeled with ^{123}I) or PET (labeled with ^{18}F) radiotracers to image the dopamine transporters in the living human brain.

Key Words: SPECT; dopamine transporters; iodine-123-β-CIT

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2β-Carbomethoxy-3β-(4-iodophenyl)tropane (β-CIT) is a potent cocaine analog with high affinity for the dopamine and serotonin (5-HT) transporters (*1,2*). When labeled with ^{123}I, β-CIT is a useful SPECT radiotracer for visualization of the dopamine and 5-HT transporters in baboons (*3–5*) and humans (*6–8*). SPECT studies in patients with idiopathic Parkinson's disease demonstrated a significant reduction of striatal uptake of [^{123}I]β-CIT (*6*). Thus, SPECT imaging with [^{123}I]β-CIT is a promising new technique for diagnostic evaluation of Parkinson's disease.

The uptake of [^{123}I]β-CIT in human striatum is characterized by slow kinetics. The striatal activity increases for 15–20 hr after bolus injection of the tracer. Thereafter, the striatal activity stabilizes at a constant value, and no significant washout is observable up to 30 hr after injection. The stable level of activity between 20 and 30 hr satisfies conditions of prolonged equilibrium (*7*). Consequently, one acquisition performed on the day after the injection provides all the information needed to