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Accumulation of glucose in keloids with FDG-PET

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Objective: Glucose metabolism has not been investigated in human (*in vivo*) keloids. In the present study, we performed positron emission tomography (PET) with fluorine-18-fluorodeoxyglucose (FDG) to examine glucose metabolism in keloids. ***Materials and Methods:*** Five patients (2 men and 3 women) with typical keloids having a thickness of more than 5 mm were studied. HEADTOME-IV SET-1400W-10 (Shimadzu, Tokyo, Japan) was employed for PET studies. Transmission scanning was performed on each patient. After fasting for more than 4 hours, the patients were injected intravenously with FDG 185–370 (MBq) following each transmission scan. Emission scans were performed 40–55 min after injection. For quantitative evaluation, the regions of interest (Circles ROIs: 6 mm in diameter) were placed on all the keloid lesions and surrounding tissues, and then their standardized uptake value (SUV = the tissue concentration/the activity injected per body weight) was calculated. ***Results:*** FDG was defined as showing the accumulation in keloids when its uptake was relatively higher in the keloid than that in the surrounding tissue. The SUV of the keloids ranged from 1.0 to 2.74, with a mean of 1.79. ***Conclusion:*** FDG-PET was performed in 5 patients with keloids and low-grade accumulation of FDG was observed in all lesions. This indicated that glucose metabolism was accelerated in keloids.

Key words: keloids, FDG-PET, glucose metabolism

INTRODUCTION

KELOIDS are skin abnormalities that are unique to humans and are characterized by excessive deposition of collagen in the dermis and subcutaneous tissues secondary to trauma, inflammation, surgery, or burns.[1–3]

Usually, wounds under normal healing develop asymptomatic fine linear scars, but some wounds unaccountably show abnormal healing resulting in keloids. Clinically, keloids are elevated red lesions and extend beyond the borders of the wounds and rarely regress over time.[2]

The cause of this abnormal wound response is unknown, but abnormal cellular responses may account for the abundant connective tissue deposition.[1] These fibrous growths typically generate significant disfigurement and unwanted symptoms, such as pruritis and pain.[3]

Various *in vitro* studies have been performed to investigate the etiology of keloids, and it has been reported that metabolic activity is accelerated in these lesions. However, as described above, keloids are unique to humans and thus are difficult to examine in animal experiments. For this reason, no *in vivo* human studies have yet been performed to examine the metabolism of keloids.

Positron emission tomography (PET) can be used to evaluate glucose metabolism *in vivo* with fluorine-18-fluorodeoxyglucose (FDG). FDG-PET has been employed to differentiate between benign and malignant tumors, determine the effect of anticancer therapy and locate foci of inflammation.[4–6]

Therefore, we considered that glucose metabolism in human (*in vivo*) keloids could be evaluated by FDG-PET since increased metabolic activity has been reported in these lesions.

This paper reports the results of FDG-PET examination

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Table 1 Patient characteristics, accumulation and SUV of FDG-PET in keloids

	Sex	Age	Cause of disease	Lesion location	Previous treatment	Duration of disease	Accumulation	SUV	Chief complaint
Case 1	M	69	Surgery	Chest + Abdomen	Laser	10	Moderate	2.52	Pruritus
Case 2	F	40	Acne	Chest	Laser + Corticosteroids	15	Moderate	1.48	Pain
Case 3	M	73	Surgery	Chest + Abdomen		10	Moderate	2.74	Pruritus
Case 4	F	65	Surgery	Abdomen		9	Low	1.1	Pruritus
Case 5	F	25	Surgery	Chest		2	Low	1.01	Ugliness

Note: SUV; standardized uptake value, Laser; dye laser therapy, Corticosteroids; injection of corticosteroids, Age; year, Duration of disease; year

in 5 patients with typical keloids.

MATERIALS AND METHODS

Five patients (2 men and 3 women) with the typical keloids having a thickness of more than 5 mm were studied. They consulted the Department of Plastic Surgery during 2003 and were diagnosed as having typical keloids.

They were aged from 25 to 73 years, with a mean age of 54.5 years. The keloids had been present for 2 to 15 years (mean: 9.2 years), were located on the chest and/or abdomen, and were caused by surgery in 4 patients and acne in 1 patient. None of the keloids were infected.

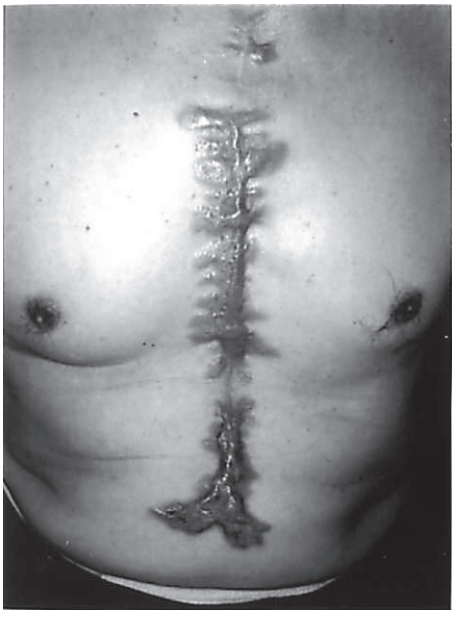
Three of the 5 patients had not received treatment for their keloids. One had been treated by injection of corticosteroids plus pulsed dye laser therapy and the other had received pulsed dye laser therapy alone (Table 1).

HEADTOME-IV SET-1400W-10 (Shimadzu, Tokyo, Japan) was employed for the PET studies. Transmission scanning was performed on each patient. After fasting for more than 4 hours, patients were injected intravenously with FDG 185–370 (MBq) following each transmission scan. Emission scans were performed 40–55 min after injection. For quantitative evaluation, regions of interest (Circles ROIs: 6 mm in diameter) were placed on all keloid lesions and surrounding tissues, and then the standardized uptake value (SUV = tissue concentration/activity injected per body weight) was calculated for each ROI.

RESULTS

Fasting blood glucose was high (145 mg/d*l*) in Case 4, but was normal in the other subjects.

FDG was defined as showing the accumulation in the keloids when its uptake was relatively higher in the keloid than in the surrounding tissue. Low or moderate accumulation of FDG was observed in all of the keloids examined (Figs. 1–3). The SUV of the keloids ranged from 1.0 to 2.74, with a mean of 1.79.



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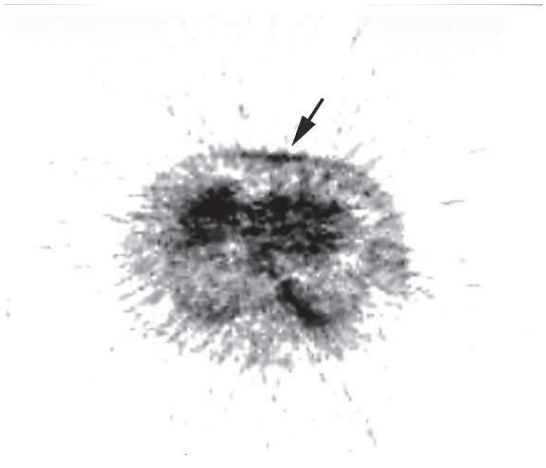

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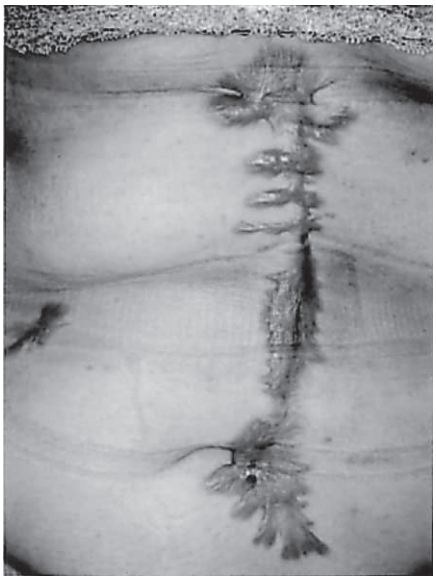
Fig. 1 A 69-year-old man with a keloid (Case 1 in Table 1). A. Keloid arising from a surgical wound extending down the chest to the abdomen. B. Axial FDG-PET image: Moderate degree uptake of FDG is observed (*arrow*) compared with the surrounding skin.



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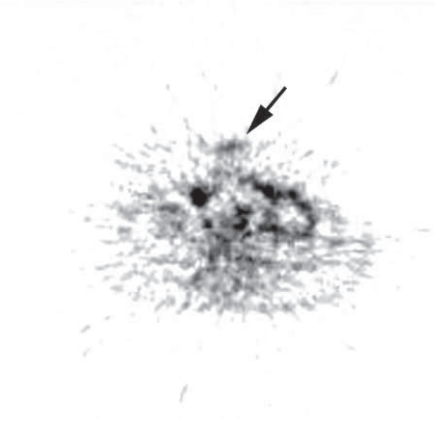

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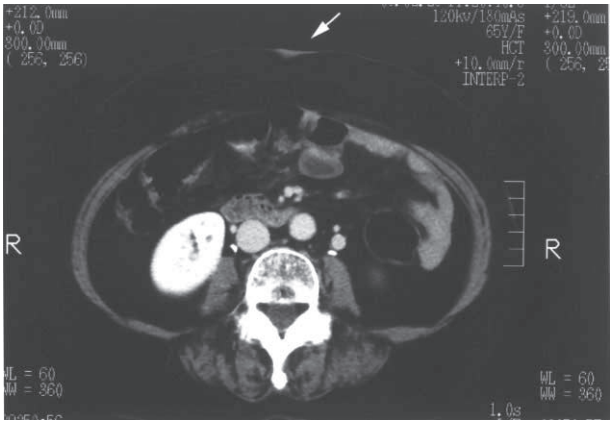

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Fig. 2 A 65-year-old woman with a keloid (Case 4 in Table 1). A. Keloid arising from an abdominal surgical wound. B. Axial FDG-PET image: Low degree uptake of FDG is observed (*arrow*) compared with the surrounding skin. C. CT scan obtained at a position close to that of Figure 2-B. The arrow indicates the site of the keloid.

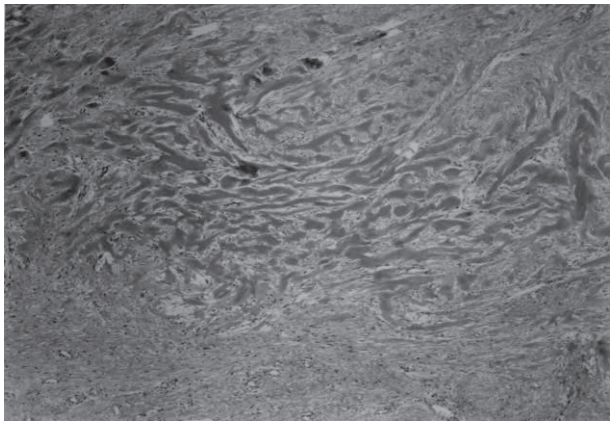

Fig. 3 High-power microscopic view of the keloid with HE staining (Case 5 in Table 1). Thick collagen bundles and fibroblasts are seen.

DISCUSSION

Usually, wounds under normal healing that develop asymptomatic fine linear scars, but some wounds unaccountably show abnormal healing resulting in keloids. Keloids are proliferative dermal growths that develop after skin injury and extend beyond the borders of the original wound and rarely regress over time. In addition to the cosmetic disfigurement these scars represent to affected patients, they can be complicated by secondary infections.

At present, FDG is the most widely used tracer for PET imaging studies to detect altered glucose metabolism in pathophysiological processes by means of radionuclide imaging.[4,5]

FDG initially distributes in proportion to the perfusion of the organs, whereby it follows the same uptake metabolic route as glucose, but FDG is phosphorylated to FDG-6-phosphate. By this mechanism and also due to its low membrane permeability, it becomes trapped and is accumulated within the cells.[4–6] Therefore, PET can detect a signal that reflects increased glucose metabolism, which may represent rapidly growing and/or inflamed tissue.

Malignant tumors show high uptake of FDG because proliferation requires accelerated glucose metabolism compared with that of normal tissue. Therefore, FDG-PET has been used to differentiate benign from malignant tumors and to determine the effect of anticancer therapy.

In addition to malignant tumors, inflammatory lesions and some benign tumors have also been reported to show uptake of FDG. In the case of inflammatory lesions, this may occur because FDG accumulates in inflammatory cells, such as macrophages and neutrophils.[7]

In the present study, all 5 patients showed low or moderate accumulation of FDG-PET in their keloids.

One possible reason for such accumulation may be

acceleration of metabolic activity in the keloids. In general, keloids contain more extracellular matrix than normal skin. It has been suggested that hyperplasia of the extracellular matrix may partially explain the development of keloids, and that acceleration of metabolic activity may occur because the matrix requires more energy for hyperplasia and infiltration of the surrounding tissues. Previous *in vitro* studies have shown that keloids have a high metabolic activity, as demonstrated by increased levels of adenosine triphosphate[8] and glycolytic enzyme activities and glycoprotein synthesis[9–11] than in normal skin cells. Therefore, FDG may accumulate in human keloids because of their accelerated metabolic activity.

The presence of macrophages in keloids may be another reason for the accumulation of FDG. Keloids contain more macrophages than normal skin, and it has been suggested that the release of growth factors and cytokines by macrophages may be partially responsible for the development of these lesions.[11] Macrophages may be responsible for the accumulation of FDG in keloids because these cells induce its accumulation in inflammatory lesions.

Since PET was not performed before and after treatment of keloids during the present study, changes in SUV in association with improvement or aggravation of cosmetic disfigurement, pruritus, and pain remain unclear. We plan to compare the FDG-PET findings before and after treatment in more patients to determine whether this technique can be used to objectively determine the effect of treatment.

Since the keloids examined in this study were located on the chest or abdomen, movement with respiration might have influenced SUV values and may have led to underestimation due to motion artifact. Also thin layer of the keloid may be a cause of underestimation.

In summary, FDG-PET was performed in 5 patients with keloids, and low-grade accumulation of FDG was observed in all of the lesions. This indicated that glucose metabolism is accelerated in keloids.

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