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Effect of Absolute Ethanol Injection into Solid Tumors Estimated by ^{133}Xe Tumor Blood Flow on a Mouse and a Human

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Abstract The tumor blood flow was calculated by ^{133}Xe clearance curves. Absolute Ethanol injection shuts off the tumor blood flow very powerfully. In the case of a nude mouse, 0.05 ml of absolute ethanol decreased the tumor blood flow to 60% and 0.10 ml of it decreased to 11 % markedly. The latter tumor fell and cured 2 weeks later, but the former still grew. In a human, two cases who had metastatic tumors at the chest walls were treated in the same way. In the first case, 20 ml of it was injected and the tumor blood flow was decreased to 27%. In the second case, 25 ml of it was injected and the tumor blood flow was decreased to 2.4%. The enhanced Computed Tomography scans showed massive tumor necrosis occurred a week later in the both cases. The decreased tumor blood flow correlated to the tumor responses to absolute ethanol injections on both a mouse and a human.

Key Words : Absolute Ethanol Injection, ^{133}Xe Tumor Blood Flow, Mouse, Human

Introduction

Absolute ethanol coagulates proteins, dehydrates cells and necroses both normal and malignant tissues. At clinical aspects, its injection is available for nerve blocking¹⁾²⁾, gastric bleeding³⁾, cystic lesions⁴⁾⁵⁾ and solid tumors⁶⁾⁷⁾⁸⁾.

In this short report, the tumor blood flow was measured by ^{133}Xe before and after its injections and then tumor responses were shown on a mouse and a human.

It is demonstrated that an absolute ethanol injection is one of the powerful, hopeful and safe cancer treatments regarding to choking the tumor blood flow.

Material and Methods

Tumor bearing mouse

HeLa S3 cells were cultured in Dulbecco's Modified Eagle Medium supplemented by 10 % calf serum at 37 °C in 5 % CO₂ gas incubator. Male 6-week-old BALB/cAJcl-nu/nu mice were purchased from Kyushu Experimental Animal Co., Ltd., Japan. 10⁶ cells were inoculated to the back of the nude mouse and grew up to a solid tumor a month later. Its diameter was 1 cm and its volume was approximately 0.5 to 0.6 cm³.

Patients

Case 1 ; A 74-year-old male patient suffered from lung cancer of the stage IV. He had a

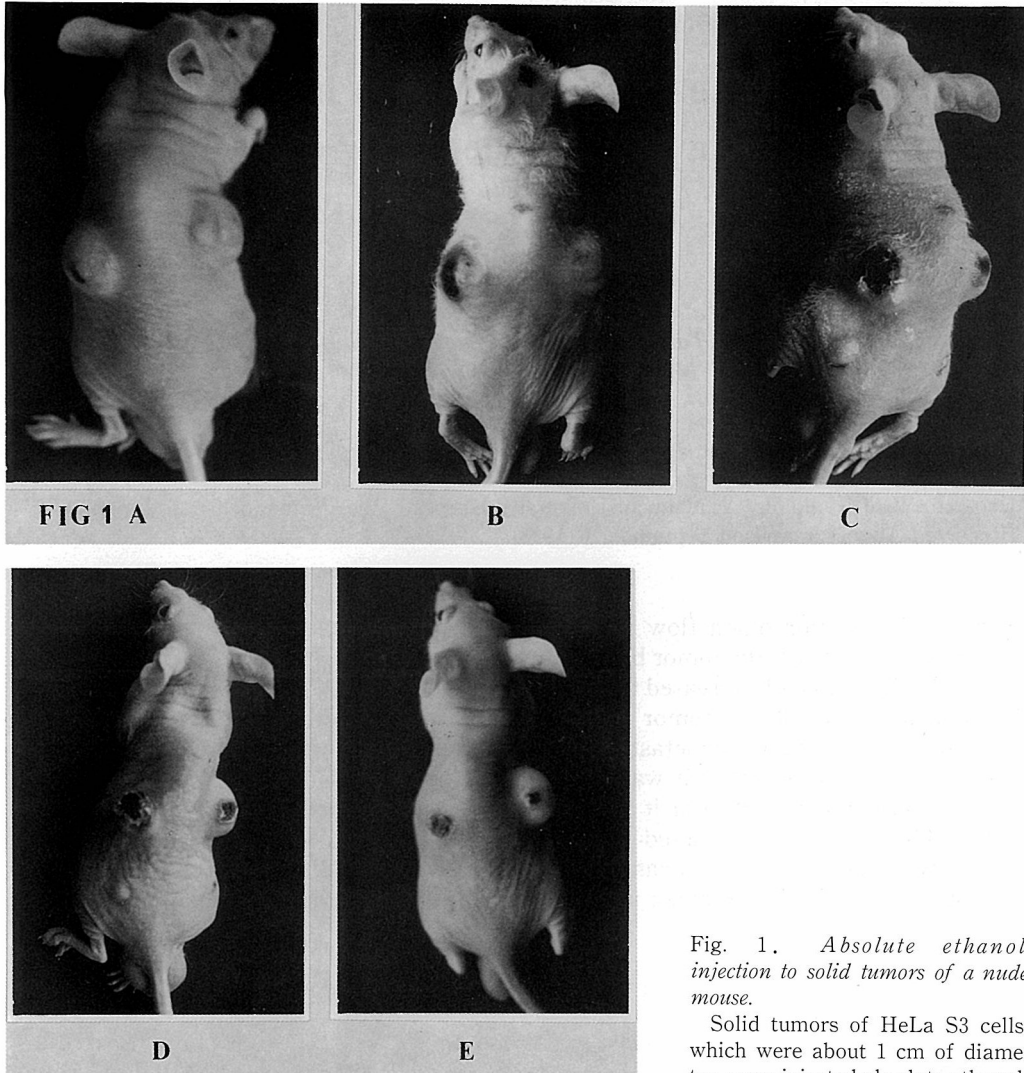


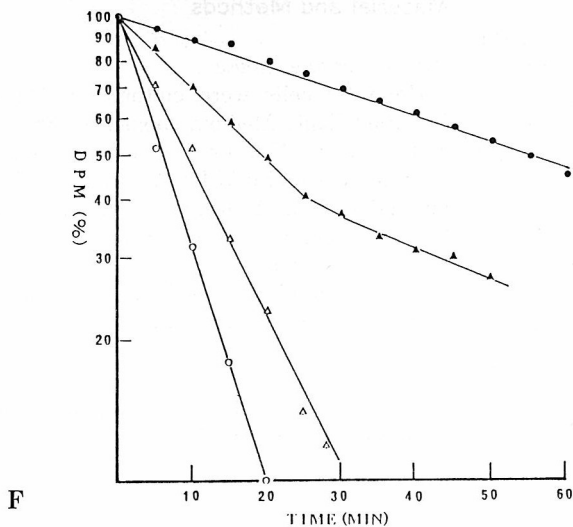
FIG 1 A

B

C

D

E



F

Fig. 1. Absolute ethanol injection to solid tumors of a nude mouse.

Solid tumors of HeLa S3 cells, which were about 1 cm of diameter, were injected absolute ethanol. The left tumor was injected 0.10 ml and the right tumor was done 0.05 ml. The tumor blood flow was measured by ^{133}Xe clearance curve. Panel A ; both tumors before injections. B ; a day after injections. C ; 5 days after. D ; 10 days after. E ; 2 weeks after. The left tumor was cured but the right one grew up. F ; ^{133}Xe clearance curves. The blood flow of the left tumor was calculated 12.3 ml/100 g/min (100 %) before the injection (○) and decreased to 1.4 ml/100 g/min (11.4 %) 10 minutes after (●). The blood flow of the right tumor was calculated 8.2 ml/100 g/min (100 %) before the injection (△) and decreased to 4.9 ml/100 g/min (60 %) 10 minutes after (▲).

metastatic tumor at his right back. Histopathological diagnosis showed carcinosarcoma. The tumor size was $10 \times 5 \times 3\text{cm}$.

Case 2; A 54-year-old male patient suffered from lung cancer of the stage IV. He had a metastatic tumor at his left anterior chest wall. Histopathological diagnosis showed adenocarcinoma. The tumor size was $10 \times 8 \times 3\text{cm}$.

^{133}Xe clearance curve

50 μCi of ^{133}Xe solution (Amersham) was injected to a tumor of a nude mouse before and 10 minutes after an absolute ethanol injection. 2 mCi of it was injected for a human solid tumor in the same way as a mouse. The radioactivity of ^{133}Xe was counted by a γ -Camera GCA 401-5 (Toshiba Co., Ltd.) each minute for an hour for a human and by a Nal Scintillation Counter (Aloka Co., Ltd.) for a mouse.

The clearance curve was depicted in the way of semi-logarithm.

The blood flow was calculated as follows: When the mono-componented curve; $F(\text{ml/g/min}) = (\lambda/\rho) (\log_e 2/T_{\text{hal}})$ When the double-componented curve; $F = (\lambda \cdot \log_e 2/\rho) (A/T_{\text{Ahal}} + B/T_{\text{Bhal}})$ λ (partition coefficient) = 1.07⁹⁾, ρ (specific gravity of tumor) = 1.0, T_{hal} (half time of ^{133}X clearance), A (proportion of A component), B (proportion of B component), T_{Ahal} (half time of A component), T_{Bhal} (half time of B component).

Computed Tomography (CT)

CT scans were performed for each patient before and a week after an absolute ethanol injection by a TCT-900S (Toshiba Co., Ltd.). Contrast medium was used to reveal the necrotic tissue clearly.

Results

Animal Studies

An experiment of a nude mouse is shown in Fig. 1. The right tumor was injected by 0.05 ml of absolute ethanol. The tumor blood flow was decreased to 60% 10 minutes after the absolute ethanol injection. On the other hand, the left tumor was done by 0.10 ml of it. The tumor blood flow was decreased to 11% (Fig. 1F). The nude mouse was kept feeding and taken pictures. On the left tumor, necrosis started a day after (Fig. 1B) and defected 5 days after (Fig. 1C). Crusta was

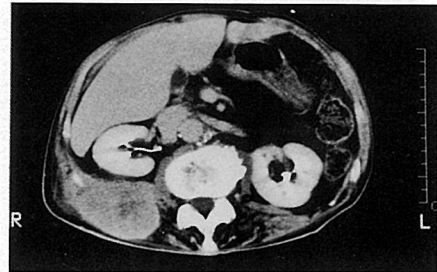
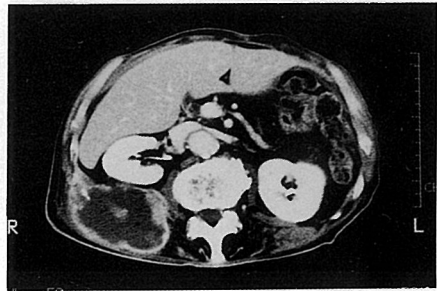


FIG 2 A



B

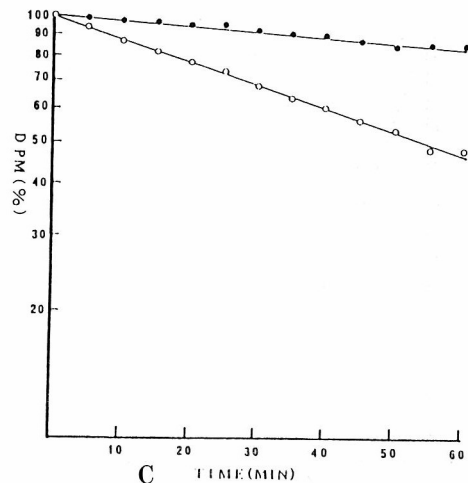


Fig. 2. Case 1

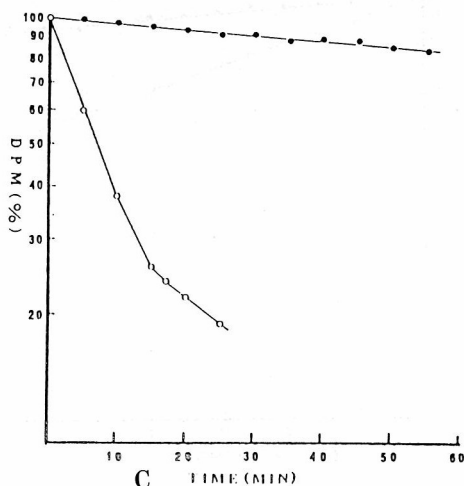
A 74-year-old male patient suffered from lung cancer of the stage IV. Panel A; Enhanced CT showed a metastatic tumor at his right back. It was $5 \times 3\text{cm}$ in size. B; Enhanced CT showed a massive necrosis in the same tumor a week after 20 ml of absolute ethanol injection. Gases were shown in the low density area. C; ^{133}Xe clearance curve. The tumor blood flow was calculated 1.4 ml/100 g/min (100%) before the injection (O) and 0.38 ml/100 g/min (27.1%) 10 minutes after (●).



FIG 3 A



B



Case 2

A 54-year-old male patient suffered from lung cancer of the stage IV. Panel A; Enhanced CT showed a metastatic tumor at his left anterior chest wall. It was 8×3 cm in size. B; Enhanced CT showed a massive necrosis a week after 25 ml of absolute ethanol injection. Gases were also shown in the low density area. C; ^{133}Xe clearance curve. The tumor blood flow was calculated 1.4 ml/100 g/min (100 %) before the injection (○) and decreased to 0.33 ml/100 g/min (12.4 %) 10 minutes after (●).

formed 10 days after (Fig. 1D) and fell 2 weeks after (Fig. 1E). On the right tumor, necrosis was observed partially but still grew up. Shutting off 89 % of the tumor blood flow was good enough to cure the tumor regarding to this experiment.

Case Reports

Case 1 (Fig. 2); The metastatic tumor was treated by 20 ml of absolute ethanol. The tumor blood flow was decreased to 27 % 10 minutes after the injection (Fig. 2C). As to CT findings, massive tumor necrosis was shown as a low density area which was not enhanced by contrast medium. In addition, gases in the necrotic tissue were shown (Fig. 2B). As to clinical findings, his chest pains subsided and he was very easy to raise his right arm a few days after the therapy.

Case 2 (Fig. 3); The metastatic tumor was treated by 25 ml of absolute ethanol. The tumor blood flow was decreased to 2.4 % 10 minutes after the injection (Fig. 3C). CT findings were the same as case 1 (Fig. 3B). As to clinical findings, his chest pains subsided a day after.

Discussion

We have described ^{133}Xe tumor blood flow was shutted off by absolute ethanol very powerfully on both a mouse and a human. This finding correlated to the tumor responses at the clinical aspects. As to CT findings, gases were shown in the low density areas of the tumor. They might be products of necrotic tissues¹⁰⁾¹¹⁾.

It seems that absolute ethanol injection is one of very hopeful therapies for many kinds of cancer as well as hepatoma⁶⁾. Because nowadays needle injections to a tumor can be done very safely under Ultrasound Sonography (US) or CT. If neither US nor CT is available it can be operated under open surgery. We are trying absolute ethanol injections to a gastric cancer under endoscopy⁷⁾. A disadvantage of this treatment was that local pains appeared for both patients during injections. It continued for a minute.

^{133}Xe clearance curves showed that absolute ethanol choked the tumor blood flow.

But the mechanism hasn't been clarified yet.

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