Successful monotherapy with autologous formalin-fixed tumor vaccine for a stage IV uterine cancer patient rejecting rational chemotherapy and immune-checkpoint-inhibitor treatment

Katsuhiko Fukuda[1] and Tadao Ohno[2]

[1]Integrated Medical Center Fukuda Internal Medicine Clinic
[2]Cell-Medicine, Inc.

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Abstract

A patient with stage IV uterine cancer displaying circulating tumor cells and high microsatellite instability who had rejected standard chemotherapy and immune-check-point inhibitor treatment received monotherapy with autologous formalin-fixed tumor vaccine (AFTV). The treatment resulted in shrinkage of multiple lung metastases, suggesting that AFTV will be an attractive treatment option.

CASE REPORT

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Katsuhiko Fukuda[1] and Tadao Ohno[2]

[1] Integrated Medical Center Fukuda Internal Medicine Clinic, Agenogi 9-4-25, Matsue-shi, Shimane 690-0015, Japan

[2] Cell-Medicine, Inc., Sengen 2-1-6, Tsukuba Science City, Ibaraki 305-0047, Japan

Correspondence

Tadao Ohno, Cell-Medicine, Inc., Sengen 2-1-6, Tsukuba Science City, Ibaraki 305-0047, Japan

Tel: +81-852-27-1200, Fax: +81-852-67-1711, E-mail: tad-ohno@cell-medicine.com

ORCID ID: Tadao Ohno, 0000-0002-8996-5997

Funding Information

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Ethics approval

The ethics committee of Cell-Medicine, Inc. has allowed to co-work with Integrated Medical Center Fukuda Internal Medicine Clinic on the autologous formalin-fixed tumor vaccine (AFTV) treatment.

Patient Consent

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Clinical trial registration

None. The treatment described below has been carried out in daily clinical practice.

Abstract

A patient with stage IV uterine cancer displaying circulating tumor cells and high microsatellite instability who had rejected standard chemotherapy and immune-check-point inhibitor treatment received monotherapy with autologous formalin-fixed tumor vaccine (AFTV). The treatment resulted in shrinkage of multiple lung metastases, suggesting that AFTV will be an attractive treatment option.

Key Clinical Message (max. 250 characters)

Doctors who met strong rejection of a rational treatment because of patient's fear of severe adverse effects of the proposed treatments should consider a mild immunotherapy with a cancer vaccine such as the autologous formalin-fixed tumor vaccine.

KEY WORDS

Cancer vaccine, monotherapy, uterine cancer, immunotherapy

Authors' contributions

KF carried out vaccination with AFTV. TO prepared AFTV. Both authors read and approved the final manuscript.

1 INTRODUCTION

In clinical settings for cancer patients, doctors may have experienced strong rejection of a rational treatment because of patient's fear of severe adverse effects of the proposed treatments. If no more options are available among the governmentally-approved treatments, we should have to select unapproved but humane treatments for the patient without considering health insurance. Autologous formalin-fixed tumor vaccine (AFTV) is one of such treatment options that has been exceptionally allowed in Japan and Germany. Here, we report on a patient with a stage IV uterine carcinoma who initially rejected chemotherapy and anti-PD-1 antibody treatment despite the presence of apparent circulating tumor cells (CTC) that were sensitive to paclitaxel and carboplatin and carried microsatellite instability (MSI).

2 CASE REPORT

A 56-year-old female was diagnosed with uterine endometrioid adenocarcinoma stage I2b in April, 2020. She underwent a simple hysterectomy, bilateral salpingo-oophorectomy, greater omentum segmental resection, lymphadenectomy of pelvis, paraaortic, and retroperitoneum. She strongly rejected the standard chemotherapy. We found that her CTC level was high (6.2 cells/6.5 mL by Oncocount RGCC, Research Genetics Cancer Center (RGCC) International GmBH, Switzerland). Pathological tests revealed her CTC to be sensitive to chemotherapeutic agents, i.e., carboplatin and docetaxel, and MSI-high. However, she also rejected treatment with immune-checkpoint inhibitors. Then, we found multiple metastases in both sides of her lungs by computed tomography (CT) (Fig. 1, a-g, series i) and a positive signal in paraaortic lymph nodes on the hilum of left kidney by positron emission tomography (PET)-CT (Fig. 1, h, i) in October, 2020.

We therefore selected AFTV treatment. From November, 2020, to January, 2021, she was treated with three intradermal injections of AFTV, each of them two weeks apart. AFTV was made from the patient's own resected, formalin-fixed uterine carcinoma tissue, similar to the procedure reported in cases of glioblastoma.[1] No problematic adverse event has been observed (erythema and induration at the injection sites, all less than CTCAE grade 2). Subsequently, we found by CT imaging apparently reduced, almost faint, nine lung metastases in December, 2021, as shown in Fig. 1, a-g, series ii. Especially, the lung metastasis observed in Fig. 1, g, i (arrowhead with asterisk) had disappeared in Fig. 1, g, ii, suggesting that AFTV monotherapy was effective towards the lung metastases.

To our surprise, however, she was unwillingly guided towards the standard chemotherapy at a regional big hospital in order to suppress the remaining metastases. Reluctantly, she received one dosis of chemotherapy with carboplatin and docetaxel (70 mg/m^{2}and AUC 5, respectively) that resulted in several typical, severe adverse effects such as nausea, diarrhea, stomatitis, anorexia, numbness, psilosis, and transient leukopenia. She quickly rejected further chemotherapy and was then switched back to two more AFTV injections in January and February, 2021, in our clinic. The CT and PET-CT images revealed complete response of her lung- and paraaortic lymph node metastases, as shown in Fig. 1, a-h, series iii. She is living well at present (cut-off, January 31, 2022).

3 DISCUSSION

As far as we know, monotherapy of stage IV carcinoma with cancer vaccines, except AFTV, has had dismal outcomes. AFTV made from resected formalin-fixed and paraffin-embedded autologous tumor tissue has been effective in glioblastoma,[1-4] bone-metastatic triple-negative breast cancer,[5, 6]upper tract urothelial carcinoma,[7] advanced hepatocyte carcinoma,[8, 9] malignant histiocytoma,[10] peritoneal serous carcinoma recurrent after chemotherapy,[11] gall bladder cancer,[12] advanced colon cancer,[12]uterine cervical small cell carcinoma.[13] Almost all of these tumors, at advanced stages, are known to be refractory to chemotherapy and immune-checkpoint inhibitors.

In the present case of advanced uterine carcinoma, early cancellation of the standard chemotherapy (carboplatin-docetaxel, only one injection) may have preserved her bone marrow in a healthy condition from where immune competent T lymphocytes were released without impairing cell proliferation and differentiation capacity. AFTV is capable of stimulating these cells to differentiate into cytotoxic T lymphocytes (CTL) in vivo.[9] The basic mechanism of CTL induction in formalin-fixed paraffin-embedded tumor tissue sections has been shown in our prior publication.[14]

Although monotherapy with AFTV was three injections in the present case, all of the nine lung metastases of the carcinoma shrunk apparently to less than half of their original sizes (Fig. 1, series ii). Although we are not quite able to conclude that the complete responses of all of the lung metastases (Fig 1, series iii) and the paraaortic lymph node (Fig. 1, h, iii) are solely due to the monotherapy with AFTV, the course of the present case strongly implies that AFTV monotherapy followed by, if necessary, one injection of cytotoxic agents will be an attractive treatment option for patients fearing severe adverse effects of standard chemotherapy.

Conclusion

Treatment with AFTV will be suitable for a patient who rejects standard chemotherapy of his/her advanced cancer.

Acknowledgement

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Conflict of Interest

None declared.

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Figure legends

Figure 1. CT images of the lung and PET-CT images of a paraaortic lymph node.

a-g (series i), CT images before the AFTV treatment. Nine metastases (arrows) of the uterine cancer were observed. h, i, a PET-CT image indicating a small hotspot at a paraaortic lymph node (arrow).

a-g (series ii), images after the initial AFTV monotherapy. Three intradermal injections of AFTV were performed two weeks apart. The arrowhead with a red asterisk shown in g, i has disappeared in g, ii. No PET-CT image was available at h, ii.

a-h (series iii), images after the one-time injection of the chemotherapy with carboplatin and docetaxel plus additional two injections with AFTV. Complete response was observed.