

[ CASE REPORT ]

## Spontaneous Regression of Recurrent Undifferentiated Carcinoma of the Endometrium

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### Abstract:

We herein report a very rare case of spontaneous regression of recurrent undifferentiated carcinoma of the endometrium. An 80-year-old woman had undergone total hysterectomy with bilateral adnexectomy for undifferentiated carcinoma of the endometrium. The cancer recurred locally 10 months after surgery and then metastasized to the lung and liver. After she and her family elected to receive supportive care without active treatment, the local recurrences dramatically decreased, and the metastases of the lung, liver, and peritoneum also disappeared. This case showed that spontaneous regression can occur even with malignant tumors showing an extremely poor prognosis, such as undifferentiated carcinoma of the endometrium.

**Key words:** spontaneous regression, undifferentiated carcinoma, endometrial carcinoma

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### Introduction

Spontaneous regression (SR) of malignant tumor was defined as “the partial or complete disappearance of a malignant tumor in the absence of all treatment or in the presence of therapy which is considered inadequate to exert a significant influence on neoplastic disease” by Everson and Cole in 1956 (1). SR in cancer is rare, with an estimated incidence of no more than 1 in 60,000-100,000 cases (2). Furthermore, undifferentiated carcinoma is a rare cancer of the endometrium with an extremely poor prognosis.

We herein report a very rare case of SR after postoperative recurrence of undifferentiated carcinoma of the endometrium.

### Case Report

A 77-year-old woman without any family history of cancer underwent total gastrectomy for gastric cancer with stage IIA (pTNM) in Japanese Red Cross Ishinomaki Hospital.

Follow-up computed tomography (CT) performed 3 years after gastrectomy, at 80 years of age, demonstrated a tumor in the uterus without any findings of recurrent gastric cancer (Fig. 1). She underwent total hysterectomy with bilateral adnexectomy after clinical stage IB endometrial carcinoma was diagnosed. Postoperatively, a histological examination confirmed undifferentiated carcinoma of the endometrium (Fig. 2, 3).

Out of consideration of the patient's age, she and her family suggested not initiating postoperative adjuvant chemotherapy, but instead maintaining regular observation. Local recurrences of carcinoma of the endometrium together with pleural effusion, ascites, and bilateral hydronephrosis were observed at 10 months after hysterectomy with adnexectomy. The cancer subsequently metastasized to the lung, liver, and peritoneum at 17 months after surgery (Fig. 4). As she and her family decided against undergoing surgery, chemotherapy, or other active treatments, they selected best supportive care. She continued to attend our outpatient clinic for nephrostomy tube management of hydronephrosis but did not receive any active treatment for the

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cancer. She was working energetically on her vegetable garden and also showed a good appetite without any weight loss or pain. Surprisingly, follow-up CT at 38 months after surgery (28 months post-recurrence) showed that all lung and peritoneal recurrences had disappeared, and that the liver and local recurrences had dramatically decreased in size (Fig. 5). When abdominal surgery was performed again to treat strangulated intestinal obstruction at 44 months after surgery (34 months post-recurrence), the laparotomy find-



**Figure 1.** Follow-up CT reveals tumor in the uterus (arrow).

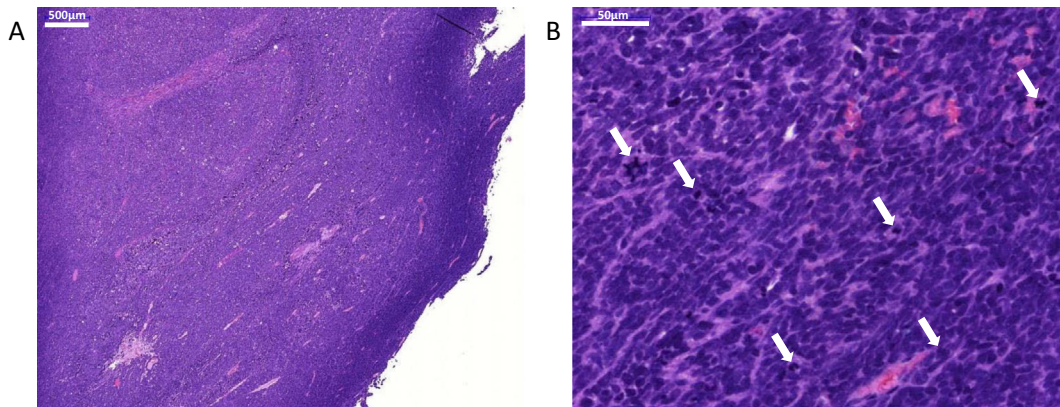
ings showed limited adhesions without any sign of peritoneal dissemination or other obvious recurrence of cancer. A cytological examination of the ascites showed no signs of malignancy, so the findings did not support cancer as the cause of intestinal obstruction.

At 45 months after hysterectomy with adnexectomy (35 months post-recurrence), follow-up CT still showed no signs of lung, liver, or peritoneal recurrences, but regrowth of the local recurrence in the pelvis was noted (Fig. 6). The patient ultimately died of unknown cause at 53 months after surgery. Her family declined to consent to an autopsy, but post-mortem CT revealed no recurrences in the lungs, liver, or peritoneum, with limited local recurrence and bilateral pleural effusion.

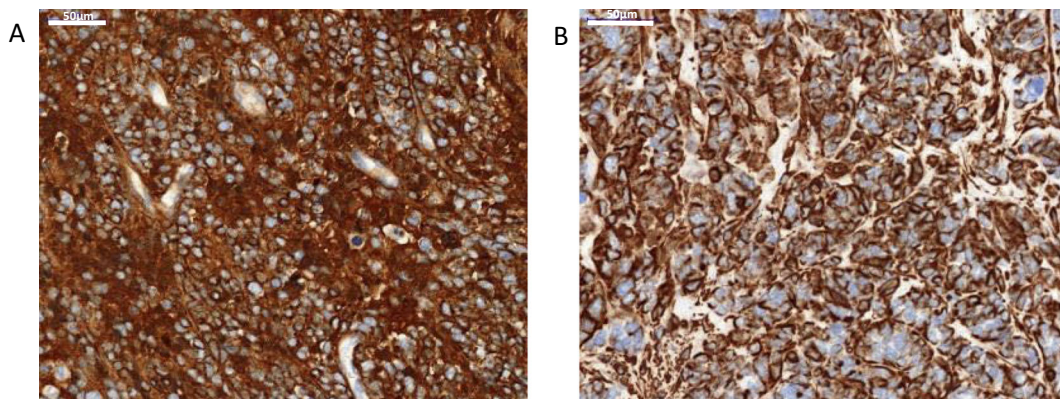
## Discussion

A PubMed search using the search terms “spontaneous regression” and “endometrial carcinoma” yielded only three reports worldwide of SR of endometrial carcinoma (3-5). We encountered a very rare case of SR of recurrent undifferentiated carcinoma of the endometrium.

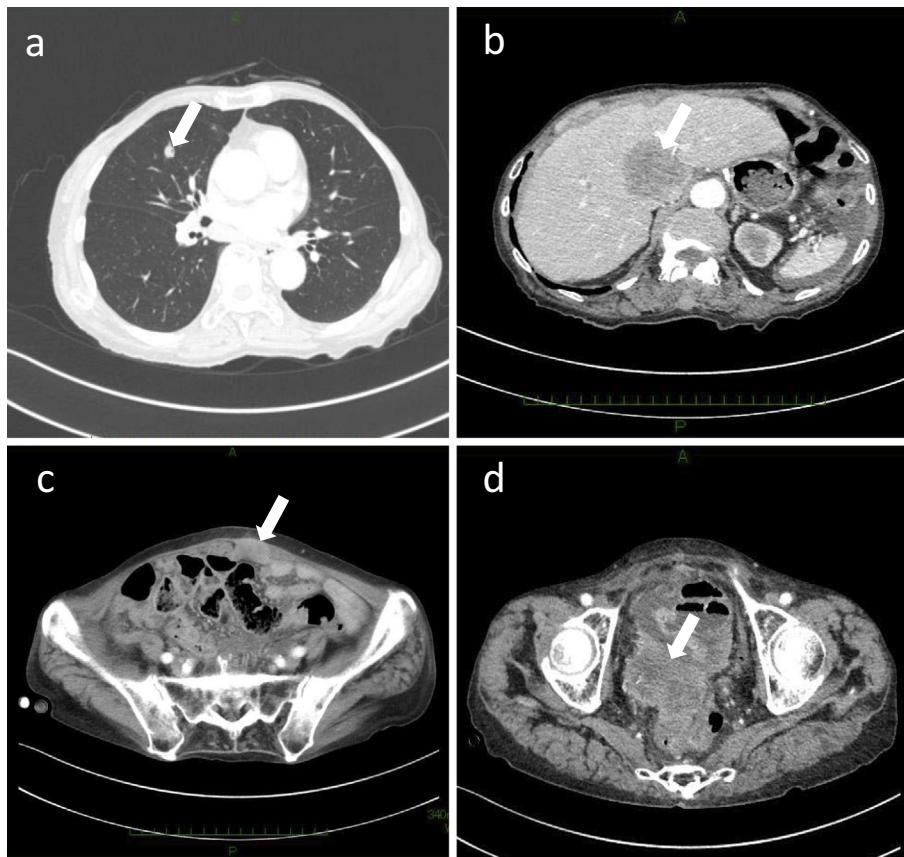
To our knowledge, so far only five cases of SR of endometrial carcinoma have been reported. Everson reported



**Figure 2.** (A) The tumor comprises small, uniform cells arranged without any obvious nested or trabecular architecture, and with no gland formation. (B) The tumor shows many atypical mitoses.



**Figure 3.** Tumor cells are positive for the epithelial cell marker pan-keratin (A), and for vimentin (B), which is positive in endometrial carcinoma.



**Figure 4.** CT at 17 months postoperatively reveals exacerbation of the lung (a; arrow), liver (b; arrow) and peritoneal (c; arrow) recurrences, and slight exacerbation of the local recurrence (d; arrow).

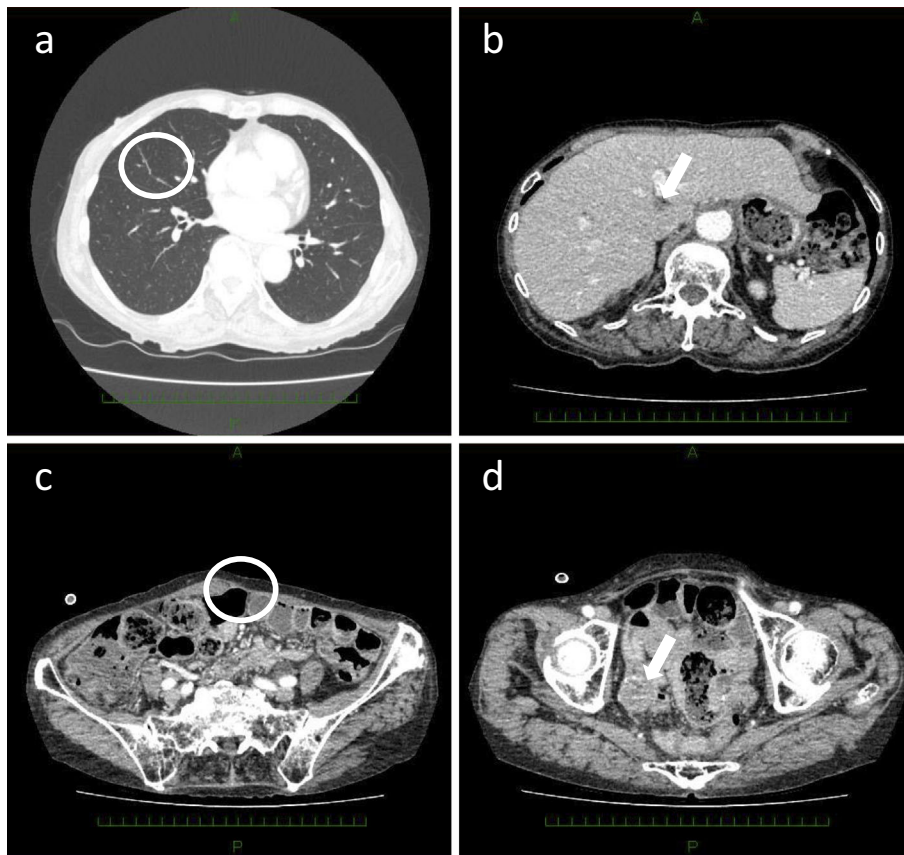
two cases of SR of endometrial carcinoma (6). One of the cases involved a 33-year-old woman with inoperable glandular-type carcinoma of the uterus with a vaginal mass and abdominal nodules. When she died 3 years after vaginal operation (6.5 years after the diagnosis), an autopsy revealed regression of the uterine cancer. The second involved a 67-year-old woman with highly anaplastic endometrioid adenocarcinoma who died 3 years after apparent regression of abdominal tumor masses, although an autopsy was not performed for that patient. In those two cases, SR of the peritoneal tumor nodules and abdominal metastases occurred following removal of the primary tumor by hysterectomy. Beller et al. reported the case of a 56-year-old woman with endometrial carcinoma that metastasized to the vagina and para-aortic lymph nodes at clinical stage IV (3). She underwent total hysterectomy and bilateral salpingo-oophorectomy to stop vaginal bleeding, but the para-aortic lymph nodes remained. She then received local radiation to the vagina (total dose, 6,000 rads). She underwent partial treatment but lived without recurrence for 18 years from the diagnosis. Parker et al. reported the case of a 73-year-old woman with stage IV clear cell carcinoma of the endometrium (4). The findings from total abdominal hysterectomy, bilateral salpingo-oophorectomy, and omentectomy performed five weeks after the diagnosis showed that the endometrial tumor was almost entirely necrotic. That patient remained alive and clinically

free from endometrial carcinoma for six years. Because she had a history of essential thrombocytosis and the platelet count continued to remain high, the authors speculated that the mechanism of SR in that specific case was thrombosis due to essential thrombocytosis. Cheng reported the case of a 41-year-old woman with metastatic endometrial adenocarcinoma (5). Ascites, omental infiltration, peritoneal seeding, and levels of carbohydrate antigen 125 were reduced after she commenced the “Lim Lifestyle”, which includes drinking organic and unregimented vegetable juices, practicing Qigong to harmonize the body-mind-spirit condition, and maintaining a minimal stress environment. The author speculated that this “holistic approach” might have contributed to her SR.

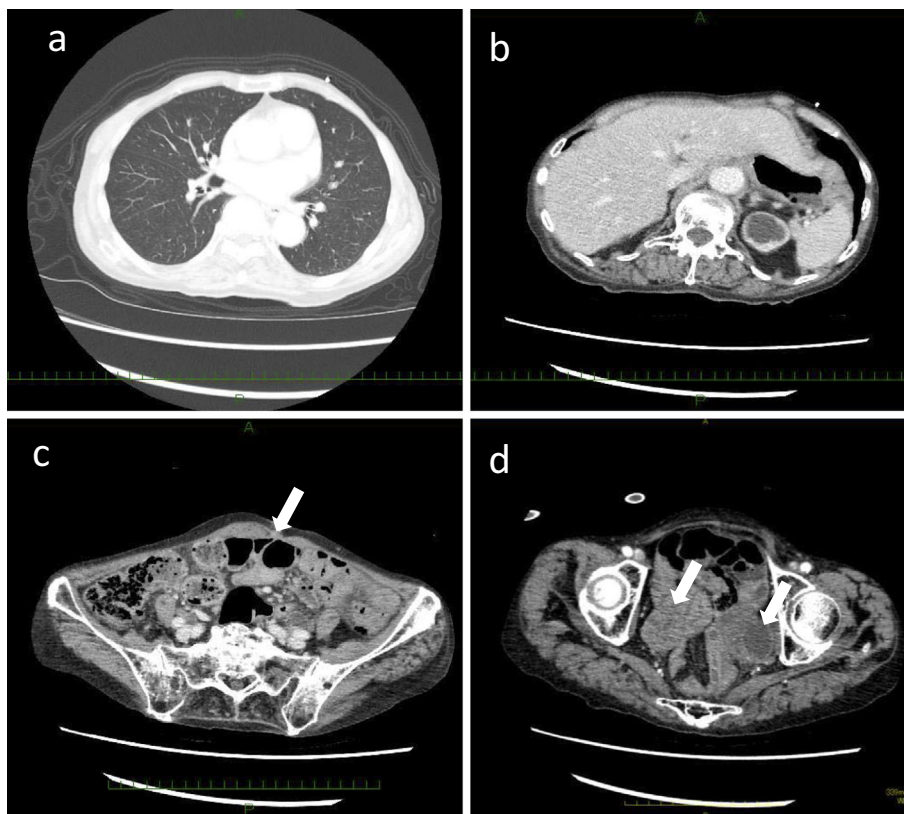
These five cases of SR demonstrated a relatively long-term survival with SR. In our case, local recurrence regressed from 38 to 44 months after surgery, and lung and liver metastases regressed from 38 months after surgery to death. This case seems to represent a case of temporary regression in the primary region with complete remission of metastases.

Cole reported that more than half of SR cases in cancer belong to four types: renal cell cancer, neuroblastoma, malignant melanoma, and choriocarcinoma (7). The reasons for SR of cancer remain unclear, but previous reports of SR in small cell lung cancer, melanoma, or other cancers have





**Figure 5.** CT at 38 months postoperatively reveals that all lung (a; circle) and peritoneal (c; circle) recurrences have disappeared, and that the liver (b; arrow) and local recurrences (d; arrow) have dramatically decreased in size.



**Figure 6.** CT at 45 months postoperatively reveals no signs of any lung (a), liver (b) or peritoneal recurrences (c; arrow), but regrowth of the local recurrence in pelvis is apparent (d; arrows).

suggested the possibility of mechanisms such as alteration of the immune system (8-10). Immunological mechanisms have recently been regarded as important for cancer regression. Immune checkpoint inhibitors, such as anti-cytotoxic T lymphocyte antigen-4 antibodies, anti-programmed cell death-1 (PD-1) antibodies, or anti-PD-1 ligand 1 antibodies, have been applied to the treatment of various tumors, such as melanoma. Studies of immune checkpoint inhibitors for some cancers support the notion of cancer immunity as a key point involved in regression (11-13). Immune checkpoint inhibitors are reported to be highly effective for tumors with a high mutation burden, a state that has been proven to induce neoantigens by the tumor mutation burden. Immunogenicity sometimes results from lifestyle habits, but the present patient had no habits of smoking, drinking alcohol, or excessive exposure to ultraviolet radiation or chemicals that might have led to an elevated tumor mutation burden. SR occurred after she had decided to receive best supportive care for the recurrences that developed following surgery to remove the primary cancer. She had been living happily, working in her vegetable plot every day and surrounded by her caring family, without engaging in any particular folk therapies or taking any supplements, and thus had been mentally fulfilled, living life positively and without stress. This condition is somewhat similar to the conditions reported by Cheng (5). Mental stress can obviously influence natural immunity, and conditions without mental stress might activate the body's natural immunity against cancer. However, these discussions remain purely hypothetical, and further studies are required in the future to investigate the mechanisms underlying both SR and regrowth.

### Conclusion

Although the precise mechanisms underlying the SR of the malignant tumors in the present patient are unknown, this case showed that SR can occur even in malignant tumors with an extremely poor prognosis, such as undifferentiated carcinoma of the endometrium.

**The authors state that they have no Conflict of Interest (COI).**

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