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Case Report

Adrenocortical carcinoma with multiple liver metastases controlled by bland transarterial embolization and surgery resulting in long-term survival[☆]

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ABSTRACT

Adrenocortical carcinoma (ACC) is a rare malignant tumor with a poor prognosis. Local recurrence or distant metastases occur in more than 50% of cases. Patients with metastases have limited treatment options, and <15% have a 5-year survival time. Herein, we describe a 44-year-old woman with ACC and who underwent retroperitoneal tumor resection. Multiple liver and lung metastases were found 1-year postresection. Mitotane therapy started as systemic treatment. Lung metastases were controlled but liver metastases were progressive. The liver metastases were treated by performing 2 resections and 6 bland transarterial embolization (bland TAE), and are presently controlled with only 2 liver metastases of <20 mm. The present case showed that bland TAE can achieve long-term prevention of the progression of liver metastases of ACC. The ultraselective bland TAE for selective embolization supported by the latest computed tomography analysis techniques during arteriography could minimize liver damage caused by embolization and allowed multiple treatments which prolonged survival. We conclude that bland TAE can be effective for controlling liver metastases of ACC.

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Introduction

Adrenocortical carcinoma (ACC) is a rare malignant tumor with a poor prognosis [1]. Many ACC cases are diagnosed in the late stages with distant metastases. Complete surgical resection is the only curative method for localized disease. However, local recurrence or distant metastases occur in more than 50% of cases. Patients with metastases have limited treatment options, and < 15% have a 5-year survival time [2,3]. Mitotane is the only available drug specific for ACC, and treatment options are limited owing to their serious side effects and the very narrow range of treatment. Fassnacht et al. showed improvement of progression-free survival by etoposide-doxorubicin-cisplatin-mitotane (EDP-M) compared with streptozocin-mitotane in patients with stage III–IV disease [4]. Thus, EDP-M has become the standard chemotherapy for ACC. However, the survival benefits of nonchemotherapy treatments remain lacking. Transcatheter arterial chemoembolization (TACE) and bland transarterial embolization without an anticancer agent (bland TAE) for liver metastasis are very effective treatment options with good results. Indeed, TACE and bland TAE have been widely used in the treatments of hepatocellular carcinoma (HCC) [5–8] and liver metastases from neuroendocrine tumor [9–12], colorectal cancer [13,11], and lung cancer [11]. However, there are still few reports of TACE or bland TAE for the treatment of ACC liver metastasis [14–16]. Herein, we reported an ACC patient who achieved a long-term survival of 8 years or more by a combination of repeated bland TAE, surgery and mitotane therapy. Additionally, some liver metastases showed a high rate of complete response to bland TAE alone.

Case report

A 44-year-old woman presented with abdominal distention as the chief complaint. There were no other specific complaints including appetite or weight loss. She had no medical history without medications or family history. Abdominal contrast-enhanced computed tomography (CT) showed a 160 mm retroperitoneal tumor which deviated the caudal side of the left kidney without metastasis. Blood samples showed no hormonal abnormalities. Retroperitoneal tumor resection was performed. The pathological diagnosis was left ACC Stage II under the UIC/WHO classification stage (T2N0M0).

One year postoperation, multiple liver and lung metastases were found. Thus, mitotane therapy was started. 1 year after starting mitotane therapy, the lung metastases were controlled but the liver metastases progressed. Therefore, 2 cycles of EDP-M therapy were administered, but there was no treatment response. Liver metastases were distributed predominantly in the posterior segment (60 mm and 50 mm in S7; 50 mm in S6; 25 mm in S5). The progression rate of the liver metastases was higher than that of the lung metastases, suggesting liver metastases as a prognostic factor. Posterior segmentectomy plus S5 partial hepatectomy were thereafter performed. 1 year after the hepatectomy, new multiple liver metastases were observed. The patient decided not to undergo

any surgical resection, thus other options were discussed. Liver metastases were enhanced strongly in the arterial dominant phase (Fig. 1A), suggesting that bland TAE or TACE may be effective.

In our country, there are still no anticancer agents arterially administered for ACC treatment. Therefore, bland TAE was selected as a treatment option. Bland TAE was repeated when necessary, adopting a usage policy when the maximum size of the liver metastases was >2 cm. For the embolic materials, 100–300 μm microspheres were used. Before the bland TAE, CT during arteriography was performed for feeding artery analysis. Catheterization was performed as selective as possible by using selective microcatheter with 1.5F or 1.7F tip for ultraselective bland TAE (Fig. 1B,C). Bland TAE was performed 6 times over a 3-year period. 8 liver metastases were treated, of which 5 lesions showed a complete response (Fig. 1D). 1 lesion on the hepatic surface of S4 was fed by some branches via the internal thoracic artery. As the parasitic artery could not be controlled by bland TAE alone, partial resection was added for this nodule. The other 2 lesions were <2 cm and are currently under follow-up. During the course of the disease, the liver functional reserve has been maintained. As for the lung metastases, they showed a slow increase. The patient remains alive 8 years after the initial surgery. Clinical course was summarized in Fig. 2.

Discussion

ACC is a rare malignant tumor with a poor prognosis, particularly in patients with metastatic disease [1–3]. The lung and liver are the 2 most common organs where distant metastases occur. In particular, liver metastases greatly affect the prognosis of ACC. The control of liver metastases prolongs survival. TACE and bland TAE are reported to be very effective treatments for liver malignancy. However, evidence of the survival benefits of TACE and bland TAE for ACC liver metastases remains very limited.

Theoretically, bland TAE induces local ischemia by stopping arterial blood flow to ACC, leading to tumor cell death. Therefore, bland TAE is more effective in hypervascular tumors than in hypovascular tumors. ACC liver metastases have very high vascular density at $573.2 \pm 185.2/\text{mm}^2$ [17]. This density is about twice that of HCC ($297 \pm 88/\text{mm}^2$) [18]. Therefore, bland TAE for ACC liver metastases can be expected to have the same favorable therapeutic effect as that for HCC [14]. In the present case, CT also showed the hypervascularity of the liver metastases. Bland TAE was very effective as suggested, resulting in the complete response of many nodules.

Some reports have shown the effectiveness of TAE and TACE for liver metastasis. Tanaka et al. reported that repeated bland TAE at 100 μm microsphere was very effective against chemoresistant liver metastases of colorectal or gastric cancer [19]. Shimohira et al. showed that bland TAE mainly at 100–300 μm microspheres was effective for hypervascular liver metastases refractory to standard treatment. They reported overall response and disease control rates of 52% and 72%, respectively. However, the complete response rate was only 8%

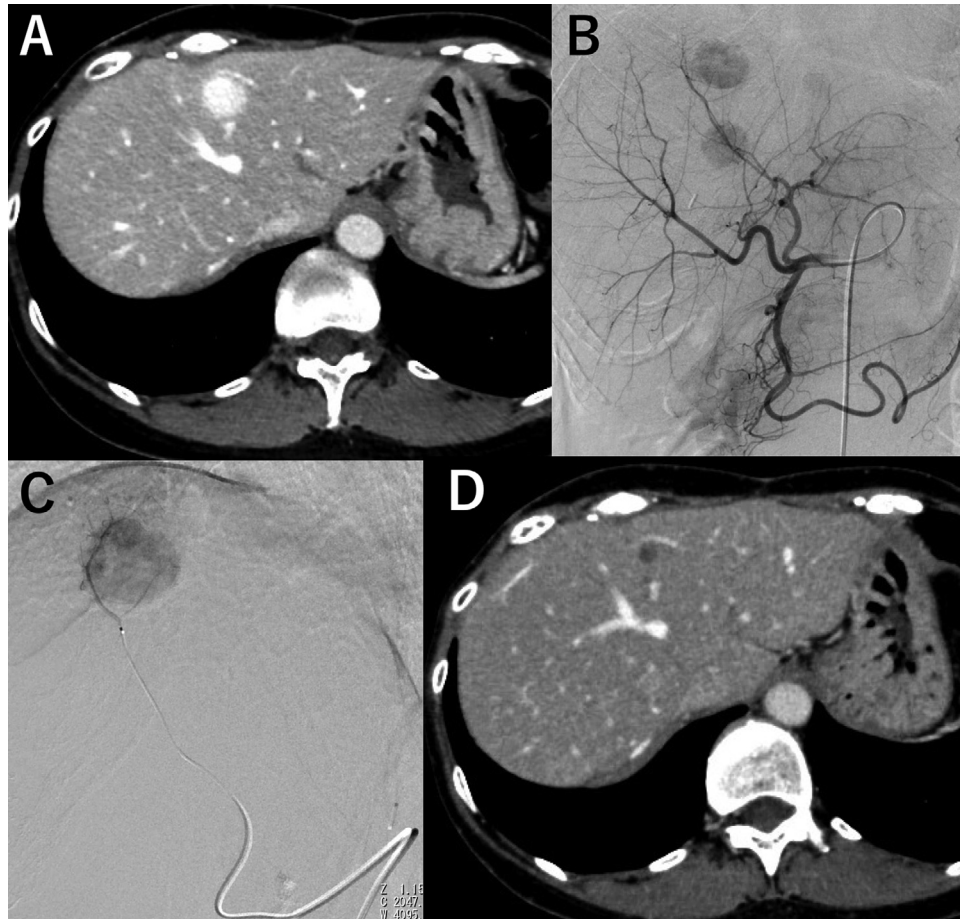


Fig. 1 – (A) Arterial phase of CT before first embolization showed all the liver metastases (S4, S8, S1, S2) were enhanced strongly. **(B)** Arteriography via common hepatic artery showed multiple strong tumor enhancement. **(C)** Ultra-selective arteriography via the branch of A4 by using microcatheter showed strong tumor stain and then ultra-selective bland transarterial embolization with 100-300 μ m microspheres performed. **(D)** Arterial phase of CT 2 month after bland transarterial embolization showed the loss of tumor enhancement. Note: S; segment, A4; medial branch of hepatic artery

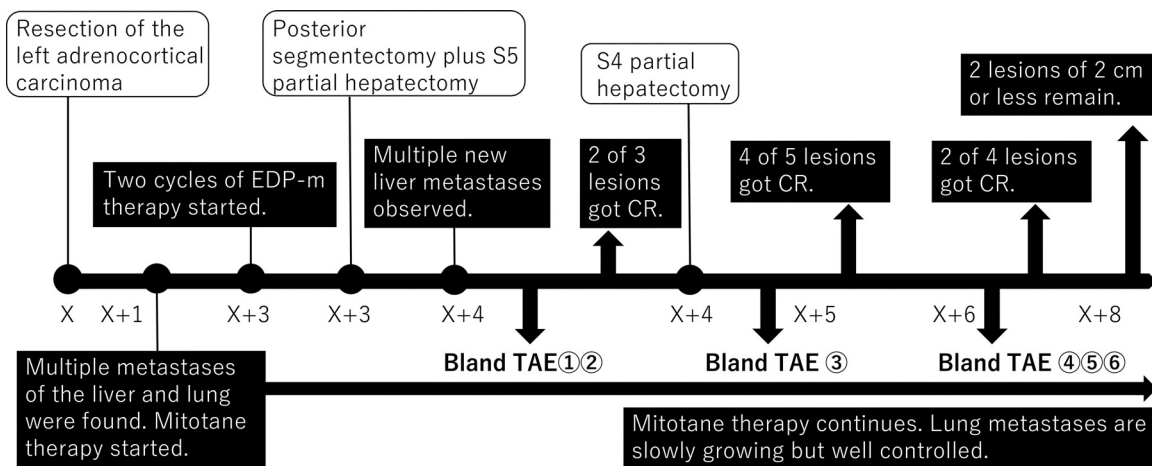


Fig. 2 – Clinical course Note: TAE; transarterial embolization, S; segment CR; complete response, EDP-m; etoposide-doxorubicin-cisplatin-mitotane. X indicates the initial surgery year. X+1, etc. indicate that signify years after initial surgery

[11]. With reference to this report, we used 100-300 μm microspheres as the embolic material.

Reports of TACE and bland TAE for ACC liver metastases are even more limited. Wong et al. reported a complete response of liver metastases in a patient who underwent conventional TACE with doxorubicin, mitomycin, and iodized oil after EDP-M chemotherapy [16]. Their limitation was that the lesions were evaluated only by positron emission tomography. Soga et al. described a complete response of liver metastases in 2 patients who underwent bland TAE after EDP-M [14]. Owen et al. reported that patients receiving additional local therapies such as TACE or selective internal radiation therapy had a significantly longer survival time than patients who did not [20]. These previous reports are expected to further improve the treatment outcomes of TACE and bland TAE. Cazejust et al. reported the analysis of a large number of patients ($n = 29$) with ACC liver metastases who underwent conventional TACE with cisplatin and iodized oil. In their study, the response rate was only 21%. There are several possible reasons for this poor result. First, conventional TACE with iodized oil may not be effective for ACC liver metastases. Second, CT analysis was not yet mature, and super selective embolization with feeder detection was not possible. In the present case, ultra selective bland TAE as a selective embolization treatment supported by the latest CT analysis techniques during arteriography could minimize TAE-induced liver damage and made it possible to perform multiple treatments which prolonged survival. Additionally, the surgical excision of the tumors refractory to bland TAE also produced a favorable outcome. Based on the present case, we conclude that bland TAE can be effective for ACC liver metastases, and it should be considered as a selective embolization treatment for ACC similarly to HCC.

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