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## Case report

# Cured giant hepatocellular carcinoma after transarterial embolization complicated with liver abscess formation ☆☆☆

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## ABSTRACT

Many patients with hepatocellular carcinoma cannot be treated surgically because of the advanced stage of the tumor and/or coexisting cirrhosis. Transcatheter arterial embolization (TAE) represents an alternative therapeutic approach for some of these patients. However, it is not a curative measure, and an additional therapy is required to eradicate the residual disease.

In this communication, we report a case of 55-year-old man with giant hepatocellular carcinoma located in the right lobe of the liver that was successfully treated with TAE. TAE completely devascularized the tumor in one session. Despite of postembolization antibiotic therapy, complete tumor necrosis led to abscess formation. After 57 days of abscess drainage, necrotic tumor tissue was completely evacuated from the drained cavity; no viable tumor tissue was identified by computed tomography/magnetic resonance imaging scan on a 5 year follow-up.

TAE procedure can be suggested as a modulator of antitumor immune response, by exposing tumor antigens after necrosis leading to inflammation. In addition to necrosis caused by TAE, an antimicrobial acute inflammatory reaction in the treated area led to the complete destruction of the giant tumor.

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## Introduction

Hepatocellular carcinoma (HCC) is the most common primary liver cancer, with over half a million new cases diagnosed annually worldwide. It represents the second leading cause of cancer related mortality in the world [1]. Classical treatments for HCC include surgical resection, liver transplantation, and local ablative therapy [2–4]. Fewer than 40% cases are operable, and the rate of tumor recurrence after curative surgery is high.

Microwave and radiofrequency ablation are the most widely used ablation technique, which is effective only for small metastatic and primary tumors [5,6]. Patients with intermediate stage multinodular disease without extrahepatic metastases and sufficient liver reserve should be offered transarterial therapies. It mainly includes transarterial chemoembolization (TACE) and transarterial embolization (TAE) – so called bland embolization. Transarterial therapy is now a validated treatment for unresectable HCC [7]. The latest National Comprehensive Cancer Network (NCCN) guidelines suggest that TACE should be considered as a firstline treatment for unresectable HCC with a diameter more than 5 cm. However, it is debatable whether TAE gives the same survival advantage as TACE [8–10].

TACE according this novel schedule is feasible and associated with a higher response rate than TAE alone. However, the survival benefit of TACE over TAE is not documented [7].

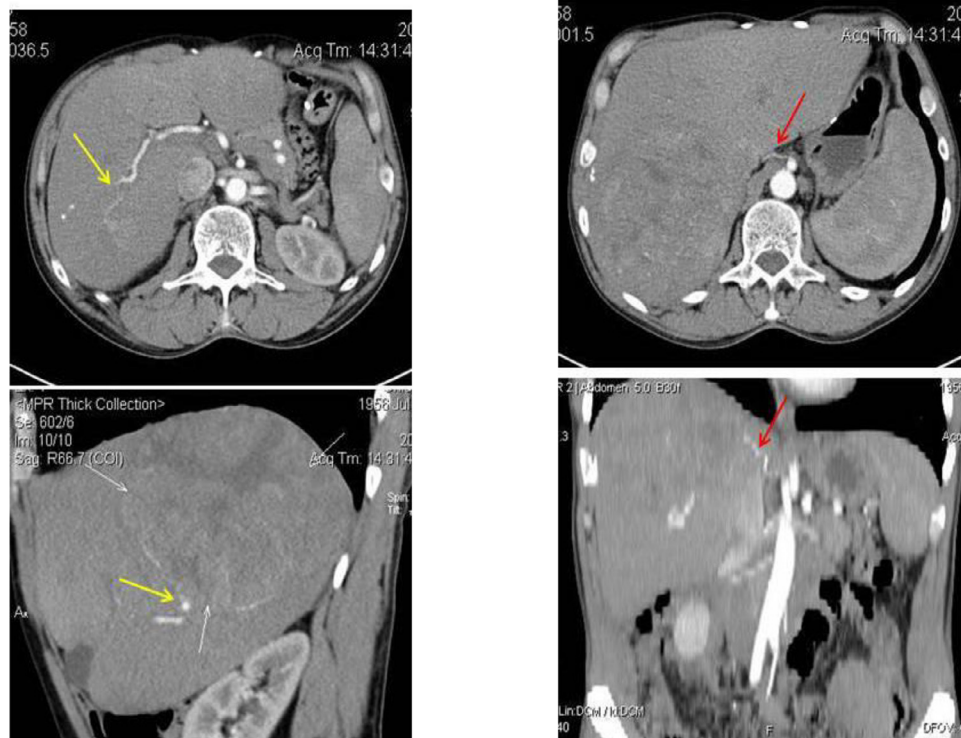
The risk of liver abscess after TACE appears to be related to the extent of liver infarction. While some degree of infarction in the necrotic affected area is probably inevitable, abscess formation is rare [11]. When abscess occurs, it is due to colonization of necrotic tumor from either enteric organisms or from bacteria introduced exogenously during the procedure [12]. Up to 60% of organisms are Gram-positive [13].

Here, we report the case of an HCC patient treated with TAE complicated with the abscess formation. After abscess drainage the tumor had regressed and completely disappeared.

## Case report/Case presentation

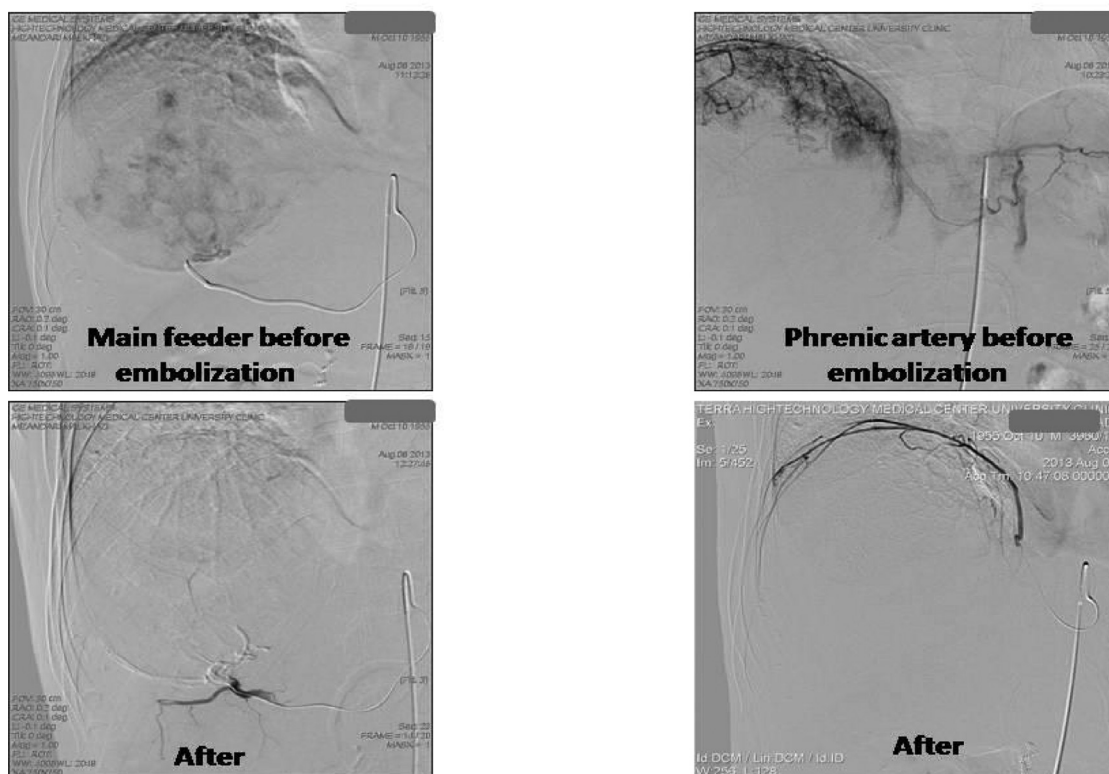
A 55-year-old Caucasian male patient presented with fatigue, weight loss, and dull right upper quadrant pain. Ultrasound and computed tomography (CT) scan revealed a giant (maximal diameter, 15 cm; volume, 1100 mL) inoperable right liver lobe hypervascular tumor with contrast wash-out in the venous phase (Fig. 1). Patient was anti-HCV-positive (with chemiluminescence immunoassay >30) and alpha-fetoprotein was elevated (AFP– 11.68).

TAE was performed using 100-300 and 300-500 micron microparticles and sponge gel to the main feeder branches originating from the right hepatic artery and secondary feeders from the right inferior phrenic artery; Figure 2 shows the right



**Fig. 1** – The initial CT scan (arterial phase; upper images axial –plane, lower images – saggital and coronal planes) shows giant (maximal diameter- 15 cm; volume- 1100 mL) hypervascular tumor in the right liver lobe. Main feeder – RHA (Yellow arrow), secondary feeder – right inferior phrenic artery (red arrow). (Color version available online.)

## Embolization - TAE



**Fig. 2 – The hepatic arteriography. A large hypervascular tumor within the right lobe of liver. The hepatic angiography after TAE procedure occluded branches of right hepatic and phrenic artery with some collateral vessels and remarkable tumor reduction.**

phrenic and right hepatic artery before and after bland embolization. TAE completely devascularized the tumor in one session, as shown by a postembolization CT scan (Fig. 3). The patient tolerated the embolization procedure without any early complications. Forty-five days after TAE, the patient returned to hospital with signs of infection: high fever (up to 39), chills and right upper quadrant abdominal pain. Blood tests revealed severe inflammation – white blood cell count showed  $17.5 \times 10^9/L$ , C-reactive protein level – 143 mg/L. In spite of postembolization antibiotic therapy, complete tumor necrosis led to abscess formation. A CT scan revealed 1550 mL of gas containing cystic mass – abscess (Fig. 4), which was drained under CT guidance using a 14Flocking loop catheter. Organoleptically purulent content was received, which may be the result of sterile inflammation caused by tumor necrosis, since no microorganisms were cultured. Abscess drainage was performed on an outpatient basis and was easily tolerated by the patient. AFP level was decreased to 2.43 (N <5.8) in few weeks. Fifty-seven days after drainage, necrotic tumor tissue was completely evacuated from the drained cavity; no viable tumor was identified at that moment on a follow-up CT scan (Fig. 5).

At a 5-year follow up, the patient was asymptomatic, without any signs of distress. He had normal liver tests, AFP was

3.17 (N <5.8) and no tumor recurrence was seen on follow-up magnetic resonance imaging (Fig. 6). After 6 years, health-related quality of life, evaluated by using the standard 4-item set of Healthy Days core questions (CDC HRQOL- 4), is excellent. This report demonstrates the full eradication of giant HCC documented by magnetic resonance imaging after the follow-up of 63 months after TAE procedure.

### Discussion/conclusion

HCC has a 5-year survival rate of <5% and there are at least 1 million novel cases per year [14]. TAE/TACE is a widely accepted treatment option for unresectable HCC. The final goal of TAE treatment is to obtain complete necrosis of the malignant tissue by disruption of the blood supply to the tumor tissue.

TAE/TACE therapy may cause several major complications which include hepatic failure, liver abscess, liver rupture, biliary tract injury, renal failure, necrotizing pancreatitis, cerebral lipiodol embolism, and hepatic encephalopathy [15–18]. The reported mortality rates due to embolization complications range from 13.3% to 50% [19,20].



**Fig. 3 – CT follow-up documents complete response to TAE (Multiphasic Contrast CT including 3 D reconstruction images).**

Liver abscess formation is a rare and potentially fatal complication of TAE/TACE. The incidence of post-TAE/TACE liver abscess for liver cancer varies from 0% to 1.1% according to the previous works [21–23].

The incidence of post-TAE/TACE liver abscess is statistically discrepant among different studies, which is likely attributed to the heterogeneous populations, variation in embolization treatment, and numbers of involved patients [24].

Effective management of liver abscess relies on a clear understanding of its pathogenesis, improvement of the diagnosis, clarification of its imaging characteristics, administration of sufficient doses of sensitive antibiotics in a timely manner, and active abscess cavity puncture aspiration and drainage [25]. Those with larger abscesses and those with more advanced age has worse outcomes [26].

Despite of its severe and fatal outcome abscess formation may lead to complete tumor resolution, according to previous studies [26, 27]. Among the 10 reported postremobilization liver abscess out of 3878 TAE procedures, one resulted in tumor shrinkage following abscess resolution (from 13 to 4 cm). Surgery was subsequently performed and the patient remained tumor free for a period of 4 years and 9 months after the operation before a small new growth was detected [26]. In the same study, another patient experienced total tumor regression after resolution of the abscess. He remained tumor free for the next 3 years and 7 months before new growth was detected. There is also a report of the patient who survived 5.5 years with a regressed giant HCC after TAE procedure complicated with liver abscess.

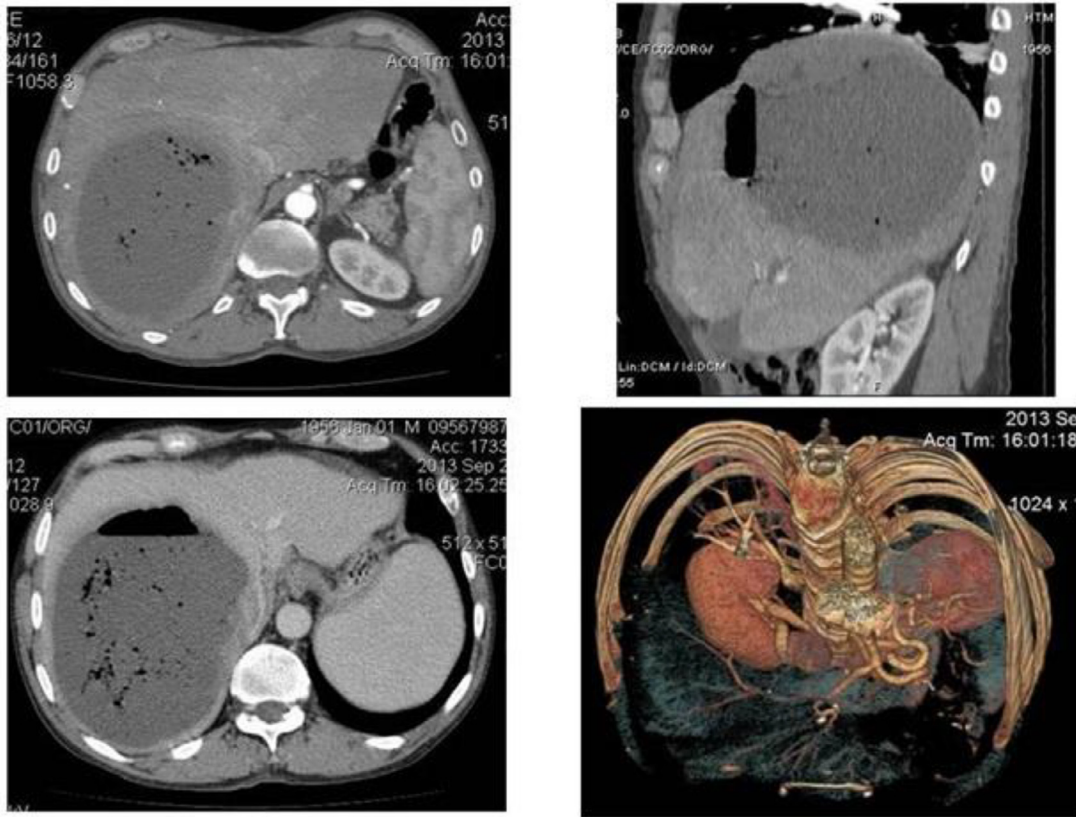
As an established notion, TAE destroys a tumor by the induction of necrosis and/or apoptosis and causes inflammation with cytokine production, which may favor immune activation and presentation of tumor-specific antigens [28], however, this effect is not sufficient for complete tumor resolution. Desirable outcome might be achieved synergizing TAE procedure with immunotherapeutic approaches [29].

For at least 2 centuries, there were reports that cancer patients infected with various bacteria demonstrated spontaneous remission [30]. Thus, bacteria or their extracts were further used in the treatment of cancer [31,32]. Bacteria, their toxins or extracts can stimulate the immune system against tumors. Even more, Bacteria can directly attack and eradicate tumors by invading cancer cells [33].

Streptococcal preparation OK-432 has been used as antitumor agent for more than 20 years, and its safety is well established [34, 35]. OK-432 promotes the functional maturation of imIL-4-DC through ligation of TLR4 [36] and TLR9 [37], and this maturation correlates with the upregulated expression of CD80, CD83, and CD86, thus promoting the effective induction of antigen-specific T cells [37]. It is also reported that following OK-432 activation, human mIL-4-DCs can specifically kill tumor cells via a novel CD40/CD40 ligand-mediated mechanism, without affecting normal cells [38].

In the case reported herein, an accidental infection of the tumor, following TAE procedure can be suggested as a modulator of antitumor immune response, by exposing tumor antigens after necrosis leading to inflammation. In addition to necrosis caused by TAE, the microbes generate an antimicrobial inflammatory response and a severe acute inflammatory

## 45 days after TAE – abscess formation. Abscess vol. -1550 ml



**Fig. 4 – Complication of TAE. Patient presented with signs of infection. A CT scan revealed 1550 mL gas-containing cystic mass – abscess with “air-fluid level”.**

reaction. A strong immune response, caused by necrosis and an infectious agent, led to the complete destruction of the giant tumor. Thus, this procedure became curable.

Complete removal of cancer without damage of normal tissues, which is the ideal performance of cancer treatment, has been achieved with the formation of a liver abscess after TAE. TAE induced a tumor-specific immune response and infection probably acted as adjuvant therapy that enhanced the anti-tumor effect of TAE procedure. As a result, a combination of these processes led to the complete destruction of the tumor. Exploration of the underlying mechanism behind this rare phenomenon might be cardinal to find curative treatments for advanced cancer.

### Statements

**Statement of Ethics:** The case are presented in accordance with the World Medical Association Declaration of Helsinki.

The study protocol was approved by Tbilisi State Medical University ethical committee on human research. The patient has give her written informed consent to publish their case (including publication of images).

### Author contributions

MM and TA performed all medical procedures and patient monitoring. MM and TC designed the report. NT and NN collected and analyzed the data. IP, NK and TC wrote the manuscript. NJ edited the manuscript.

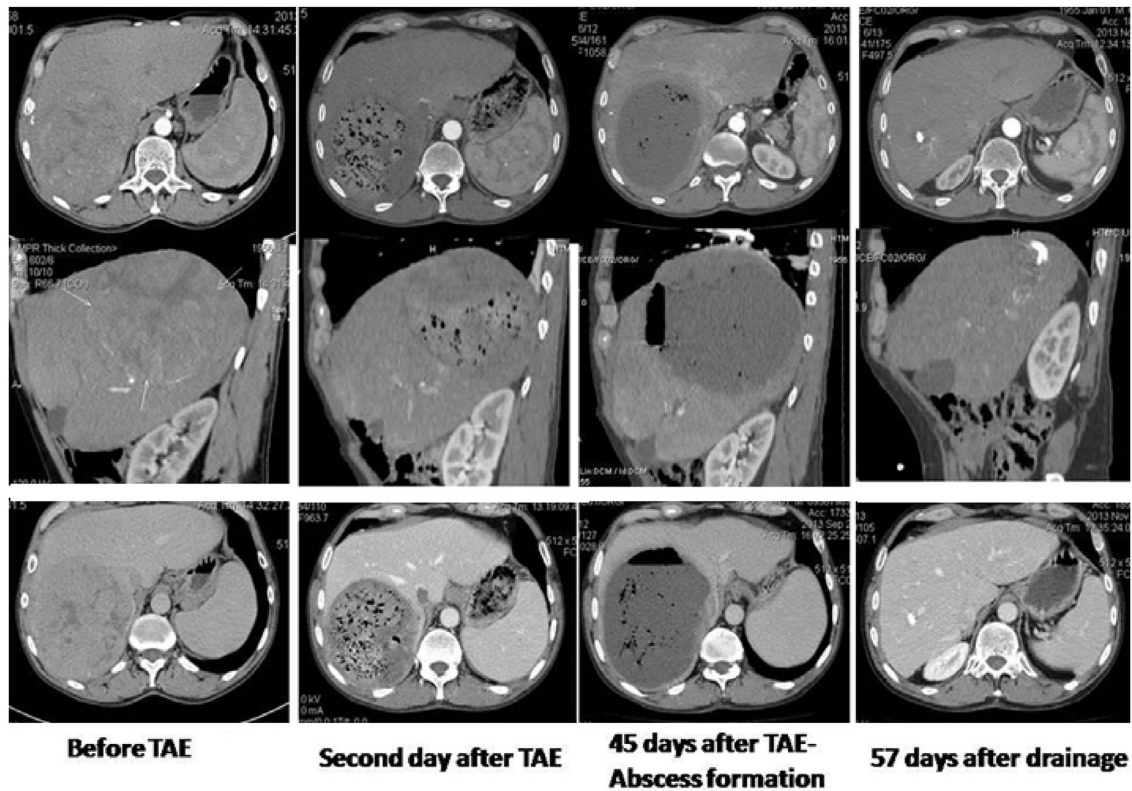


Fig. 5 - CT follow-up.

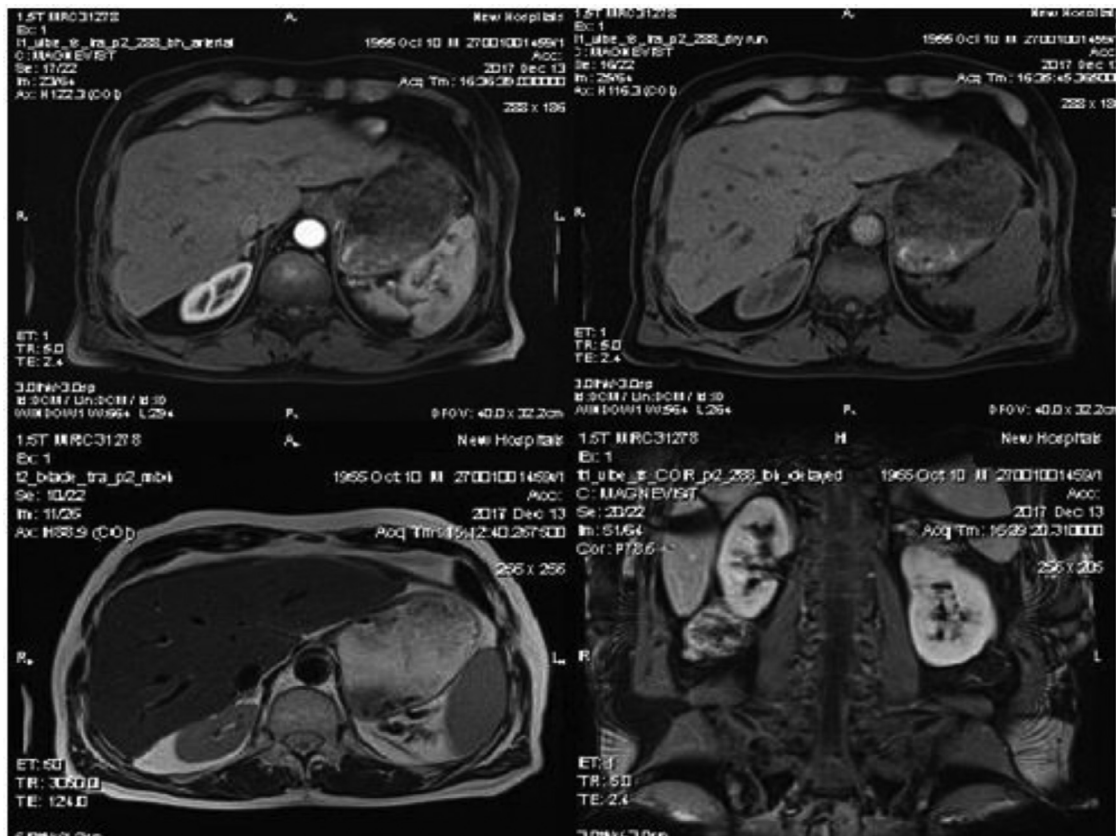


Fig. 6 - Follow-up MRI after TAE (5 years after treatment). No recurrence of liver tumor.

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