

## Introduction

- Patients with intermediate grade hepatocellular carcinoma (BCLC-B) receive trans-arterial chemoembolization (TACE) with or without microwave ablation (MWA) or radiofrequency ablation (RFA), as standard non-curative therapy.
- TACE has established survival benefit, with complications typically involving hepatocellular damage from treatment though the exact mechanism of this outcome remains unclear.
- Here we discuss two patients, one treated with standard TACE alone and one with TACE + MWA for LIRADS-5 HCC, for whom initial positive response was followed by subsequent rapid disease progression- a rare but important complication meriting future exploration.

## Case Presentation- Patient 1

Patient 2- 52M h/o cirrhosis d/t long-standing use of seizure medications. He had increased AFP with CT W/ showing a 3.7 cm lesion in segment VII (LR-5).

He underwent standard TACE alone. 2-month follow-up imaging showed 3.4 cm calcified lesion in the same area w/ decreased AFP. He then re-presented to our center 5 months later w/ abdominal pain and MRI showed 7.1cm x 7.5cm infiltrative mass of the R hepatic lobe w/ extrahepatic extension of 4.1 cm x 11.3 cm involving the diaphragm, and R hepatic vein thrombosis (LR-5, LRT-IV).

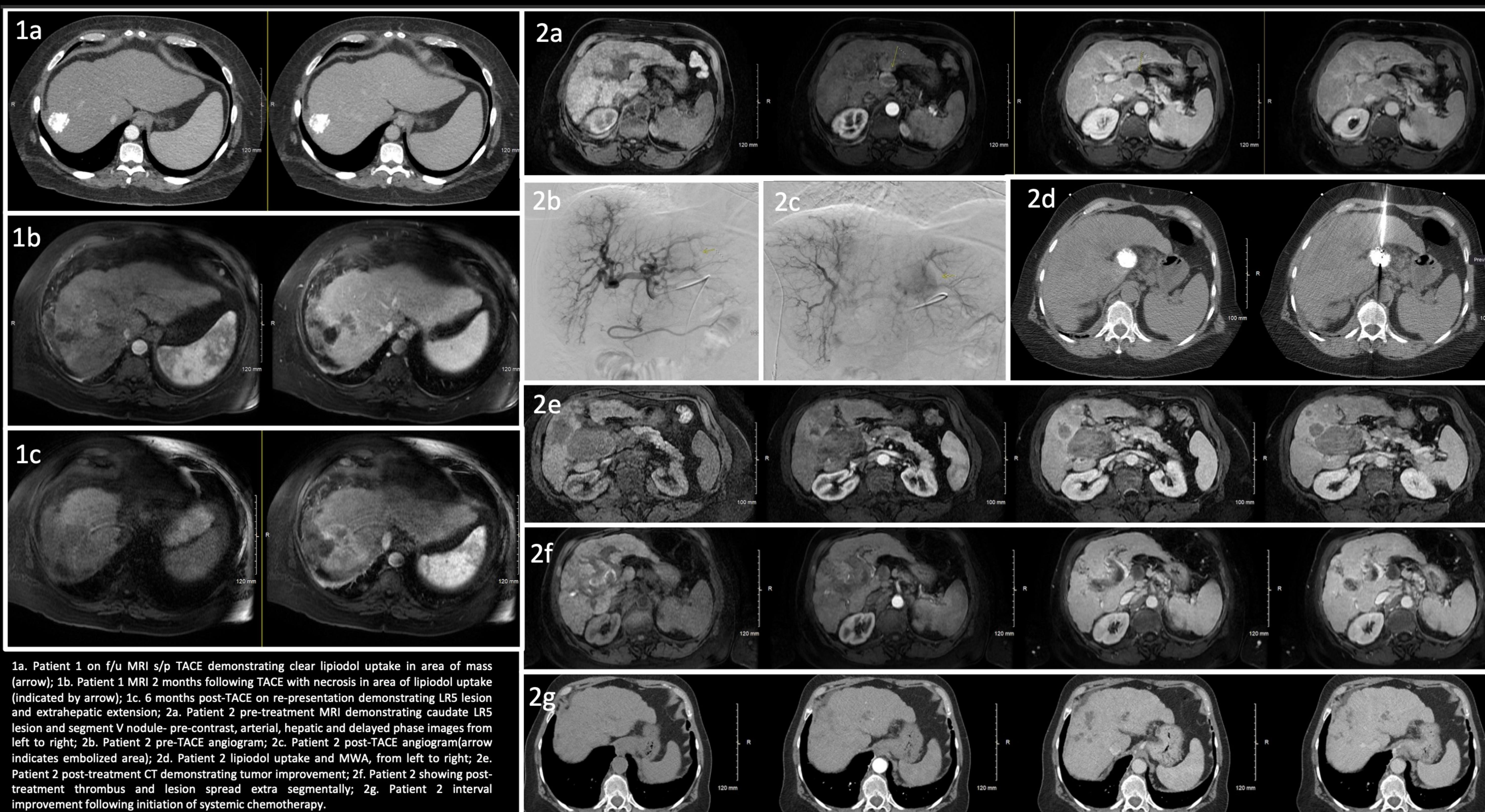
Systemic chemotherapy was recommended but he ultimately succumbed to respiratory failure from VRE bacteremia one month later.

## Case Presentation- Patient 2

Patient 1- 66F h/o HCV cirrhosis undergoing surveillance MRI following serial AFP elevation. This showed arterial phase enhancing lesions of 2.8 cm size in the caudate lobe (LR-5) and 9 mm in segment V (LR-4). Patient underwent TACE and MWA ablation. Follow-up MRI scan at 2 months was improved.

However, 3-month interval CT showed large irregular mass w/ central arterial enhancement and washout involving the central aspects of left and right lobes, and extensive tumor thrombus of portal veins and SMV (LRT-IV).

She began systemic chemotherapy at this point, which has been well tolerated.



1a. Patient 1 on f/u MRI s/p TACE demonstrating clear lipiodol uptake in area of mass (arrow); 1b. Patient 1 MRI 2 months following TACE with necrosis in area of lipiodol uptake (indicated by arrow); 1c. 6 months post-TACE on re-presentation demonstrating LR5 lesion and extrahepatic extension; 2a. Patient 2 pre-treatment MRI demonstrating caudate LR5 lesion and segment V nodule- pre-contrast, arterial, hepatic and delayed phase images from left to right; 2b. Patient 2 pre-TACE angiogram; 2c. Patient 2 post-TACE angiogram (arrow indicates embolized area); 2d. Patient 2 lipiodol uptake and MWA, from left to right; 2e. Patient 2 post-treatment CT demonstrating tumor improvement; 2f. Patient 2 showing post-treatment thrombus and lesion spread extra segmentally; 2g. Patient 2 interval improvement following initiation of systemic chemotherapy.

## Discussion

- Aggressive extra segmental intrahepatic recurrence of HCC following TACE or TACE combined with RWA is quite rare.
- A proposed mechanism is the induction of HIF-1 via hypoxia in tumor remnant after TACE, adding rationale for augmentation with MWA/RFA and making a case for potential added benefit of combination therapy with systemic antiangiogenic therapies such as sorafenib.
- A recent study demonstrated a marked increase in progenitor cell markers such as cytokeratin 19 (CK19) and epithelial cell adhesion molecule (EpCAM) following TACE in a rodent model
- Our patients further demonstrate the need to identify similar cases and build on established radiologic risk stratification, as well as further explore the mechanisms underlying TACE and other minimally invasive therapies to augment their efficacy even further.