

中文題目：末期肝細胞癌合併肝衰竭瀕死病人接受反覆性短療程肝動脈灌注化療之成功案例

英文題目：Successful management of a patient of Child-Pugh class C advanced hepatocellular carcinoma in moribund status with repetitive short course hepatic arterial infusion chemotherapy

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## ***Introduction***

Late diagnosis combined with liver cirrhosis and high HBV DNA titers may contribute to the poor prognosis of hepatocellular carcinoma (HCC) in Taiwan. For patients who are not eligible for curative treatment, systemic therapies such as chemotherapy, targeted therapy, or local transarterial chemoembolization (TACE) are the current treatment options. In Japan, hepatic arterial infusion chemotherapy (HAIC) is often given to patients with localized advanced HCC; however, HAIC has not been established as a standard treatment for advanced HCC, because survival benefits have not been evaluated in large scale prospective randomized trials. Cisplatin and 5-FU are most commonly used chemotherapeutic agents in HAIC, which have been shown to achieve great response and improve survival rates. It was also reported that the average survival of patients with advanced HCC was 4 months from the onset of symptoms and 2 months from the time of admission [1].

## ***Case Presentation***

This 37-year-old man, a hepatitis B carrier, presented to the hospital in 2016/03, with symptoms of general weakness and abdominal fullness. The abdominal ultrasound revealed a 14 cm mosaic-like mass, and the  $\alpha$ -fetoprotein (AFP) was 1460 ng/ml. Abdominal CT scan showed the tumor occupying the right lobe of liver with multiple satellite nodules and right intrahepatic portal vein thrombosis (PVT) was also noted (Figure 1). Radiologically, extrahepatic lymphadenopathies were also seen in the portal hepatic and para-aortic region. CT-guided tumor biopsy was taken and the pathology showed hepatocellular carcinoma. Clinically, the disease was Barcelona classification (BCLC) stage C; cT3bN1M0 stage IVA. As a result of his advanced stage disease, he underwent image-guided intensity modulated radiotherapy with 50Gy in 25 fractions for PVT between 2016/4/25 and 2016/05/27. Sorafenib was also given concurrently and subsequently after the radiation [2]. Besides, he underwent TACE with hepasphere and Doxorubicin via right segmental hepatic arteries for three cycles between 2016/07 and 2016/10. Post-TACE, he sustained good performance, and general stable condition without any constitutional symptoms. His daily activity was independent and self-fulfilling.

In 2017/01, he experienced left upper arm soreness. As such, palliative radiotherapy with 30 Gy in 10 fractions was administered to his left humeral bone metastasis. However, his general condition got worsened progressively despite of maintenance Sorafenib treatment (Table 1). He manifested jaundice, tense abdomen, and lost significant weight. Sorafenib was discontinued in view of his hepatic failure (Child-Pugh score C), and hospice care was recommended (Figure 2). However, a turning point emerged after a multidisciplinary team discussion. A HAIC infusion catheter was placed to the left hepatic artery, which is distal to the origin of gastric branches (Figure 3) via the left subclavian artery. The regimen composed of Cisplatin 20 mg/4 hours/d1-3 and 5-FU 1000 mg/12 hours/d1-3 every three weekly. A total number of 6 courses were delivered between 2017/04 and 2017/08. He tolerated the HAIC well and the lab data has shown significant

improvement (Figure 5). In our first encounter with the patient, he was in moribund liver failure and usually considered as a hospice candidate. Surprisingly his Child score went down from C (score=13) to B (score=8). ECOG was reversed from 3 to 1 in 2017/07. Overall, he had made a great clinical improvement and shown good tumor response (Figure 4).

### ***Discussion***

HAIC using low dose, continuous infusion of chemotherapeutic agents has shown benefits for patients with advanced HCC, who were ineligible for any local treatment, or have failed all conventional therapy [3-5]. In retrospect, instead of maintaining an apparently failure Sorafenib, he should have undergone more local treatments before being referred to a multidisciplinary team in desperate. It's always the norm to deny a wrong candidate from HAIC by a conventional wisdom. However, the team concluded the imminent cause of death would be hepatic failure, rather than a minimal nonthreatening bone metastasis. After a heated debate, the team reached a heroic consent to salvage him with HAIC. To our surprise, our patient survives and still lives up to now with good performance and quality of life.

The lessons learned from our success are firstly, the importance of early HAIC intervention once exhausted all conventional means. Secondly, the selection criteria of contemporary studies for advanced HCC patients should be expanded to accommodate more patients who may benefit from the procedure. Thirdly, we should make HAIC aware to more specialists in treating HCC, despite its cumbersome procedure, catheter related complications and prolonged hospital stay.

### ***Conclusion***

Early HAIC intervention is useful as a therapeutic option after failing all other local treatments for advanced HCC. The eligibility for HAIC could be relaxed to benefit a broader spectrum of advanced HCC patients, such as Child Pugh classification C group in a hope to improve the survival and quality of life in palliative endeavors.