

中文題目：一個轉移性肝癌患者經 Atezolizumab + Avastin 治療失敗的成功二線治療經驗

英文題目：A successful second line therapy in a case of metastatic HCC patient after Atezolizumab + Avastin treatment failure .

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Introduction:

HCC (hepatocellular carcinoma) is the second leading cause of cancer-related death in Taiwan . For locally advanced and metastatic HCC , Atezolizumab , a immune checkpoint inhibitor (ICI) , targeting PD-L1 (programmed death ligand 1) plus Avastin , a VEGF (vascular endothelial growth factor) monoclonal antibody (AA regimen) was considered as the new standard first line treatment since 2020 . But there was no standard salvage treatment after AA failure . We report a metastatic HCC case who achieved complete remission after failure of AA .

Case presentation:

A 52-years-old male patient had underlying disease of liver cirrhosis , Child A , chronic hepatitis B related . He experienced dry cough , progressive right upper abdominal pain for 2 weeks and body weight loss 6 kg in half year . CT scan on 2021/07/19 (Fig 1) revealed huge liver mass with bilateral lung small nodules . HCC with lung mets was diagnosed by typical wash-out pattern on CT scan and high alfa fetoprotein (AFP) : 147176 ng/ml . He received Avastin + Atezolizumab every 3 weeks as first line therapy. However , abdominal fullness persisted and dyspnea developed after 3 cycles treatments . AFP increased to 247677 ng/ml and enlarged both liver HCC and lung mets was proved by CT scan on 2021/09/29 (Fig 2). After discussing with family , he agreed another VEGF TKI : Lenvatinib as salvage treatment . Besides ,another immune checkpoint inhibitor (ICI) , pembrolizumab (Keytruda) , used as lower dose (100 mg every 3 weeks) was also prescribed . Serum AFP level drop significantly to 567 ng/ml after 4 cycles treatment .

CT scan was repeated again on 2021/12/08 (Fig 3) and almost complete remission of lung mets and cystic change of liver HCC was found . Except mild higher blood pressure , there was no any grade 3 or higher adverse effect

Discussion:

For locally advanced or metastatic HCC , sorafenib has been the standard treatment for a long time since 2007 after SHARP trial . All of the standard second line treatments , including TKIs (regorafenib , carbozantinib) , VEGF monoclonal Ab (ramucirumab) and ICIs (nivolumab & pembrolizumab) are designed after sorafenib failure. In 2020 , AA was shown to have significant survival benefit than sorafenib in a global phase III clinical trial : IMbrave 150 and become the new standard first line

treatment . However, there was no randomized , well-designed , second line treatment to prove if current second line therapy is still effective after AA regimen . Although atezolizumab and Keytruda were all the immune check point inhibitors but they still had different mechanism of action. Atezolizumab targeted PD-L1 but Keytruda targeted PD-1 . The targeted site difference cause fewer adverse side effect of PD-L1 inhibitor and maybe also cause better tumor response in HCC . We do not have a good explanation for the difference between these two similar therapy .

Because of economic reason , the patient received lower dose of lenvatinib + Keytruda as second line treatment . Although Keytruda plus lenvatinib have similar acting mechanism as AA regimen , we still very shocked about the totally different tumor response between first and second line treatment .

Conclusion:

We report a metastatic HCC patient , who progressed after AA regimen to had very good tumor response by using Keytruda plus lenvatinib as salvage treatment. We still needed large , multicenter and randomized trial to confirmed the effect of Keytruda + Lenvatinib and to find the predictive markers in second line setting of metastatic HCC .

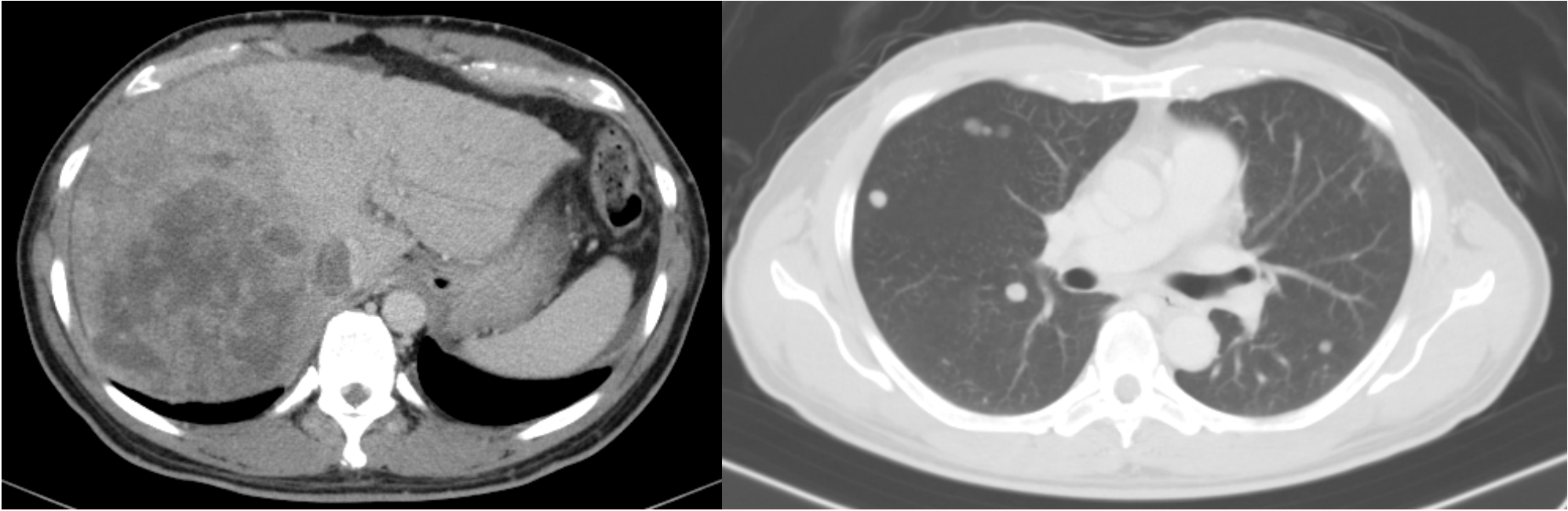


Fig 1 : 2021/07/19 CT scan : HCC with portal vein thrombosis multiple lung mets.

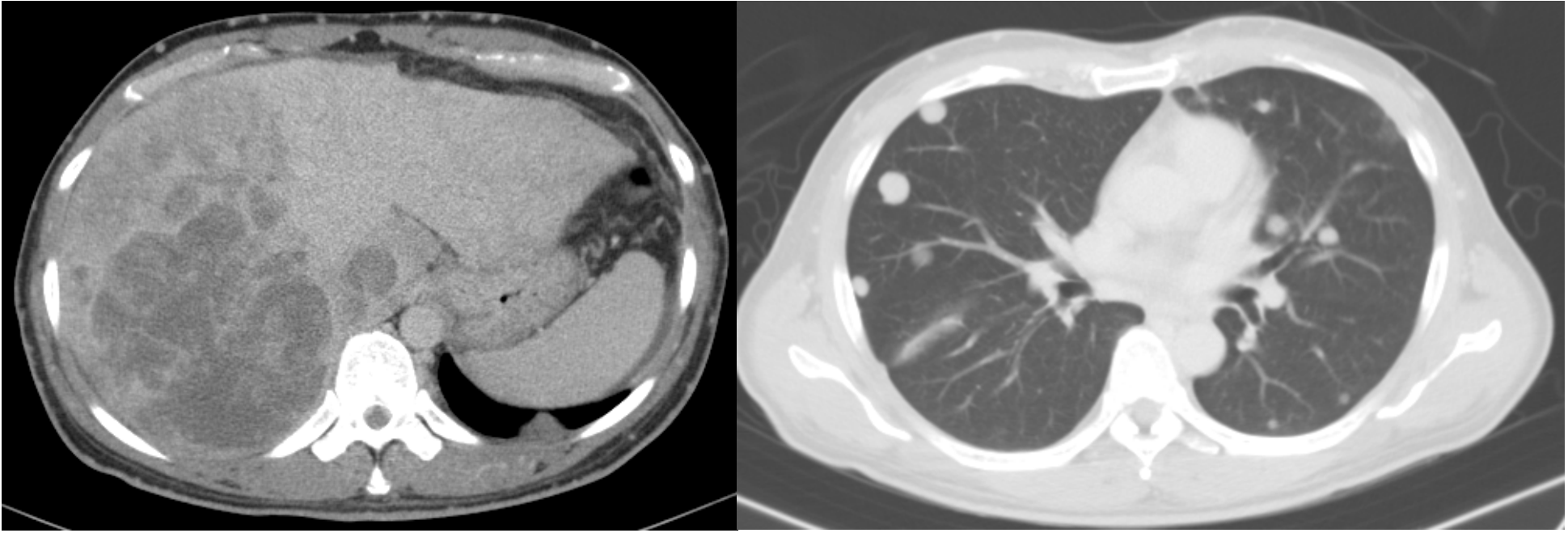


Fig 2 :2021/09/29 CT scan : tumor progression after 3 cycles AA therapy.

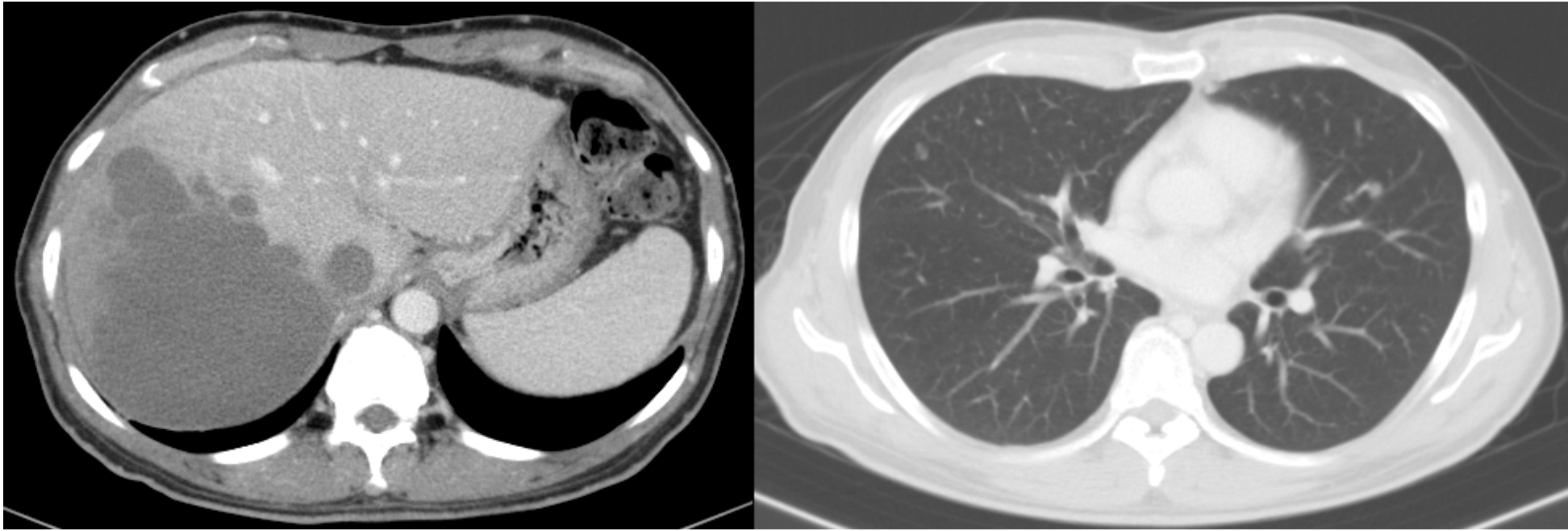


Fig 3 : 2021/12/08 CT scan : almost cystic change of HCC and lung mets.