

A Single Case of Fibrolamellar Hepatocellular Carcinoma Diagnosed and Treated By Sorafenib

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Abstract— Fibrolamellar carcinoma is a rare primary malignant neoplasm of the liver, different than the well-known hepatocellular carcinoma and affecting young patients with no underlying disease (1). Most of the knowledge about this cancer is obtained from small series due to its scarcity.

The survival outcomes is better than the classical hepatocellular carcinoma but remains poor in the locally advanced and metastatic setting.

This case is about a 34 year old patient with a locally advanced fibrolamellar carcinoma diagnosed in a context of thrombosis of the lower limb and treated with sorafenib in first line with a good clinical response.

Index Terms— Fibrolamellar hepatocellular carcinoma , surgery , sorafenib , targeted therapy .

I. INTRODUCTION

The fibrolamellar hepatocellular carcinoma (FLHCC) is a unique and rare tumor of the liver that was first described in 1956 as a subtype of hepatocellular carcinoma (HCC) , it is accounting for 0.8 to 16% of all hepatocellular malignancies (1).

In a recent study, Ramaïet et al. found that FLHCC has a slight male predominance, a bimodal age distribution, and does not tend to a specific ethnicity (2). Also, recent studies have found that FLHCC is associated with the presence of DNAJB-PRKACA fusion mutations (7).

Something important to point is that no underlying liver disease has been found (8).

Abdominal pain, distention due to abdominal mass and anorexia were the most common symptoms, the serum alpha-feto protein can also be elevated but rarely (10 % of cases) conversely to the HCC (9).

It is also worth noting that most patients are in advanced stages at the time of diagnosis with 40-50% with distant metastasis (11-12).

Histologically tumor cells in FLHCC are well differentiated, large, polygonal with eosinophilic hyaline cytoplasmic bodies, large vesicular nuclei and prominent nucleoli.

The immunohistochemical profile is similar to that of the HCC but the immunostaining for CD68 and epithelial membrane antigen (EMA) are specific for FLHCC (13-16).

Radiologically , Unlike the strong peripheral enhancement with subsequent wash out in the portal venous phase for HCC on CT-SCAN , the FLHCC demonstrate heterogeneous hyperenhancement compared to the rest of the liver and a central scars which is considered a distinguish feature and help in the diagnosis (10).

Curative surgery is the mainstay of therapy with a survival rate at 5 years of 70-76%, but the recurrence rate is very high up to 90%(17).

For the locally advanced and metastatic settings the systemic and targeted therapy is used but the prognosis in this situations remains poor.

II. CASE REPORT :

34 years old male was presented to the emergency units with an edema of the lower limb
The echodoppler showed a thrombosis and a mass in the liver

A thoraco-abdominal scan(CT-Scan) confirmed the thrombosis and the enormous liver mass spontaneously hypodense presenting a pseudo-nodular enhancement in the arterial phase and becoming hypodense with the presence of a central scarring , the tumor was also responsible for repression of the inferior vena cava with an echogenic thrombus extending to the right and left primary iliac veins. Total bilirubin was 14 umol (3-20 umol/l) , direct bilirubin 10 umol/ l (0-8.6 umol/l) , Gamma-glutamyl transferase (GGT) 410 ui/l and alpha-fetoprotein >2000 ng/ml.

A biopsy was consistent with fibrolamellar HCC . The case was discussed on the tumor board and the FLHCC was found unresectable.

The decision was then to start the sorafenib and the clinical evolution was quite spectacular with a decrease in the abdominal distention and disappearance of the pain.

In term of secondary effects, they were diarrhea, hand-foot syndrome and fatigue but all in all the treatment was well tolerated as these secondary effects were mainly a grade 1-2 at most.

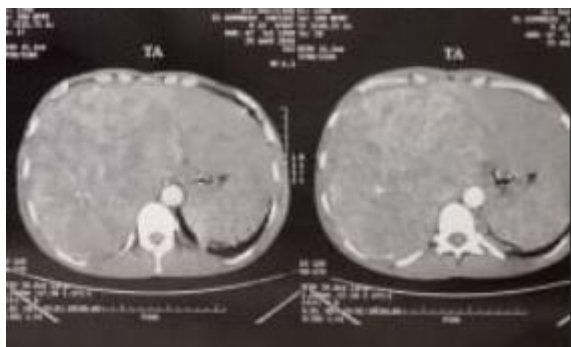


Figure 1 : heterogeneous hyper-enhancement of the tumor

III. DISCUSSION

Since the first description of the FLHCC by Edmondson in 1956, little progress has been made in the treatment of this entity(1).

As mentioned previously, it's a rare entity and thus most of the clinico-pathological and survival data are derived from report cases or small series of patients(1-2).

The surgery is the pivotal curable treatment, but the recurrence rate is very high even when it is a R0 resection(17).

Also there wasn't a demonstrated benefit from adjuvant and neoadjuvant therapy in resectable FLHCC (17).

for patients with non-resectable tumors like our patient , there have not been a consensus about the best approach and most of the therapeutic decisions have either been extrapolated from the classical HCC or based on report cases and small series .

Unfortunately chemotherapy with 5-Fluorouracil does not offer potential benefit, as for targeted therapy namely sorafenib some series reported a possibility of stabilization under it while others reported progression (18).

As for the role of checkpoint inhibitors , their efficacy has been established in solid tumors especially those with high mutational burden or genomic instability , improving the overall survival , but in the case of FLHCC and from the little series found in the literature , the effectiveness of

immunotherapy is controversial and therefore there are a need to explore more this pathway (17).

IV. CONCLUSION

There is still a lot of shadow zones in the diagnostic and treatment of the FLHCC as it is a different entity than the classical HCC .

Until now , the treatments used didn't show a great response in the metastatic setting , as for the localized FLHCC the rate of recurrence after surgery is really high even with a radical resection.

Future studies that evaluate various therapeutic strategies targeting molecular pathways and genetic alterations would help better understanding of the natural history of this disease

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