

CASE REPORT

Curative lung metastectomy and complete pathological response after neo-adjuvant GEMOX chemotherapy for relapse fibrolamellar hepatocellular carcinoma

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SUMMARY

Fibrolamellar hepatocellular carcinoma (FL-HCC) is a rare variant of hepatocellular carcinoma. It is commonly reported in the younger population with no underlying chronic liver disease and free of viral Hepatitis B and C. Local recurrence and distant metastasis are common despite better prognosis compared to conventional hepatocellular carcinoma. Complete surgical resection is associated with higher median survival and is the mainstay treatment option for localized FL-HCC. Multi-modality therapies such as TACE can be used to downstage upfront unresectable FL-HCC. Complete response with GEMOX chemotherapy has been reported in advanced metastatic FL-HCC and should be considered in upfront unresectable or metastatic disease. We present a case of biopsied proven relapse FL-HCC with oligo- left lung metastasis who successfully underwent a left lung lobectomy after neo-adjuvant GEMOX chemotherapy, and is disease free at 24 months follow up.

INTRODUCTION

Fibrolamellar hepatocellular carcinoma (FL-HCC) was first described in 1956 by Edmondson as a rare variant of hepatocellular carcinoma with distinctive histology predominantly affect the younger individuals with non-cirrhotic liver.¹ Compared to conventional HCC, FL-HCC is associated with better prognosis² with a higher incidence in the Caucasian population. Currently, surgical resection is the mainstay of treatment even for resectable metastatic lesion,² as it is associated with longer survival rate. Multi-modality therapies³ have been used to downstage non-resectable tumour. We present a case of biopsied proven relapsed FL-HCC with left lower lobe lung oligometastases. The patient was treated with neo-adjuvant GEMOX chemotherapy with a good clinical response and subsequently underwent a successful left lower lobectomy.

CASE REPORT

A 46 years old lifelong non-smoker lady with no significant past medical illness presented with an enlarging epigastric mass in December 2010. Multiphase CT showed a large multicentric mass, 19cm x 20cm at the right lobe of liver highly suggestive of FL-HCC. Her AFP was raised at 43.2 ng/dl. Hepatitis Bs antigen and Hepatitis C antibody were

negative. In view of huge tumour burden, Transarterial Chemoembolization (TACE) via DC bead was given for 4 times before an extended right hemi-hepatectomy was done successfully in March 2012. Histopathology report confirmed FL-HCC with clear resection margins. CECT Abdomen post operation showed no residual disease and her AFP normalized. Subsequently, the patient was followed up regularly with 6 monthly CECT Abdomen and AFP.

The patient was well until she re-presented in February 2014 with an episode of frank hemoptysis. AFP was elevated at 19.6IU/mL Repeated CECT Thorax and Abdomen showed multiple lung nodules, coalesced at left lower lobe measuring 7.3cm x 7.7cm suggestive of lung metastasis with no evidence of local recurrence. PET CT confirmed oligometastases with FDG avid left lower lobe lung nodules, which was proven to be relapsed FL-HCC on biopsy. Upfront surgery was attempted but failed, and the patient was subsequently referred to our oncology centre. We commenced the patient on two weekly neo-adjuvant Gemcitabine-Oxaliplatin combination chemotherapy (GEMOX) with an aim for downstaging and curative metastectomy. Reassessment CT scan post 6 cycles of GEMOX showed good partial response with significant reduction size of lung metastasis to 3.1 x 5.1cm and no other disease site.

The patient subsequently underwent a successful left lower lobe lobectomy in January 2015. Post-op she developed a left pneumothorax which resolved with a left chest tube insertion. Histopathology review showed complete pathological response with extensive necrosis and no malignancy cells seen. The patient was given another six cycles of adjuvant GEMOX (total of 12 cycles) starting 6 weeks post op without any complication. Latest surveillance CT Thorax, Abdomen and Pelvis (TAP) 24 months post adjuvant GemOx showed no evidence of disease recurrence.

DISCUSSION

The incidence of Fibrolamellar hepatocellular carcinoma (FL-HCC) - a rare variant of hepatocellular carcinoma (HCC) is low, representing only 0.6 to 8.6% of all HCC. While typical HCC has an average presentation age of 60 years old, FL-HCC is more common amongst the younger generation, and usually occurs in patients with no hepatitis, cirrhosis² or

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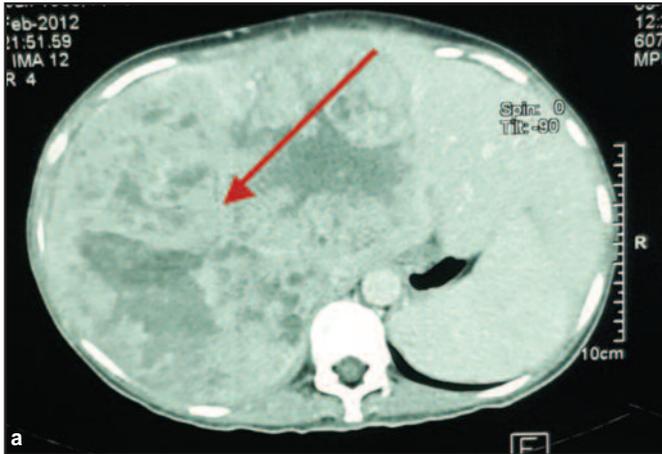


Fig. 1a: Shows the abdomen computed tomography (CT) image before resection with huge hepatoma at the right lobe of the liver.

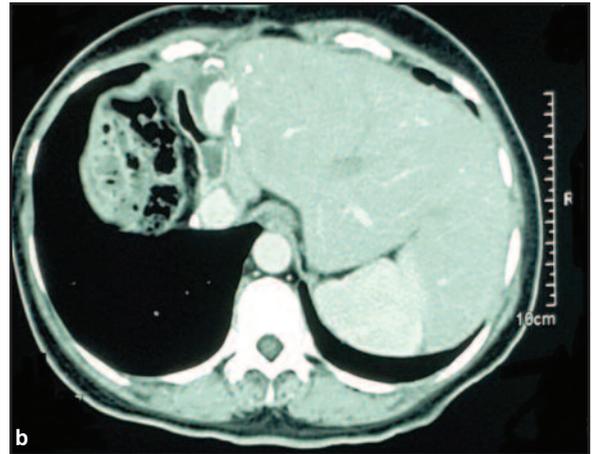


Fig. 1b: CT image of post-resection.

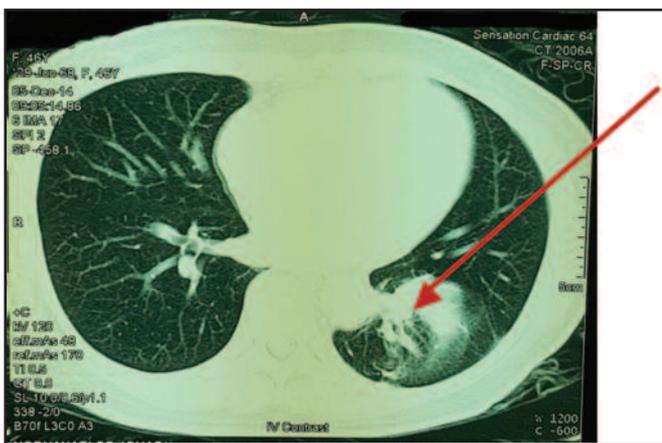


Fig. 2: Left lower lobe lung metastasis measuring 7.3cm x 7.7cm

elevated AFP >200ng/ml. Also, it appears to be less aggressive than typical HCC with a significantly better prognosis.²

Currently, surgical resection is the mainstay treatment for resectable FL-HCC. 5 years survival rate after partial hepatectomy alone is reported to be as high as 70-85% while unresectable patients have median survival of only 12 months.² However, the recurrence rate either locally or distant metastasis for FL-HCC is high with about 50 to 60% of patients reported to require second resections.³ However, as in our case, upfront surgical resection may not always be possible due to the locally advanced disease at presentation. Other local regional modalities, radiotherapy and chemotherapy have been used to downstage the disease prior to contemplating surgery though it has yet to be established which is the best therapy for FL-HCC.^{3,4}

At her initial presentation and diagnosis, our patient was given a total of four transarterial chemoembolization (TACE) with DC beads with good tumour shrinkage rendering it resectable. Figure 1 shows the abdomen computed tomography (CT) image before resection with huge

hepatoma at the right lobe of the liver. CT image of post-resection is shown in figure 2.

Largely due to the rarity of the disease, there is limited data on the effectiveness of systemic chemotherapy for the treatment of FL-HCC. As for advanced typical HCC, there is no validated data for systemic chemotherapy, and the role of tyrosine kinase inhibitors such as sorafenib for FL-HCC is not known. Clinical trials are still going on for the drugs like the combination of cisplatin, doxorubicin, 5-fluorouracil and alpha-interferon, but the most extensive study is on a combination of gemcitabine and oxaliplatin (GEMOX).⁵ This regime is the most promising as it lacks renal and hepatic toxicity in cirrhotic patients as shown in the studies.

To date, there are a few published case reports of locally advanced and metastatic FL-HCC successfully treated with GEMOX with a prolonged complete response, though there is no standardised regimen and optimal duration of treatment is not established. Our patient re-presented with upfront unresectable oligometastasis at left lower lobe ~ two years after right hemi-hepatotectomy. Figure 3 shows CT images of lung metastasis in our patient. We used 85mg/m² of oxaliplatin, 1000mg/m² of gemcitabine two weekly and assessed the patient with a CXR after every two cycles of GEMOX and repeat a re-assessment CT after 6 cycles. She tolerated the treatment well and as she had achieved complete pathological complete response post neo-adjuvant GEMOX chemotherapy with no measurable disease post resection, we treated her for a total duration of 6 months (12 cycles).

At her last review 24 months post her last cycle of adjuvant GEMOX and 28 months post left lobectomy, our patient remains in remission and well.

CONCLUSION

FL-HCC is a rare variant of hepatocellular carcinoma with a better prognosis than typical HCC. Surgical resection improves overall survival and remains the mainstay

treatment for FL-HCC even for metastatic disease. GEMOX chemotherapy appears to be an effective and tolerable systemic therapy for FL-HCC and may be an option to consider for downstaging patients with unresectable FL-HCC prior to curative resection. Ongoing studies need to be conducted to establish the efficacy and optimal duration of treatment. Regular follow up with tumour markers and surveillance CT post curative surgery and systemic therapy is recommended.

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