THE ROLE OF HUMAN U THREE PROTEIN 14A AS A PREDICTOR FOR HEPATOCELLULAR CARCINOMA RECURRENCE AFTER MICROWAVE ABLATION

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Introduction

- Hepatocellular carcinoma (HCC) is one of the most common cancers worldwide. Cirrhosis is the most important risk factor for the development of HCC. The most widely adopted staging system is the Barcelona Clinic Liver Cancer (BCLC) algorithm, which links prognosis of HCC with the best treatment option based on strong clinical evidence. One of the loco-regional interventional therapies that plays a major role in the current therapeutic management of HCC, is microwave ablation (MWA). The applied electromagnetic field causes water molecules to rotate billions of times per second, which leads to heat generation and cellular death via coagulation necrosis. The prognosis of HCC remains unsatisfactory, thus novel molecular markers are needed to predict tumor biology and identify patients with higher risk of metastasis or recurrence. Human U three protein 14a (hUTP14a), a member of the U three proteins (UTPs) family, is one of the nucleolar proteins, that play an important role in unregulated replication of defective DNA, genomic instability and progression to cancer, through promoting degradation the tumor suppressor protein p53.

Aim of the work

- The present work aimed to measure the hepatic expression of hUTP14a in cirrhotic HCC patients (tumor & non-tumor tissues); to evaluate its prognostic role as a predictor for HCC recurrence after treatment with MWA.

Subjects and Methods

- All patients included in our study were subjected to routine investigations including; complete blood count (CBC), alanine aminotransaminase (ALT), aspartate aminotransferase (AST), serum albumin, prothrombin activity, total serum bilirubin, alpha-fetoprotein (AFP), HCV Ab and HBsAg.
- Abdominal Ultrasound (US) was done to assess liver size, presence or absence of focal hepatic lesion, size of spleen, presence or absence of ascites and portal vein invasion.
- The diagnosis of HCC was confirmed by triphasic computed tomography (CT) abdomen which showed a characteristic pattern of arterial enhancement and venous washout. Immunohistochemistry for US guided fine needle aspiration from the tumor and the cirrhotic non-tumor tissue was performed. MWA procedure; was conducted with a high-power microwave ablation system with a maximum generator power of 150 W and a generator frequency of 2.45 GHz.
- All patients were followed up using triphasic CT abdomen 2 weeks after the MWA session to assess the completeness and success of the ablation. Thereafter follow up was done every 3 months for one year to be able to detect any HCC recurrence.

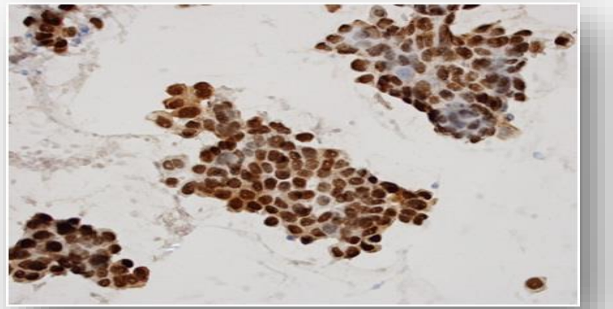
Results

- The present study was carried out on 26 HCC patients diagnosed by abdominal triphasic CT or dynamic magnetic resonance imaging (MRI). Patients were recruited from the Hepatobiliary unit, Internal Medicine Department, Alexandria University Hospital.
- Concerning the number of the focal lesions in our studied HCC cases, 16/26 patients had a single lesion (61.53%), 4/26 patients had 2 focal lesions (15.39%) and 6/26 patients had 3 focal lesions (23.08%) with a total of 42 focal lesions.
- The tumor size of our 42 studied HCC nodules was less than 3 cm in 31% and 3-5 cm in 69%.
- In our study, 12/26 studied HCC cases (46.15%) were grade II and 14/26 studied HCC cases (53.85%) were grade III according to Edmondson-Steiner (ES) grading system.

Distribution of the studied HCC cases according to tumor characteristics

	No.	%
Number of focal lesions		
1	16	61.53
2	4	15.39
3	6	23.08
Tumor Size		
<3cm	13	31.0
3–5 cm	29	69.0
ES grading system		
II	12	46.15
III	14	53.85

- 14/26 (53.85%) of the studied HCC patients were recurrence free, while 12/26 (46.15%) of the studied HCC patients witnessed recurrence within 12 months of follow up. Out of the 12 studied HCC cases who experienced recurrence, 6 cases showed local recurrences (6/12, 50%) and 6 cases had denovo HCC (6/12, 50%).
- The hUTP14a expression was observed in the form of nuclear staining in the cellular population of our HCC cases stained with the antibody.



Conclusion

- The hUTP14a has an oncogenic potential, as it is highly expressed in HCC tissues compared to surrounding non-tumor cirrhotic tissues.
- The hUTP14a expression is not related to different studied clinic-pathological parameters as Child-Pugh (CP); ES grade; size of tumors; number of tumors, however, the reverse was proved regarding serum AFP levels.
- The hUTP14a expression in tumor tissue is related to the response of HCC to MWA, where tumoral hUTP14a expression is significantly higher in patients who experienced recurrence than those who didn't experience recurrence after MWA.
- The hUTP14a could be used as a promising prognostic biomarker with high sensitivity and specificity for prediction of HCC recurrence after treatment with MWA.