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EXPRESSION OF p62/SQSTM1 IN HEPATOCELLULAR CARCINOMA AND RELATION TO TUMOR RECURRENCE AFTER RADIOFREQUENCY ABLATION

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INTRODUCTION

Autophagy is a highly regulated lysosomal-dependant cellular process that allows the degradation of detrimental components to maintain cellular homeostasis under a variety of stimuli. Dysregulation of autophagy is involved in a broad spectrum of diseases such as cancers including hepatocellular carcinoma (HCC). p62/SQSTM1 is considered as an indicator of functional autophagy, where its accumulation reflects impaired autophagy which is a key to the onset of tumorigenesis.

AIM

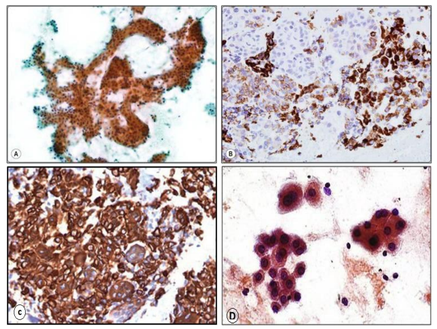
Aim to evaluate the hepatic expression of autophagy-related protein p62/SQSTM1 in HCC of hepatitis C virus (HCV)-related cirrhosis and identification of the impact of this expression on tumor recurrence after radiofrequency ablation (RFA) management.

METHOD

This study included 44 HCC patients of HCV-related cirrhosis who were candidate to RFA. Expression of p62 was measured in tumor tissue of all studied patients using immunohistochemistry, and coupled with measurement in peri-cancerous cirrhotic liver tissue as control. Follow-up of our patients was done every 3 months for one year by multiphase CT/dynamic MRI.

RESULTS

p62 expression was significantly increased in HCC tissues compared to their corresponding peri-tumor tissues (*P* =0.001). Poorly differentiated HCC among the other histological grades showed higher p62 expression level (*P* <0.001). As a prognostic marker, p62 expression level had significant positive correlations with tumor recurrence and overall mortality rates.



Cytoplasmic p62/SQSTM1 staining in different HCC grades (A: grade I; B: grade II; C: grade III; D: peri-tumor tissue).

Table (1): Levels of p62 expression in the tumoral and peri-tumoral tissues.

	Tumoral p62	Peri-tumoral p62	t	p
Min. – Max.	15.0 – 42.0	11.0 – 40.0	8.934*	0.001*
Mean ± SD	28.84± 6.53	26.75± 6.62		
Median	28.0	26.0		

t, p: t and p values for **Paired t-test** for comparing between tumoral and peri-tumoral p62
*: Statistically significant at p ≤ 0.05

Table (3): Relation between p62 expression level and disease recurrence

p62	Non recurrence (n=30)	Recurrence (n=14)	t	p
Min. – Max.	11.0 – 39.0	23.0 – 40.0	4.055*	<0.001*
Mean ± SD	24.40 ± 5.76	31.79 ± 5.56		
Median	26.0	32.0		

t: Student`t-test
p: p value for comparing between the studied groups
*: Statistically significant at p ≤ 0.05

Table (2): Tumoral and peri-tumoral p62 expression in relation to HCC grade

	HCC grade			F	P
	Grade I (n=3)	Grade II (n=31)	Grade III (n=10)		
Peri-tumoral p62 • Min. –Max. • Mean± SD • Median	16.0-19.0 17.33±1.53 17.0	11.0-30.0 25.61±4.18 26.0	33.0-40.0 36.20±2.53 36.0	45.529*	<0.001*
Significance between groups	p_1= 0.008* ,p_2<0.001* ,p_3<0.001*				
Tumoral p62 • Min. –Max. • Mean± SD • Median	18.0-20.0 19.33±1.15 20.0	15.0-31.0 26.58±3.57 28.0	35.0-42.0 38.70±2.26 39.0	66.770*	<0.001*
Significance between groups	p_1= 0.002* ,p_2<0.001* ,p_3<0.001*				

F,p: F and p values for ANOVA test. Significance between groups was done using Post Hoc Test (Tukey).
*: Statistically significant at p ≤ 0.05
p_1: p value for comparing between grade I and II
p_2: p value for comparing between grade I and III
p_3: p value for comparing between grade II and III

CONCLUSIONS

Over-expression of p62 in cancerous tissue can identify a subset of HCC patients with unfavorable prognosis and higher tumor recurrence after RFA management.

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