Macrotrabecular Growth Pattern is Associated with Poor Prognosis in Patients with Hepatocellular Carcinoma

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Disclosure: Nothing To Disclose (The authors of this abstract have indicated that they have no conflicts of interest that relate to the content of this abstract).

Background

- Recent studies have shown hepatocellular carcinoma (HCC) with macrotrabecular (MT) pattern may be a distinct aggressive HCC subtype.
- The aim of this study is to evaluate the clinicopathologic significance of MT growth pattern in HCC patients.

Design

- We included HCC patients who underwent surgical resection at 2 large health systems between Jan 2008 - Dec 2017.
- HCC histologic features were recorded including tumor focality, size, grade, necrosis, macro and micro- lymphovascular invasion, and inflammatory cell infiltrates.
- Presence and percentage of HCC histologic patterns were assessed including conventional/trabecular, steatohepatitic, pseudoglandular, compact/solid, clear cell, pleomorphic/giant cell and and macrotrabecular (MT) variants.
- Fisher exact test was used to compare demographics, clinical and tumor characteristics between patients with and without MT.
- Univariable and multivariable Cox regression analyses were used to compare survival between the two groups.

Results

- We identified 97 eligible patients. Median age was 62 (27-90 years), and 70 (72.2%) patients were male.
- The most common liver disease etiologies were hepatitis C (63.9%), non-alcoholic steatohepatitis (16.5%), and hepatitis B (11.3%).
- Most lesions (93.8%) were unifocal, and median tumor size was 3 (range 1.2 – 16.7) cm.

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Variable	Adjusted HR	95% CI
MT pattern	2.47	1.04 – 5.86
Unifocal lesion	0.57	0.24 – 1.38
Tumor size	1.03	0.95 – 1.13
Tumor grade	1.25	0.68 – 2.30
Microvascular invasion	1.53	0.64 – 3.65

Table1: Factors associated with survival among patients with HCC undergoing surgical resection

- MT was identified in 41 (42.2%) patients.
- MT appeared more common in hepatitis B patients (8 of 10), although the proportion with MT did not significantly differ by liver disease etiology (p=0.15) or presence vs. absence of cirrhosis on surgical specimen (p=0.22).
- MT was significantly associated with larger tumor size (3.5 vs. 2.7 cm; p=0.03), increased microvascular invasion (MVI; 80.5% vs. 30.4%; p<0.001), higher grade (53.7% vs. 14.3%;p<0.001), and less infiltrating lymphocytes (41.5% vs. 63.5%, p=0.06).
- MT patients had higher serum AFP levels (median 41 vs. 11 ng/mL) but this did not reach statistical significance (p=0.21).
- MT patients had increased residual disease or early recurrence after surgical resection (33.5% vs. 4.0%, p=0.001).
- In Multivariable Cox regression, MT pattern was independently associated with increased mortality risk (HR 2.47, 95%CI 1.04-5.86) after adjusting for tumor focality, size, grade, and MVI. (Table 1)

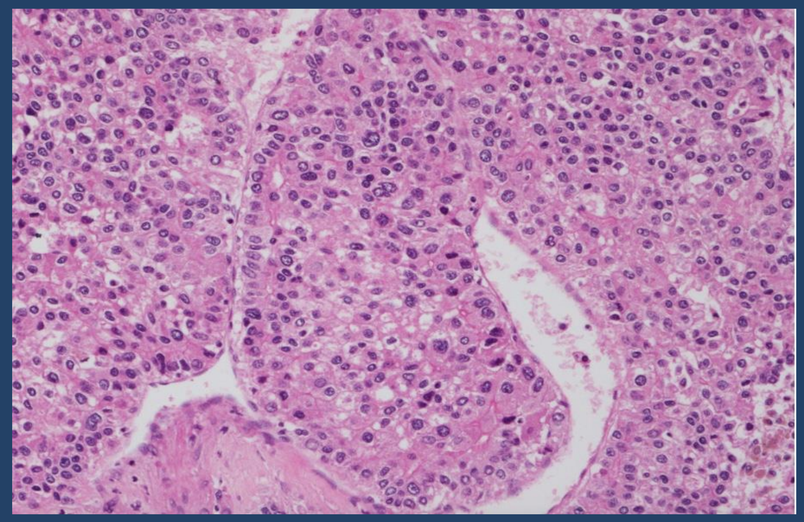

Figure 1. Histological appearance of MT-HCC. The tumor consists of a macrotrabecular pattern, with trabeculae of more than six cells thick surrounded by vascular spaces (H&E X20)

Conclusions

The presence of MT growth pattern is independently associated with poor prognosis in HCC patients including increased high-risk pathologic features, decreased response to treatment, and worse overall survival.

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