Short communication

Tumour budding in gallbladder carcinoma

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Available evidence strongly suggests that tumour budding (TB), especially in the gastrointestinal tract [1], is an adverse prognostic factor that can help stratify patients into more significant risk groups than tumour-node-metastasis staging alone. Most importantly, it has the potential to guide decision-making [2]. Its presence has been associated with significantly worse outcomes in various cancers, so the assessment of budding could be critical in treatment algorithms [3]. Unfortunately, there are no studies regarding its occurrence in gallbladder cancer.

For the considerable prognostic power of TB to be fully accepted, agreed-upon criteria for its evaluation must be established to guide further research in this area and provide practicing pathologists with reporting guidelines. Although a recent consensus has been published, there is still room for optimisation [4].

We studied a series of 59 cases of gallbladder cancer. We identified a predominance in women (53 cases, 88.1%) with a median age of 62 years (range 43–83). Most of the patients had gallstones (47 cases, 79.7%), and the median CA-19.9 level was 9.32 IU/ml. 55.9% of the cases were in stage IV. In our series, only 16 cases (27.1%) had lymph nodes sampled, and only 9 patients (15.3%) had nodal metastases. Regarding histological characteristics, 16.9% of the cases were poorly differentiated, and 53 cases (88.1%) demonstrated budding, with a median of 5 (range 0–11). Similarly to the classification of TB in the colon, we found grade 1 in 29 cases (49.2%), grade 2 in 10 (16.9%), and grade 3 in 20 (33.9%). We divided our population into 2 groups, with low budding (0–4 buds/0.785 mm^2) and high budding (> 5 buds/0.785 mm^2) (Table I).

Table I. Clinicopathologic features of gallbladder cancer according to tumour budding grade

Parameters	Low budding group (n = 40)	High budding group (n = 19)	p-value
Age (mean, SD)	61 (10)	61 (9)	0.959
Sex			
Female	37 (92.5)	15 (78.9)	0.133*
Male	3 (7.5)	4 (21.1)	
Cholelithiasis			
No	8 (20)	4 (21.1)	0.925
Yes	32 (809	15 (78.9)	
CA 19-9 (median, min–max)	8.08 (0–7201)	26.2 (0–11271)	0.506
CEA (median, min–max)	2.65 (0.6–261)	3.19 (0.72–1449)	0.126
Grade			
G1	10 (25)	2 (10.5)	0.249*
G2	25 (62.5)	12 (63.2)	
G3	5 (12.5)	5 (26.3)	

Table I. Cont.

Parameters	Low budding group (N = 40)	High budding group (N = 19)	p-value
pT			
pT1	7 (17.5)	2 (10.5)	0.013*
pT2a	28 (70)	8 (42.1)	
pT2b	5 (12.5)	9 (47.4)	
Stage			
III	18 (45)	8 (42.1)	0.834
IV	22 (55)	11 (57.9)	
# Lymph nodes resected (median, min–max)	0 (0–13)	0 (0–11)	0.467
# Lymph node metastasis (median, min–max)	0 (0–3)	0 (0–2)	0.440
Lymph nodes sampled			
No	28 (70)	15 (78.9)	0.470
Yes	12 (30)	4 (21.1)	
Lymph nodes metastasis			
No	35 (87.5)	15 (78.9)	0.393*
Yes	5 (12.5)	4 (21.1)	
Lymphovascular invasion			
No	32 (80)	16 (84.2)	0.698
Yes	8 (20)	3 (15.8)	
Perineural invasion			
No	35 (87.5)	13 (68.4)	0.079*
Yes	5 (12.5)	6 (31.6)	
Adjuvant			
No	26 (65)	15 (78.9)	0.277
Yes	14 (35)	4 (21.1)	
Status			
Alive	33 (82.5)	14 (73.7)	0.432*
Dead	7 (17.5)	5 (26.3)	
Recurrence			
No	20 (50)	9 (47.4)	0.850
Yes	20 (50)	10 (52.6)	
Follow-up (median, min–max)	16 (4–78)	11 (4–70)	0.107

When comparing the variables between groups, the only one associated with high budding was a higher pathological stage (pT2b). In the survival analysis, we did not identify any variables related to mortality.

Our study did not identify clinical or pathological characteristics associated with the various degrees of TB. Likewise, TB did not influence survival. Tumour budding on the invasive front has recently been suggested as a potential index of aggressiveness and poor prognosis for various types of cancer [5, 6]. An essential advantage of this index is its simplicity and reproducible measurement. It is easily adaptable to routine histopathological examination based on H and E stains without additional expensive techniques. This feature is crucial and may have therapeutic implications for patients with gallbladder carcinoma. To date, the prognostic importance of TB in gallbladder cancer has not been investigated. Our study shows no evidence that TB has prognostic significance in overall survival.

In conclusion, the only clinical characteristic of gallbladder carcinoma associated with high TB

was pT2b stage; however, TB is unrelated to overall survival in this carcinoma.

The authors declare no conflict of interest.

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