Newsletter

Time to take notice of tumour budding in colorectal carcinoma specimens

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The term tumour budding denotes that at the invasive front of colorectal adenocarcinomas tumour cells, singly or in small aggregates, become detached from the neoplastic glands and migrate into the surrounding stroma. (Morodomi et al, 1989; Hase et al, 1993; Ueno et al, 2002b). Tumour budding, is a histomorphological biomarker associated with an adverse outcome. It represents de-differentiation of epithelial cells into more invasive phenotypes in a process known as epithelial–mesenchymal transition. Tumour budding in colorectal carcinoma has shown to be significantly associated with lymphatic invasion, lymph node metastases, and is a negative prognostic indicator in terms of recurrence and overall survival. Incorporation of this histological finding into the CRC staging algorithm is imminent, but will require standardization of the pathological description of tumour budding.

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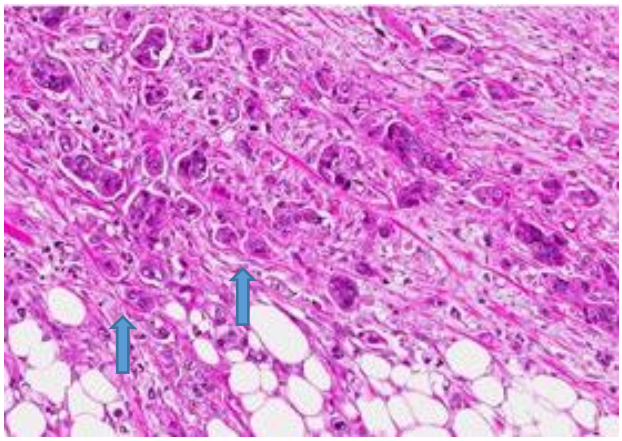

Figure 1: Tumour budding at the invasive front of colorectal carcinoma (H & E x 40)

A panel of experts discussed the issues related to standardized reporting of tumour budding in colorectal carcinoma, at the International Tumour Budding Consensus Conference (ITBCC) held in Bern, Switzerland, in November 2016. The primary goal of the ITBCC was to reach agreement on an international, evidence-based standardized scoring system for reporting of tumour budding. The consensus recommendations of the ITBCC has been

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incorporated into the CAP cancer protocol for the examination of specimens from patients with primary carcinoma of the colon and rectum, to be used along with the 8th edition of the American Joint Committee on Cancer (AJCC) staging manual. Of the 11 total recommendations, 10 statements achieved consensus, with 10 of 11 recommendations agreed upon by 100% of the panel members and 1 statement (No. 5 below) achieving 96% (22 of 23) agreement. These recommendations / statements, are as follows;

1. Tumour budding is defined as a single tumor cell or a cell cluster of up to 4 tumor cells.
2. Tumour budding is an independent predictor of lymph node metastasis in pT1 colorectal cancer.
3. Tumour budding is an independent predictor of survival in stage II colorectal cancer.
4. Tumour budding should be taken into account along with other clinicopathologic factors in a multidisciplinary setting.
5. Tumour budding is counted on hematoxylin-eosin (H&E).
6. Intratumoral tumor budding in colorectal cancer has been shown to be related to lymph node metastasis.
7. Tumour budding is assessed in 1 hotspot (in a field measuring 0.785 mm^2) at the invasive front.
8. For tumour budding assessment in colorectal cancer, the hotspot method is recommended.
9. A 3-tier system should be used along with the budding count to facilitate risk stratification in colorectal cancer.
10. Tumour budding should be included in guidelines/protocols for colorectal cancer reporting.
11. Tumour budding and tumour grade are not the same.

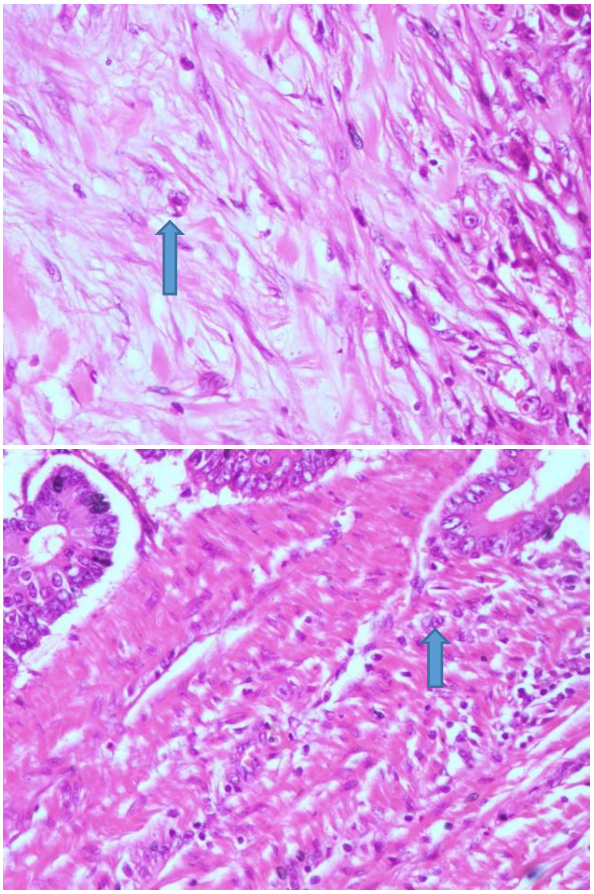

Figure 2: Tumour budding- Detached single cells at the invasive front of the tumour (H & E x 40)

Statements 1, 5, 7 through 9, and 11 were directly incorporated into the CAP cancer protocol as the advocated method for assessing and reporting tumour budding in colorectal carcinoma. The ITBCC is also acknowledged in the pathology reporting guidelines for colorectal carcinoma issued by The Royal College of Pathologists of the United Kingdom (V4, December 2017). The consensus method requires scanning the entire invasive front of the tumor on routine H&E-stained slides, selecting a single “hotspot,” and counting the number of tumour buds (defined as single tumor cells or clusters of up to 4 tumour cells) with a ×20 objective lens. Given variable field diameters, application of a correction factor may be

necessary to report the number of tumour buds in the equivalent of a 0.785-mm^2 field. A tumor bud score should also be reported by using a 3-tiered system based on the number of tumour buds in a 0.785-mm^2 field (low, 0–5 tumor buds; intermediate, 6–9 tumour buds; high, 10 or more tumour buds). However, it is widely acknowledged that additional studies will be required to further refine the methodology and address the challenges in uniform reporting of tumour budding.

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