Deeper sections reveal residual tumor cells in rectal cancer specimens diagnosed with complete pathological regression following neoadjuvant treatment

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Background and Objective

Rectal cancer is one of the most common malignancies in the world and a significant cause of cancer death. In locally advanced rectal cancer, standard treatment consists of neoadjuvant chemo- and radiotherapy and subsequent surgical resection. Complete pathological response is observed in 10 – 20% of patients. To diagnose complete regression, the whole tumor bed must be embedded, and there must be a complete absence of residual tumor on microscopic examination. Current Danish guidelines recommend examining one HE section per tumor block, whereas the corresponding British guidelines recommend three sections per block. We examined the consequences of this inconsistency for diagnostic accuracy and prognosis.

Methods

All patients diagnosed with complete pathological regression of rectal cancer from 2015 to 2020 in our department were included (n = 23). Three additional deeper sections at 200 µm intervals were cut from each block and stained with HE. Slides were reviewed by two pathologists for presence of residual tumor cells. All patients were clinically followed for 1 to 36 months.

Results

Additional sections revealed residual viable tumor cells in seven patients (30.4%) originally diagnosed with complete pathological regression. Of these, three patients (42.9%) later had local recurrence or distant metastasis during the follow-up period, compared with one patient (6.3%) in the group with no residual tumor cells in deeper sections (Fisher's exact test; p = 0.07). In four of the seven patients with residual tumor cells, careful examination of the original slides revealed minute foci of tumor cells or areas suspicious for residual tumor. These areas were interpreted as non-malignant or overlooked at the time of diagnosis. The residual tumor was more obvious and easily recognized in the deeper sections.

Conclusion

Systematic use of deeper sections in evaluation of tumor regression in rectal cancer reveals the presence of residual tumor cells in a subset of patients diagnosed with complete pathological regression based on a single section. Furthermore, additional levels probably reduce the risk of overlooking small tumor foci. Our results indicate that presence of residual tumor may increase the risk of recurrence, although not significantly.

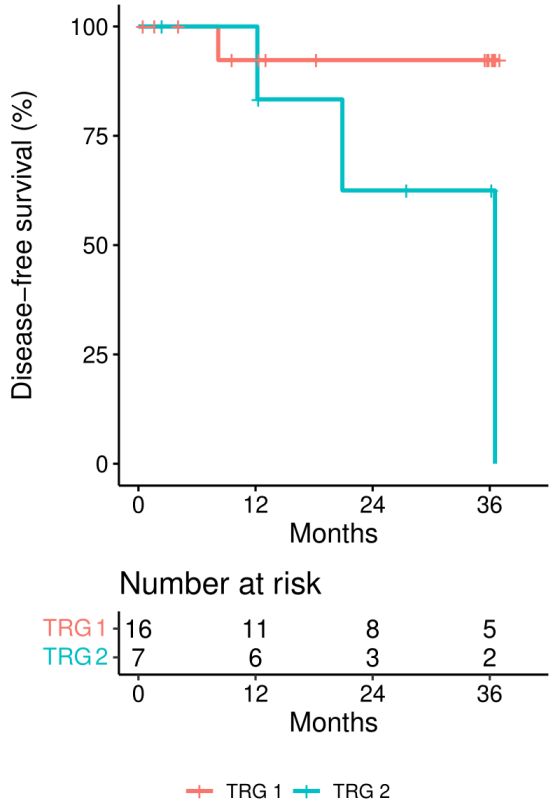

Figure 1. Patients with residual tumor in deeper sections showed a nonsignificant reduction in disease-free survival (log-rank; p = 0.08).

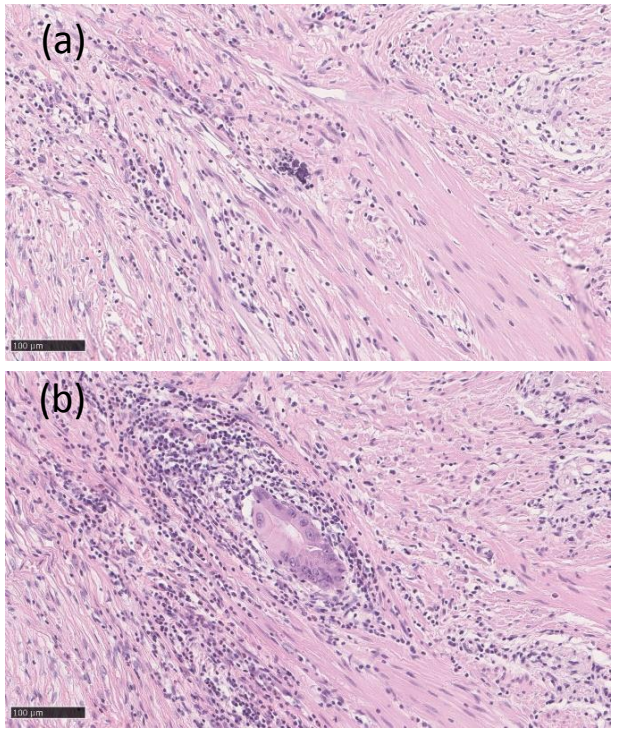

Figure 2. (a) Original HE section shows absence of tumor cells and presence of calcifications in the tumor bed. (b) Deeper section reveals residual tumor cells. Scale bars are 100 µm.

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Department of Pathology, Zealand University Hospital. The authors report no conflicts of interest.