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Well-Differentiated Rectal Neuroendocrine Tumors: Analysis of Histology, Including INSM1 Expression, and Biologic Behavior, Involving a Large Cohort of 94 Cases

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BACKGROUND: Rectal well-differentiated neuroendocrine tumors (R-NET) are increasingly being detected by screening colonoscopy, commonly manifesting as submucosal polyps. Chromogranin-A is frequently negative in R-NETs. Insulinoma-associated protein 1 (INSM1) is a novel transcription factor that has recently shown excellent sensitivity and specificity for NE differentiation in various anatomic sites but has not been systematically evaluated in R-NET.

METHODS: A retrospective histologic review of all available R-NET was performed, and stained for INSM1 immunohistochemistry, as well as for Ki-67 and chromogranin-A, if not already available. Clinical and follow-up information was obtained from the medical chart.

RESULTS: A total of 94 R-NET were included in our cohort. Of these, 82 (87%) were < 10 mm in greatest dimension, and submucosal involvement was noted in 70 patients (74%). The tumors displayed a variety of histologic patterns, and the majority of the cases had intratumoral fibrosis (61%). Synaptophysin and INSM1 were reactive in 100% whereas chromogranin-A was reactive in 45%. The mean Ki-67 proliferative index was 1.6% (range: 0.5-5%). Median follow-up of the cohort was 30 months (80 cases, range: 3-226 months). Only three patients were identified with regional lymph node metastasis, all of which showed tumor size ≥ 10 mm and had lymphovascular invasion (LVI).

CONCLUSION: R-NET in our fairly large cohort display an indolent biologic behavior without distant metastasis. Metastatic disease in lymph nodes was associated with tumor size and the presence of LVI, but not with Ki-67 proliferative index. This is also the first systematic study documenting INSM1 as a highly sensitive NE marker in R-NET.

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