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Colorectal Intramucosal Perikarya of Ganglion Cells

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Abstract

It generally is believed that perikarya of ganglion cells in the human colorectum are confined to plexuses that lie deep to the mucosa, and that intramucosal perikarya are rare. We retrospectively reviewed 100 specimens from biopsies of normal and abnormal mucosa to further characterize intramucosal perikarya. The presence of intramucosal perikarya, their number, location, and grouping were recorded. Twenty-one specimens (21.0%) contained intramucosal perikarya. Intramucosal perikarya occurred throughout the colorectum in the muscularis mucosae or lamina propria and in normal mucosa, acute self-limited colitis, inflammatory bowel disease, cytomegalovirus-associated colitis, hyperplastic polyps, tubular adenomas, and high-grade intraepithelial neoplasia. In some specimens, intramucosal perikarya morphologically resembled microgranulomas or cytomegalovirus-infected cells. We demonstrated that intramucosal perikarya of ganglion cells are surprisingly common in normal and abnormal mucosa. Awareness of intramucosal perikarya is necessary to avoid confusion with microgranulomas or cytomegalovirus-infected cells.

The human colorectal nervous system contains many plexuses, most of which lie deep to the mucosa. Perikarya of ganglion cells are found in these plexuses, and it generally is believed that perikarya of ganglion cells in the normal human colorectum are absent from the mucosa. However, in our daily practice of surgical pathology, we commonly notice colorectal intramucosal perikarya of ganglion cells in normal and abnormal mucosa.

We examined specimens from colorectal biopsies to refine the current understanding of intramucosal perikarya, to determine relationships between intramucosal perikarya and normal and abnormal mucosa, and to alert pathologists to the diagnostic pitfall of mistaking intramucosal perikarya for other entities.

Materials and Methods

We retrospectively reviewed 4-µm-thick, H&E-stained sections from 100 randomly selected formalin-fixed, paraffin-embedded specimens from colorectal biopsies. All biopsies were performed at our institution during the interval from October 29, 2003, to September 10, 2004. Biopsies were performed with pinch forceps or jumbo forceps, with or without cautery. Perikarya were defined according to standard morphologic criteria as somata 9 to 35 µm in diameter with eccentric, large nuclei that contained finely granular nucleoplasm and 1 or 2 prominent nucleoli and variable amounts of cytoplasm and were with or without satellite cells. Perikarya were considered intramucosal when in the lamina propria or when circumscribed by smooth muscle of the muscularis mucosae. For each specimen, the presence or absence of...
perikarya, their number, location, and grouping were recorded as were the diagnoses and site of biopsy.

Immunohistochemical analysis was performed for specimens with inflammatory bowel disease and intramucosal perikarya or cytomegalovirus-infected cells using the TechMate 500 automated immunostainer (Ventana Medical Systems, Tucson, AZ) according to the manufacturer’s instructions. Automated steps included reactions with prediluted leporine polyclonal antibodies against neuron-specific enolase3 (DAKO, Carpinteria, CA) or murine monoclonal antibodies against cytomegalovirus (clones DDG9 and CCH2, DAKO) diluted 1:20 in phosphate-buffered saline, followed by reactions with avidin-biotin-peroxidase complexes.

Results

One hundred specimens were obtained from 52 patients, including 26 men and 26 women, ages 27 to 90 years. These specimens included 6 from the cecum, 19 from the ascending colon, 1 from the hepatic flexure, 8 from the transverse colon, 12 from the descending colon, 21 from the sigmoid colon, 25 from the rectum, and 8 from unspecified sites.

Of 52 patients, 19 (37%) had intramucosal perikarya, including 12 men and 7 women. Intramucosal perikarya were present in 21 specimens (21.0%), including 14 specimens from men and 7 specimens from women; the men’s and women’s ages were 28 to 82 years. These specimens included 2 from the cecum, 4 from the ascending colon, 2 from the descending colon, 4 from the sigmoid colon, 7 from the rectum, and 2 from unknown sites. A total of 96 intramucosal perikarya were present, including 64 in the muscularis mucosae and 32 in the lamina propria. Most perikarya in the lamina propria occupied the deep half of the lamina propria. Intramucosal perikarya occurred singly or in clusters. The largest cluster contained 7 perikarya.

Of the 21 specimens with intramucosal perikarya, 6 had otherwise normal mucosa and 15 had abnormal mucosa. These abnormalities included acute self-limited colitis (1 specimen) (Image 1B), inflammatory bowel disease (5 specimens) Image 2AI and Image 2BI, cytomegalovirus-associated colitis (2 specimens), hyperplastic polyps (4 specimens), tubular adenomas (2 specimens), and high-grade intraepithelial neoplasia (1 specimen). Six specimens had inflammatory bowel disease and intramucosal perikarya or cytomegalovirus-infected cells, including 2 specimens with both intramucosal perikarya and cytomegalovirus-infected cells. For these 6 specimens, immunohistochemical analysis confirmed the identity of intramucosal perikarya in 5 of 5 specimens Image 2CI and cytomegalovirus-infected cells in 3 of 3 specimens. Experiments with positive and negative external controls were performed appropriately.

Of the 79 specimens that lacked intramucosal perikarya, 37 had normal mucosa and 42 had at least 1 abnormality. These abnormalities included focal active colitis (2 specimens), acute self-limited colitis (2 specimens), inflammatory bowel disease (13 specimens), cytomegalovirus-associated colitis (1 specimen), trauma (4 specimens), spirochetosis (2 specimens), hyperplastic polyps (6 specimens), tubular adenomas (13 specimens), and sessile serrated adenoma (1 specimen).

Intramucosal perikarya were present in 6 (14%) of 43 specimens with normal mucosa and 15 (26%) of 57 specimens with abnormal mucosa and, hence, were more likely to occur in abnormal mucosa.

Some specimens from biopsies of putative colorectal polyps had initial sections that lacked polyps, and additional consecutive serial sections were obtained by the original pathologists. For these specimens, if intramucosal perikarya were present, they were often present only on 1 or 2 slides.

All specimens were negative for ganglioneuromas. To our knowledge, the clinical histories of all patients were negative for neuronal intestinal dysplasia, Down syndrome (morus Down), or irradiation.

Discussion

There are several neuronal plexuses in the colorectum. The most commonly known plexuses include the plexus submucosus internus (Meissner), the plexus myentericus (Auerbach), and the plexus submucosus externus (Henle or Schabadasch).1,4 Other plexuses have been described in animals but are less well

![Image 1A](https://example.com/image1a.png) Perikaryon in normal mucosa (H&E, ×600).

![Image 1B](https://example.com/image1b.png) Cluster of perikarya in a patient with acute self-limited colitis resembles microgranuloma (H&E, ×600).
studied in humans. These plexuses include the plexus submucosus extremus; the mucosal plexus of Cajal; the plexus of Drasch, near the muscularis propria; an additional plexus near the Auerbach plexus; and the outer muscular/serosal plexus of Stöhr.

It generally is believed that perikarya of ganglion cells in the normal human colorectum are confined to these plexuses, most of which lie deep to the mucosa. Colorectal intramucosal perikarya have been noted in ganglioneuromas, neuronal intestinal dysplasia, in patients with Down syndrome, in the appendix, after irradiation, and occasionally in response to mucosal injury such as in Crohn disease. Ganglioneuromas are proliferations of ganglion cells and Schwann cells and might be seen in multiple endocrine neoplasia and neurofibromatosis. Neuronal intestinal dysplasia is a congenital disorder of dysmotility characterized by the presence of intramucosal perikarya and giant ganglia. Rectal intramucosal perikarya occur frequently in patients with Down syndrome. In histologically normal appendices, perikarya combine with neurosecretory cells, Schwann cells, and neural processes to form intramucosal neuroendocrine complexes. Irradiation may be followed by intramucosal neuronal hyperplasia and scattering of intramucosal perikarya and neuroendocrine cells. Finally, intramucosal perikarya may be seen in Crohn disease, which is characterized by neuronal hypertrophy and hyperplasia.

To our knowledge, only 3 studies specifically address human colorectal intramucosal perikarya. These studies focus predominantly on pediatric patients and document extremely rare intramucosal perikarya. In our study of specimens from adult colorectal biopsies, intramucosal perikarya were surprisingly common and found easily. Intramucosal perikarya occupied the right colon, left colon, and rectum. This is a wider distribution than that described by Stöhr, who noted intramucosal...
perikarya only in the left colon. We found intramucosal perikarya in far greater numbers than did Scurry,6 who noted intramucosal perikarya in only 3 of 169 specimens from 26 pediatric patients, and Lassmann,9 who noted intramucosal perikarya in only 11 of 239 specimens.

Intramucosal perikarya were associated with normal and abnormal mucosa. These abnormalities included acute self-limited colitis, inflammatory bowel disease, cytomegalovirus-associated colitis, hyperplastic polyps, tubular adenomas, and high-grade intraepithelial neoplasia. Intramucosal perikarya were nearly twice more likely to occur in abnormal mucosa than in normal mucosa.

Intramucosal perikarya generally were identified readily by their characteristic morphologic features and large size, typical for adult perikarya. However, some clusters of intramucosal perikarya morphologically resembled microgranulomas of Crohn disease (Image 1B), as previously described.1 Furthermore, intramucosal perikarya occurring singly or in clusters could be mistaken for cytomegalovirus-infected cells, particularly if the examiner is unaware of the possibility of intramucosal perikarya. Of note, cytomegalovirus is common in intramucosal perikarya or cytomegalovirus-infected cells, correct interpretation required careful attention to morphologic details and confirmatory immunostains (Image 2B and Image 2C).

The presence of intramucosal perikarya is considered a criterion for the histologic diagnosis of neuronal intestinal dysplasia. If our findings are reproduced in pediatric patients, the diagnostic criteria for neuronal intestinal dysplasia might need to be updated.

We showed that colorectal intramucosal perikarya of ganglion cells are surprisingly common in normal and abnormal mucosa of adults. Awareness of intramucosal perikarya is necessary to avoid confusion with microgranulomas or cytomegalovirus-infected cells.

References