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Pathology of the Ganglionic-Aganglionic Junction in Congenital Megacolon

GHERARDO J. GHERARDI, M.D., Boston

Defective autonomic nerve supply of the bowel wall is accepted generally as the principal anatomical cause of congenital megacolon (Hirschsprung's disease)[1-3] and abnormal peristalsis as the functional effect.[4] This combination produces narrowing with obstruction in the affected segment and dilatation proximally. Numerous reviews have summarized the pathology and have described the clinical and radiological manifestations[5-7] of the common case and rarer variants. Successful surgical therapy, consisting of removal of the aganglionic segment of bowel, has been based on this foundation.[8] Biopsy has aided diagnosis by confirming a presumed aganglionosis and has refined therapy by fixing the limits of effective resection.[9,10]

Recent reports[11,12] have been aimed at descriptions of the extent of longitudinal involvement of bowel, whereas a comparison of the histology of the nerve supply in various layers at the junction of ganglionic and aganglionic bowel has not been made.

The present study has been designed to clarify the question of whether there is correspondence between the terminations of ganglion cells in Meissner's (submucosal) and Auerbach's (myenteric, intermuscular) plexuses in Hirschsprung's disease. Decisions regarding the depth or extent of biopsy needed for effective results depend on familiarity with such relationships.

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Associate Professor of Pathology, Tufts University School of Medicine.

From the Department of Pathology, Tufts University School of Medicine and Tufts-New England Medical Center.

Materials and Methods

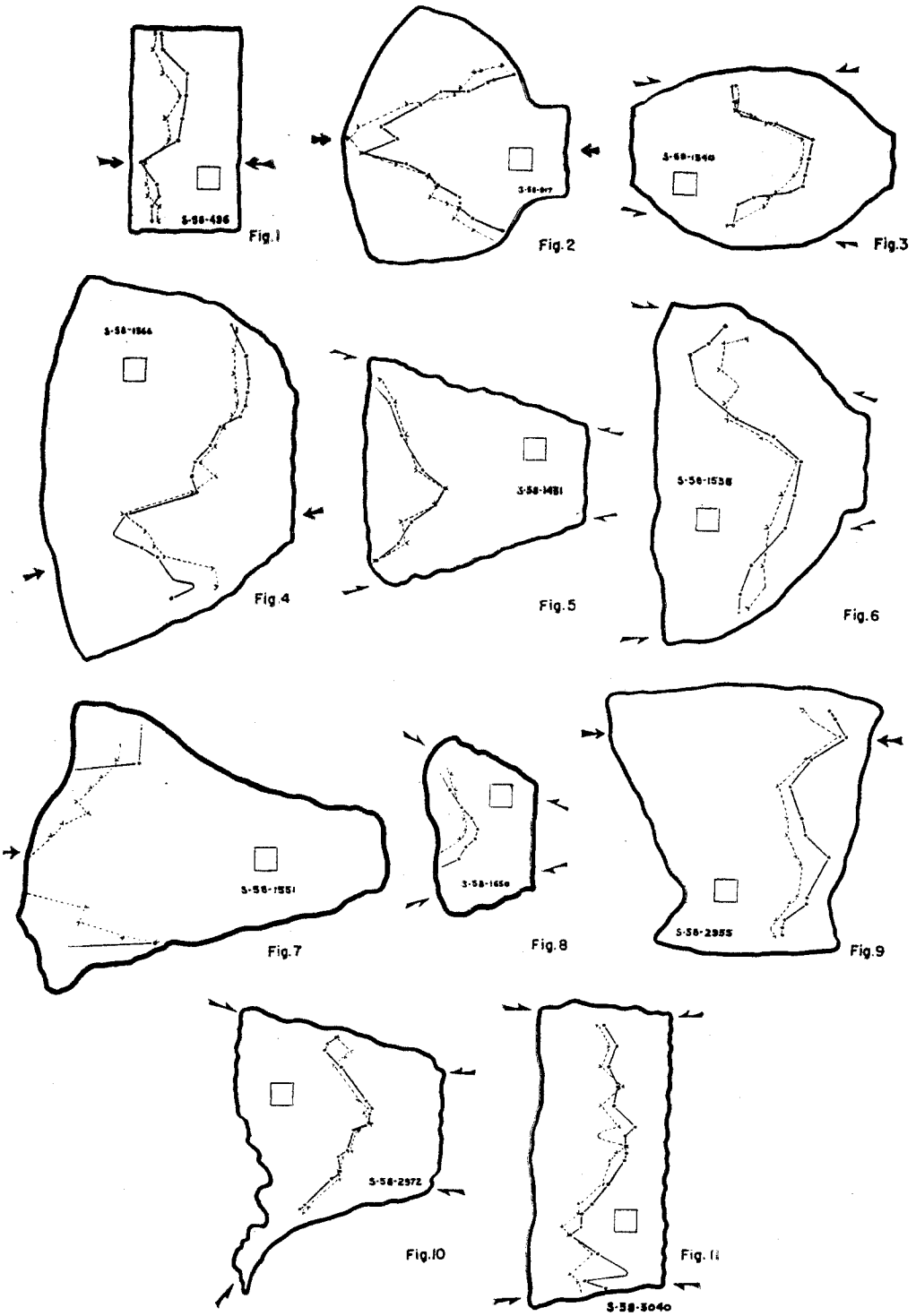
Eleven specimens of large bowel resected from cases of Hirschsprung's disease were carefully mapped out to demonstrate the location of the most caudal ganglion cells of both Auerbach's and Meissner's plexus. Only those cases were used in which a significant portion of the, or the entire, junction between ganglionic and aganglionic bowel was uninterrupted by surgical intervention and was contained within the main resected specimen. Otherwise, the cases were unselected and were studied in sequence.

The specimens were opened longitudinally along either the mesocolic or the antimesenteric line and fixed flat in 10% formalin. The approximate location of the ganglionic margin was determined by pilot samplings and was subsequently defined by semiserial longitudinal blocks taken close together, largely in parallel, along the entire circumference.

Special care was taken to include clearly the ganglion-cell termination in both plexuses within each block. The end-points were checked wherever possible in adjacent serial sections and were recorded graphically to a scale of 1:1. Only those neurons were recorded which were clearly identifiable as such, principally by their prominent nucleolus, but also by other well-established nuclear and cytoplasmic characteristics.

Observations

The change from a normally ganglionic autonomic nerve supply to totally aganglionic bowel was not completely abrupt in all cases. The presence of a zone where neurons are scanty was confirmed in some instances, but its extent and character were not evaluated. The end-points generally were fairly sharp and could be substantiated in adjacent serial microscopic sections. Such a gradual diminution of neurons, with stragglers so widely spaced as to make the level of termination indistinct, was rarely encountered.



Figs. 1-11.—Outline drawings of longitudinally opened segments of large bowel in Cases 1-11, all oriented so that the proximal margin of resection is on the left and the distal margin on the right. The most distal ganglion cells identified in the myenteric plexus are designated by dots, connected by unbroken heavy lines. The most distal ganglion cells identified in the submucosal plexus are designated by checks (v) connected by light broken lines. The arrows indicate the median line of mesenteric attachment. The small square for each specimen stands for a square centimeter.

The junction in all cases is delineated at both submucosal and intermuscular levels in line drawings (Figs. 1-11). Three main observations may be made from these.

1. The lines representing the termination of ganglion cells in the submucosal and intermuscular plexuses generally coincide.

2. The junction tends to be more caudally located opposite to the line of mesenteric attachment. Cases 2, 3, 4, 5, 6, 7, 8, and 10 bear this out clearly.

3. The submucosal ganglion cells appear to terminate either at the same level or a short distance cephalad to the intermuscular

ganglion cells. This trend is particularly noticeable in the antimesenteric portion of the bowel wall, as in Cases 1, 2, 3, 6, and 8. Minor exceptions, where the submucosal ganglion cells can be traced more distally than their intermuscular counterparts, can be found in almost every case. The discrepancy is minimal or absent in some instances (Figs. 5 and 10).

Comment

It would seem clear that the general correspondence of the junction at the submucosal and intermuscular levels has been conclusively demonstrated. The more distal extent of the ganglionic margin along the antimesenteric line and the "lag" between submucosal and intermuscular end-points appear to be of less significance, more variable, and subject to differences of interpretation.

One factor which may play an important role in bringing about the more extensive antimesenteric ganglionosis may be a mechanical one of greater dilatation opposite to the point of attachment of the bowel. In many cases the longest convexity relative to the mesocolic point of attachment lies longitudinally along the antimesenteric line. This bulge effect may produce a distribution of the neuronal units over a larger area, thereby bringing about a relative and acquired level difference rather than an absolute and developmental one. This finding cannot be ascribed to artifact of sectioning and fixation, for it is demonstrable irrespective of the line along which the bowel was opened. It is also more noticeable where dilatation is most pronounced, as indicated by the configuration of the specimens, e.g., Cases 2, 3, 4, 5, 6, 7, 8, and 10.

The findings of a minor and inconstant longitudinal "lag" between end-points must be regarded in the light of several considerations. First, the problem of fixation shrinkage becomes important: Such an effect tends to minimize these longitudinal end-point differences and to distort them where a greater contraction of muscle layers with respect to submucosa makes shrinkage a differential one.

A more random distribution of ganglionic elements in a greater volume of loose areolar tissue of the submucosa may make localization of these elements less precise than in the intermuscular layer, where they are contained in a much narrower space. The latter offers a distinct advantage for rapidity and accuracy of localization. This is particularly true when immediate diagnosis is required.

Lastly, this discrepancy may be considered on a theoretical basis with respect to the development and caudal displacement of the hindgut relative to a more cephalic source of autonomic nerve supply. In pig embryos neuronal cells accompany nerve fiber components from the pelvic plexus into the wall of the hindgut and apparently become incorporated into the enteric ganglia.[10] The appearance of ganglion cells is dependent on the penetration of these nerve fiber components. If one assumes that the ultimate position of ganglion cells in their relatively caudad migration is a linear function of the nerve fibers which join them, then any diminution in the longitudinal distance of their position from a fixed point of origin may be ascribed to lateral or transverse deflection. In the penetration of the inner circular muscle layer, such a loss, though small, might be incurred and could explain a more cephalic position of submucosal neuronal elements relative to their intermuscular counterparts.

Turning to a more practical consideration, it is clear that the absence of ganglion cells is the most reliable single diagnostic criterion in congenital megacolon, or Hirschsprung's disease. Scantiness of neurons, poor formation, their gradual diminution in the transitional segment are highly subjective and unreliable criteria. Similarly, any increase in number, or in size or complexity of nonmyelinated nerve fibers in the aganglionic portion is an inconstant finding, difficult to evaluate. On the contrary, the two muscle layers, distal to the ganglionic

margin, are frequently tightly apposed, with few intervening nerve fiber bundles.

In the employment of rectal biopsy, the choice between mucosal and submucosal biopsy and whole-thickness or muscle biopsy must be governed by several anatomical considerations. The general correspondence of ganglionosis in the two plexuses and the fact that a diagnostic biopsy specimen is generally taken in the rectum, far beyond the ganglionic-aganglionic junction, would indicate that a submucosal biopsy might suffice. Such a choice must be tempered by the realization that a positive diagnosis of Hirschsprung's disease, on which therapeutic surgical intervention is based, depends on a negative finding. This generally takes place at an age when ganglion cells, even if present, may be few, inconspicuous, small, or poorly formed, and are indentified more easily in the plexus of Auerbach. Substitution of surface sampling for full-thickness biopsy in the interest of speed and simplicity must be based on proper appraisal of the risk of diagnostic inaccuracy against the risks of possible postbiopsy complications, and should be avoided whenever possible.

Summary

The ganglionic-aganglionic junction in the autonomic plexuses of the colon in Hirschsprung's disease was studied. A general correspondence of level and configuration of the ganglionic margin was found between the submucosal plexus of Meissner and the intermuscular plexus of Auerbach. Minor details of variation were noted. The findings are discussed with regard to embryogenesis and to practical application in diagnostic biopsy.

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Department of Pathology, Tufts University School of Medicine, 136 Harrison Ave. (11).

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