How to Approach Hirschsprung Disease

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Objectives

1. Diagnosis (based on rectal biopsy)
2. Intra-operative consultation
3. Post-operative surgical pathology

RECOMMENDATIONS
Clinical History

• 3 d old male
• Failed to pass meconium in the first 48h
• Abdominal distension and vomiting

• Barium enema shows dilated sigmoid and narrow rectum (recto-sigmoid ratio <1)
Suction Rectal Biopsy

Syringe is used to create vacuum in barrel of device. 

Disposable “Cap” scored at 1 cm intervals. 

Barrel

Trigger

1. Mucosa and submucosa drawn into barrel through side port.
RECTAL BIOPSY-BASED DIAGNOSIS OF HIRSCHSPRUNG DISEASE
TOO LOW (False Positive)

TOO HIGH (False Negative)
Suction Biopsies from Multiple Levels

Less likely that all biopsies will lack sufficient submucosa.

Fewer inadequate biopsies due to sampling of anal or transitional mucosa.

Mapping data:
- "reposition" low biopsies
- very short-segment HSCR

R1: Advise surgeon to get biopsies from multiple levels in separate containers.
IN MOST CASES H&E IS SUFFICIENT

Adequate Bx

No Ganglion Cell

Nerve Hypertrophy

Experienced Pathologist

= DIAGNOSIS
R2: Routinely cut lots of sections and have a low threshold for more levels
Hypertrophic Submucosal Nerves

Monforte-Munoz et al. (1998)
Arch Pathol Lab Med 122:721-5

Experience

R3: Pay careful attention to submucosal nerve calibers
Ancillary Diagnostic Methods

• Experience varies (recognition of ganglion cells, especially immature cells, requires practice)

• Some biopsies have borderline adequacy

• Not all biopsies of aganglionic rectum contain hypertrophic nerves

• Histological quality varies

• Tissue sampling to exclude ganglion cells and large nerves is cumbersome and costly
RECOMMENDED APPROACH

controls

patient

Agang 
Gang

controls

patient

Calretinin

B-1-L3

C19

ChT Ab

B-1-L4

C19

Embed H&E

ADD 01 H&E

ADD 01 H&E

ADD 01 H&E
YOUR DIAGNOSIS?

A. Hirschsprung disease
B. Not Hirschsprung disease
C. Rebiopsy
D. Other

Calretinin

No ganglion cells

“2 cm”
Poll: Your Diagnosis?
Calretinin-immunoreactive mucosal nerves are
- present in the proximal 1-to-2 cm of the aganglionic segment in HD
- may be present in aganglionic biopsies from the distal rectum of a patient with vssHD
Intact Calretinin Innervation
Aganglionic Rectal Biopsies

R3: Pay careful attention to submucosal nerve calibers!
Recommendations

- Routinely obtain biopsies from more than one site
- Perform calretinin ihc on at least one biopsy from every patient
- Pay close attention to nerve hypertrophy, even if ganglion cells are present
- In some situations (e.g., vssHSCR), AChE histochemistry or ChT ihc may be particularly helpful
- Have low threshold for rebiopsy and/or full-thickness biopsy, especially in older patients
Intraoperative Consultation
INTRAOPERATIVE LEVELLING BIOPSY
Finding Ganglionic Bowel

HANDLING AND INTERPRETATION OF LEVELLING BIOPSY
Orientation and location are important
Myenteric Ganglion
Set a high cytological threshold
What do you advise the surgeon?

A. Do an appendectomy to exclude a skip area
B. Perform ileostomy or resection at this site
C. Obtain seromuscular biopsy of more proximal bowel to confirm ganglion cells are present
D. Other
Poll: What do you advise the surgeon?
In short-segment HSCR, the TZ is typically <5cm
INTRAOPERATIVE HISTOPATHOLOGY
Excluding Transition Zone

Find ganglion cells and make anastomosis \textbf{at least 5 cm} proximal to that point.

Conduct frozen section examination of donut from proximal margin to assess circumferential distribution of ganglion cells and submucosal nerve hypertrophy.
INTRAOPERATIVE HISTOPATHOLOGY
Excluding Transition Zone

Exclude Features of Transition Zone:
- Partial Circumferential Aganglionosis
- Myenteric Hypoganglionosis
- Submucosal Nerve Hypertrophy

Submit remainder for FFPE histology
MYENTERIC HYPOGANGLIONOSIS
≥2 submucosal nerves per high power field with diameters ≥40 µm

Coe et al. 2012
3-STEP APPROACH

1. Levelling biopsy to find ganglion cells (identify a site oral to the aganglionic segment)
2. Surgeon should perform resection at least 5 cm proximal to levelling biopsy with ganglion cells
3. Frozen section of proximal margin to exclude features of transition zone

(Repeat 2 and 3 as needed)
HANDLING THE RESECTION SPECIMEN

Open lengthwise to evaluate mucosa
Consider overnight fixation of flat specimen
improve orientation of histologic sections

Minimal goals are to
1. Confirm distal aganglionosis
2. Exclude features of transition zone at proximal margin
3. Document the length of the aganglionic segment
Guidelines for synoptic reporting of surgery and pathology in Hirschsprung disease

Laura V. Veras, Michael Arnold, Jeffrey R. Avansino, Kevin Bove, Robert A. Cowles, Megan M. Durham, Allan M. Goldstein, Chandra Krishnan, Jacob C. Langer, Marc Levitt, Hector Monforte-Munoz, Raja Rabah, Miguel Reyes-Mugica, Michael D. Rollins II, Raj P. Kapur, Ankush Gosain, On behalf of the American Pediatric Surgical Association Hirschsprung Disease Interest Group

https://hematogones.com/surg-path/hirsch
YOUR HIRSCHSPRUNG DISEASE DESTINATION

REACH is a non-profit organization committed to improving the lives of children and families affected by Hirschsprung Disease by increasing awareness, promoting education, connecting families and supporting various research around the world.