Journal of Pediatric Surgery 51 (2016) 573–576

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Rectal biopsies for Hirschsprung disease: Patient characteristics by diagnosis and attending specialty

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ARTICLE INFO

Article history:
Received 1 July 2015
Received in revised form 10 October 2015
Accepted 12 October 2015

Key words:
Hirschsprung disease
Rectal biopsy

ABSTRACT

Purpose: Hirschsprung disease (HD) is diagnosed with rectal biopsy. At our institution two services perform these biopsies: pediatric surgery and gastroenterology. Our objective was to review our institutional experience with rectal biopsies to diagnose HD and compare patients and outcomes between the two services.
Methods: We reviewed all children undergoing a rectal biopsy for the evaluation of HD at our institution over a 10-year period. Comparisons were made using multiple logistic regression models.
Results: We identified 518 children who underwent rectal biopsy for evaluation of HD; 451/518 (87%) were adequate and 56/518 (11%) were positive for HD. A positive biopsy was more likely with delayed passage of meconium ($p < 0.001$), obstructive symptoms ($p < 0.001$), trisomy 21 ($p < 0.001$), full-term gestation ($p = 0.03$), and male gender ($p = 0.02$). Pediatric surgeons biopsied younger patients with more classic symptoms for HD compared to gastroenterologists. Pediatric surgeons were more likely to take adequate (OR 6.0, 95% CI 2.9–12.4, $p < 0.001$) and positive biopsies (OR 6.7 95% CI 2.1–21.2, $p = 0.001$) compared to gastroenterologists.
Conclusion: Infants with classic symptoms can reliably be diagnosed with HD by a pediatric surgeon. The work up for HD in older children with constipation should be a collaborative effort between pediatric surgery and gastroenterology.

Rectal biopsy is considered the gold standard for the diagnosis of Hirschsprung disease (HD) [1–3]. The presence of ganglion cells in the submucosal and muscularis nerve plexuses excludes the disease, thus, to make the diagnosis it is essential that an adequate sample is obtained. The introduction of suction rectal biopsy has made biopsy for HD relatively simple, since this technique can be performed at bedside and without sedation [3]. Suction rectal biopsies, however, only allow for investigation of the submucosal plexus. Because of a lower concentration of ganglion cells in the submucosal plexus, the sample must be of good quality, and typically, more than one biopsy is obtained. Both pediatric surgeons and gastroenterologists perform suction biopsies, and given the ease of the procedure, many biopsies are taken, but few (11%–29%) result in a diagnosis [2,4,5]. A full thickness biopsy, which permits evaluation of both the submucosa and muscularis is more commonly obtained in older children or after nondiagnostic suction rectal biopsy. These biopsies are typically only obtained by a pediatric surgeon. Neither suction nor full thickness rectal biopsies are risk free, and there is some debate as to whether or not too many negative rectal biopsies are performed [2,3,6].

Our objective was to identify differences in patient populations biopsied by pediatric surgeons compared to gastroenterologists at our institution, and also to further define which patients are most likely to have adequate and positive biopsies. To our knowledge, this is the first study examining differences by service in patient characteristics and outcomes in a large volume of rectal biopsies.

1. Materials and methods

After approval by the institutional review board, we reviewed the charts of patients presenting to our center from January 2003 to January 2013 who underwent a rectal biopsy (suction rectal biopsy, full thickness rectal biopsy, adenoid punch biopsy and endoscopic biopsy) for the initial diagnosis of HD at our institution. Rectal biopsies from children who already had a diagnosis of HD, and rectal biopsies performed for other reasons were excluded from the analysis. The indication for biopsy was based on the indication described in the procedure report or in the documentation immediately preceding the

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http://dx.doi.org/10.1016/j.jpedsurg.2015.10.047
0022-3468/

biopsy by the surgical or gastroenterology team. Biopsy technique was at the discretion of the attending physician. Suction biopsies were taken in duplicate or triplicate, with an attempt to obtain specimens at least 2 cm above the dentate line. All other biopsy types are taken with the child under some form of sedation, at least 2 cm above the dentate line, with defect closure at the discretion of the attending physician. All biopsies were examined by an experienced pediatric pathologist within our institution, using paraffin imbedded tissue with hematoxylin and eosin staining. Calretinin staining became available in 2010, and was reserved for cases in which the diagnosis was in question. Biopsies were considered inadequate if evaluation for HD was not possible by pathology or if the pathologist recommended repeat biopsy for definitive diagnosis. Contrast enemas were reviewed when available. Contrast enema results from outside institutions were included if reviewed by our pediatric radiologists. Contrast enemas were considered suggestive of HD if the report stated that HD was a possible diagnosis or could not be ruled out by the study. Contrast enemas were considered not suggestive of HD if the report made no mention of HD, stated a normal rectosigmoid ratio, stated no evidence for a diagnosis of HD, or reported a normal exam. All variables were known for all subjects except gestational age, which was available for 421 subjects.

1.1. Theory/calculation

Variables of interest were evaluated and summarized using descriptive statistics. Potential predictors were compared using chi-square test, Fisher's exact test, and Student's *t*-test, where appropriate. Univariate logistic regression was performed, and individual predictors with p-values less than 0.05 were included in the final multiple logistic regression models. Only statistically significant multivariate results are presented. SAS version 9.3 (Cary, NC) was used to perform all statistical analyses, and was performed by a biostatistician.

2. Results

2.1. Demographics

A total of 518 children had a rectal biopsy for the evaluation of HD (Table 1). Rectal biopsies were performed using a variety of methods: suction rectal biopsy, full-thickness incisional, endoscopic, and adenoid punch. The indications for biopsy included chronic constipation, obstructive symptoms, delayed meconium passage, necrotizing enterocolitis, failure to thrive, and bowel perforation. Contrast enemas were performed prior to rectal biopsy in 330/518 (64%) children and were reported as suggestive of HD in 140/330 (42%) enemas. The average age at the time of biopsy was 614 ± 52 days (median age 62 days, range 1 day–17.6 years). The average gestational age was available for 421 (81%) children and was 37.2 ± 0.2 weeks (range 24–42 weeks).

2.2. Adequacy of rectal biopsies

The initial rectal biopsies were adequate to evaluate for HD in 451/518 (87%) children. The remaining 67 (13%) children had inadequate biopsies; repeat biopsy was performed in only 57% of these children (38/67), 9 of whom were ultimately diagnose with HD. Most children who did not have a repeat biopsy were ultimately diagnosed with constipation (89%, 34/38). The majority of inadequate specimens were suction biopsies (56/67, 84%). Suction biopsies were diagnostic in 352/408 (86%) children. No single biopsy type was found to be superior to another for adequacy ($p > 0.05$ for all), however numbers were low for nonsuction biopsies; adequacy rates by biopsy type are presented in Table 2. Children with an inadequate initial biopsy were older than those with an adequate biopsy (1126 ± 221 vs 520 ± 49 days, $p < 0.001$). The average gestational age did not differ between children with inadequate and adequate initial biopsies (37.7 ± 0.4 vs 37.2 ± 0.2 weeks, $p = 0.74$). Of note, calretinin immunohistochemical staining was used to evaluate 19 specimens, 4 of which were ultimately still considered inadequate for the assessment of HD. In univariate regression, the odds of having an adequate initial biopsy were higher if performed for obstruction ($p = 0.002$), in children <1 year of age ($p = 0.01$), and when performed by a pediatric surgeon ($p < 0.001$) (Table 3). In multivariate regression, younger age and pediatric surgical specialty continued to improve the odds of obtaining an adequate initial biopsy.

Table 1
Demographic information.

Variable	Surgery (n = 355, 69%)	Gastroenterology (n = 163, 31%)	Total
Type of initial biopsy			
Suction rectal biopsy	275 (67%)	134 (33%)	409 (79%)
Full-thickness excision	52 (96%)	2 (4%)	54 (10%)
Endoscopic	3 (10%)	27 (90%)	30 (6%)
Adenoid punch	25 (100%)	0 (0%)	25 (5%)
Indication for biopsy			
Chronic constipation	120 (55%)	100 (45%)	220 (42%)
Obstructive symptoms	158 (82%)	34 (18%)	192 (37%)
Delayed meconium	46 (70%)	20 (30%)	66 (13%)
Necrotizing enterocolitis	22 (71%)	9 (29%)	31 (6%)
Bowel perforation	9 (100%)	0 (0%)	9 (2%)
Age at biopsy			
0–3 months	229 (78%)	63 (22%)	293 (57%)
3–12 months	43 (56%)	35 (44%)	77 (15%)
>1 year	83 (56%)	65 (44%)	148 (28%)
Gestational age (n = 421)			
Preterm (<37 weeks)	91 (75%)	30 (25%)	121 (29%)
Term (>37 weeks)	213 (71%)	85 (29%)	298 (61%)
Associated diagnoses			
Trisomy 21	20 (61%)	13 (39%)	33 (6%)
Cardiac	15 (75%)	5 (25%)	20 (4%)
Gender			
Male	182 (68%)	85 (32%)	267 (51%)
Female	173 (69%)	78 (31%)	251 (49%)

2.3. Diagnosis of Hirschsprung disease

Rectal biopsies resulted in the diagnosis of HD in 56/518 (11%) of children. These biopsies were obtained by suction (51/56, 91%), full-thickness (3/56, 5%), and adenoid punch (2/56, 4%). The most common biopsy indications for children with HD were obstructive symptoms (29/56, 52%) and delayed passage of meconium (20/56, 36%). HD was also diagnosed in children presenting with chronic constipation (5/56, 9%) and bowel perforation (2/56, 3%). HD was not diagnosed in any children with necrotizing enterocolitis. Children with negative biopsies were older (675 ± 58 days vs 104 ± 47, $p < 0.001$). Only 3/56 (5%) children with HD were diagnosed at >1 year of age, and HD was not diagnosed in any children >6 years of age. Children with negative biopsies were more premature (37.0 ± 0.2 vs 38.5 ± 0.3 weeks, $p = 0.006$). Only 6/56 (11%) children with HD had a gestational age <37 weeks. No positive biopsies for HD were found in children with a gestational age <33 weeks. A contrast enema was performed in 79% (44/56) of children with HD, and was considered suggestive of the diagnosis in 68% (30/44). Of the 290 enemas performed on children who had negative biopsies, 110 (38%) were suggestive of HD. This yielded a sensitivity of 68% (95% CI 52–81%), and specificity of 62% (95% CI 56–68%) for contrast enema diagnosis of HD.

Table 2
Biopsy type compared to adequacy of biopsy.

Variable	Total	Adequacy
Type of initial biopsy		
Suction rectal biopsy	409 (79%)	352 (86%)
Full-thickness excision	54 (10%)	48 (92%)
Endoscopic	30 (6%)	25 (83%)
Adenoid punch	25 (5%)	24 (96%)