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Can We Rely on Frozen Sections of a Rectal Biopsy for One-stage Trans-anal Pull-through Operation in Hirschsprung's Disease?

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Abstract

Objective: Successful results after one-stage trans-anal pull-through (OSTAPT) operation for Hirschsprung's disease (HD) depend on accurate identification of the aganglionic segment in intra-operative frozen section (FS). Misinterpretation of the findings of the rectal biopsy is an anxiety-evoking pitfall for the surgeon. This study aims to describe our experiences in comparing results of FS and permanent Section (PS) rectal biopsies in children with HD who were candidates for OSTAPT in a single-step operation.

Methods: Subjects under the age of 14 years, admitted from March 2000 to July 2008 in a university-affiliated children's hospital for open rectal biopsy to diagnose HD were included in the study. All biopsies were taken 2-3 cm above the dentate line. 210 specimens of full-thickness rectal biopsy were obtained for both frozen section and permanent biopsy from all patients, examined by two well experienced pediatric pathologists for ascertaining the presence of ganglion cells, and the results were compared. Analysis was performed by SPSS Software version 11.5.

Findings: Two-hundred one infants and children underwent FS rectal biopsy to exclude HD. Positive results were seen in 63.8% of the specimens examined as PS and in 58.3% of FS samples. 93.9% of positive results in FS studies were confirmed by PS studies. 6.1% of FS reports were false positive and 21.7% were false negative ($P < 0.001$). The sensitivity of FS was 85.8% and specificity 90.2%. Positive predictive value (PPV) was 93.9% and negative predictive value (NPV) was 78.3% in FS studies ($P < 0.001$). The accuracy of FS was 80.4%.

Conclusion: Although FS of the rectal biopsy is useful in defining the aganglionic segment during operation, according to this study, it cannot be used as the sole base for performing primary pull-through operation before the results of the permanent section are on hand.

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Key Words: Hirschsprung's Disease; Frozen Section; Rectum; Biopsy; Aganglionic Megacolon

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Introduction

Hirschsprung's disease (HD) is a congenital disorder characterized by absence of ganglionic cells in the large bowel (80-85% in rectosigmoid junction) leading to functional obstruction and colonic dilatation proximal to the affected segment. HD is strongly suspected by presenting symptoms, the radiological appearance of the bowel, and by rectal manometry, but absence of ganglion cells in rectal biopsy is considered as the gold standard for the definitive diagnosis of HD^[1].

The traditional diagnostic approach is a full thickness segment biopsy. But alternatives such as suction rectal biopsy are frequently used. Although the rapid acetylcholine esterase staining method has been used for diagnosing HD with good results^[2,3,4], it unfortunately was not available in our hospital.

Suction rectal biopsy has a high diagnostic accuracy and can be performed at bedside^[5]. The most common problem in this technique is an inadequate specimen with an insufficient amount of submucosal neural plexus, so that an evaluation of ganglion cells is precluded. Is biopsy done too close to the anal sphincter and normal hypoganglionic level, the diagnosis of HD will be considerably more difficult than that of a full-thickness biopsy^[6,7].

Typical histological feature of HD includes absence of ganglionic cells plus increased number of hypertrophic nerves. These cells are better recognized in Auerbach plexus in full-thickness rectal or colonic biopsies^[2]. Full thickness biopsy can be prepared as a frozen section (FS) to be examined promptly, or as a permanent section (PS), which would take about 48 hours before the results become available.

In this study we aimed to define the diagnostic accuracy of FS and its concordance with PS in the rectal biopsies of children hospitalized with suspected HD. We intended to find out if we could go ahead with the one-stage trans-anal pull-through (OSTAPT) operation solely on the basis of the histological findings in full thickness FS rectal biopsy.

Subjects and Methods

From March 2000 to July 2008, all patients (210 cases) with clinical and paraclinical findings highly

suspicious of HD were candidates for FS rectal biopsy in Mofid Children's Hospital.

Patients with total aganglionic colon on contrast enema were excluded.

Two hundred and ten full thickness rectal biopsies (2-3cm above dentate line) were taken from 210 patients. Specimens were obtained for both FS and PS biopsies from all patients. Using cryostat machine, the specimens were prepared at about 3µm thickness and stained by routine hematoxylin and eosin (H&E) staining. Both frozen and permanent sections were examined by two well experienced pediatric pathologists for ascertaining the presence of ganglion cells.

Pathological reports with hypoganglionic or neural intestinal dysplasia were excluded and finally 201 full-thickness rectal biopsies evaluated.

The accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated. The concordance between FS diagnosis and PS diagnosis and the causal factors which led to misdiagnosis were identified. To compare the diagnostic accuracy of FS with PS McNamara test was performed.

We also report the therapeutic consequences of the actions taken on the basis of results of FS alone.

Findings

Two hundred and ten patients (151 boys and 69 girls) with mean age of 3.6 months (3 days-14 years) were included in the study. 18.9% of study population were >2 years of age. Nine pathological reports with hypoganglionic or neural intestinal dysplasia were excluded.

Comparing the results of FS with PS, findings in 201 cases were as follows:

In 18 patients, the FS falsely suggested absent ganglion cells, the final PS diagnosis revealed a normal pattern. This group comprises 7 neonates with mild enterocolitis, 3 neonates with prematurity, 3 insufficient specimens, 2 fixation artifacts and 3 specimens with pathologist's misinterpretation. In 4 out of these 18 patients, trans-anal pull-through operation was carried out solely on the basis of FS; however, in the other 14 subjects the surgeon decided to wait for the results of PS, which revealed the presence of

Table 1: The effects of discordance between FS and final diagnoses in 25 patients

No	Sex	Age	FS Dx	PS Dx	Case of discordance	Type of second operation
1	Male	7d	-	+	Enterocolitis	Nothing done
2	Female	7d	-	+	Enterocolitis	Nothing done
3	Female	6y	-	+	Prematurity	Nothing done
4	Male	6d	-	+	Enterocolitis	Nothing done
5	Male	45d	-	+	Fixation artifacts	Nothing done
6	Male	4.5m	-	+	Insufficient specimen	Nothing done
7	Male	3m	-	+	Insufficient specimen	Nothing done
8	Male	3d	-	+	Enterocolitis	Nothing done
9	Female	25d	-	+	Fixation artifacts	Nothing done
10	Male	13d	-	+	Enterocolitis	Nothing done
11	Male	13d	-	+	Prematurity	Nothing done
12	Male	12d	-	+	Enterocolitis	Nothing done
13	Male	11y	-	+	Pathologist's mistake	Nothing done
14	Male	1.5m	-	+	Pathologist's mistake	None
15	Female	3m	-	+	Pathologist's mistake	Trans-anal pull through
16	Male	35d	-	+	Enterocolitis	Trans-anal pull through
17	Female	3.5m	-	+	Insufficient specimens	Trans-anal pull through
18	Female	11d	-	+	Prematurity	Trans-anal pull through
19	Male	30d	+	-	Pathological mistake	Posterior myectomy
20	Female	3.5m	+	-	Transition zone	Posterior myectomy
21	Male	15d	+	-	Pathological mistake	Posterior myectomy
22	Male	3y	+	-	Transition zone specimen	Abominal pull-through
23	Male	2m	+	-	Transition zone specimen	Abominal pull-through
24	Female	2.5m	+	-	Transition zone specimen	Abominal pull-through
25	Female	12m	+	-	Transition zone specimen	Abominal pull-through

FS Dx: Frozen Section Diagnosis (+/- ganglionic cells) / PS Dx: Permanent Section Diagnosis (+/- ganglionic cells)

normal ganglions, thus avoiding an unnecessary major surgery.

Conversely, in 7 cases FS falsely reported normal ganglion cells and accordingly the operation was ended; but PS revealed absence of ganglionic cells. Confounding factors in this group: 5 specimens were taken from the transition zone (in low segment HD) and 2 specimens were not satisfactory for microscopic examination. In 4 of these patients abdominal pull-through operation was done and in 3 children with low segment HD, myectomy was performed (Table 1).

54.7% of FS samples and 63.8% of PS sections were positive for the presence of ganglionic cells. 93.9% of positive results in FS studies were

confirmed by PS diagnosis. 6.1 % of FS reports were false positive and 21.7% false negative ($P<0.001$). The sensitivity of FS was 85.8% and its specificity 90.2%. Positive predictive value (PPV) was 93.9% and negative predictive value (NPV) 78.3% in FS studies ($P<0.001$). The accuracy of FS biopsy was 80.4%.

Discussion

The approach to surgical treatment of HD has changed recently. Most of the affected children can

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be treated with a primary pull-through by several techniques (transanal, trans-abdominal and laparoscopic pull-through)^[8,9].

Rectal biopsies make up the cornerstone for the diagnosis of HD and subsequent surgery^[8].

Typical histological findings for HD in rectal biopsy include absence of ganglion cells in both the submucosal (Meissner's) plexus and the intermuscular (Auerbach's) plexus^[3,10].

Rectal biopsy may be obtained by means of suction or full thickness seromuscular method, both techniques having some advantages and disadvantages. The suction biopsy is difficult to interpret than full-thickness biopsy. When the diagnosis cannot be made by suction biopsy of rectum, a full-thickness posterior rectal wall biopsy should be performed^[2].

In the surgical treatment of HD, there is a trend towards primary resection without colostomy by transanal or transabdominal approach (open or laparoscopic). This renders significant importance to the evaluation of the initial pathologic specimen^[7,10,11]. In patients with strongly suspected HD, open rectal biopsy is taken and after definite diagnosis of HD by FS, definitive surgery is performed as a single-step procedure^[9].

Our research showed that in 80.4 % of cases there was complete agreement between the findings of FS and PS among the 201 children with HD. The reported concordance rates between the results of frozen sections and the permanent sections reported by other authors range from 67-100%^[6,11,12].

Factors that contribute to errors in FS as reported by other authors include: transitional zone sampling, freezing artifact, recognition of immature ganglion cells, superficial sectioning of the FS biopsy, technical difficulty in FS preparation, inexperienced pathologist, and the appendix sampling^[12,13].

In our series, the most common factors that affected FS results were: fixation artifact, insufficient biopsy samples, pathologist's mistake, and also confounding factors such as enterocolitis, short segment aganglionosis, existence of inflammation or scar in a previous biopsy site, premature neonate, and the transition zone biopsy.

Conclusion

The role of FS in the diagnosis of HD can not be denied, especially in ascertaining the presence of the ganglionic segment during surgery. Although error rate is low with a frozen section, the potentially serious clinical consequences of these errors are significant, such as unnecessary surgery or a second operation.

We recommend that the absence of ganglion cells in FS rectal biopsy for possible HD should be established by final PS diagnosis and definitive surgery should only be done if the findings are confirmed by permanent section.

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Conflict of Interest: None

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