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Association of Hirschsprung's disease with anorectal malformations: the early alarming signs for diagnosis and comorbidity related to this association

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ABSTRACT

Background and aim: The association of Hirschsprung's disease (HD) and anorectal malformation (ARM) is rare. The aim of this study is to highlight the frequency of this rare association and comorbidity that may be related to this association.

Patients and methods: Eleven cases out of four hundred forty six cases (2.5%) with ARM found to have HD association presented to Assiut University Children Hospital. All cases were diagnosed by complete clinical, radiological assessment and histopathological examination before correction. The evaluating parameters for those patients were the early warning signs for diagnosis, any unnecessary procedures done and any associated morbidity related to misdiagnosis of this association.

Results: Age at presentation of these eleven cases ranged from 2 days to 10 years. The diagnosis started early during neonatal period only in four cases either by change of bowel caliber or nonfunctioning stoma. In the remaining seven cases the diagnosis was delayed because of unsuspected association. Fecal fistula after closure of stoma and wound dehiscence followed by incisional hernia is evident associated comorbidity.

Conclusions: The incidence of HD in ARM population seems to be more common than its incidence in the general pediatric population. Caliber change of the bowel during the first operation or nonfunctioning stoma is early alarming sign for diagnoses of such association and should direct the attention for stomal biopsy.

1. Background

Hirschsprung's disease (HD) and anorectal malformation (ARM) are reported as a rare association [1–4]. Most of the reported cases were published as case reports. HD usually presents early during neonatal or infancy period. However if HD is associated with ARM, this presentation may be delayed because of misinterpreted symptoms which may lead to morbidity and even mortality [5,6]. The aim of this study is to detect the frequency of this association and the warning signs for early diagnosis to avoid unnecessary surgical procedures and morbidity.

2. Patients and methods

A retrospective study was conducted at Assiut University Children Hospital from December 2002 to December 2013. The study included all cases with anorectal malformation (ARM) proved to have Hirschsprung's disease (HD) association. A full clinical, radiological and histopathological examination was done to all patients to reach complete diagnosis. All histopathological specimens were formalin fixed, routinely processed at Pathology Laboratory, Assiut University Hospital. Sections were stained by hematoxylin and eosin (H&E) and examined by light microscopy. Immunohistochemistry for chromogranin was done to confirm absence of ganglion cells.

An informed written consent was obtained from the parents before any procedure taken. Approval of the ethical committee of Assiut University was taken to conduct this study. The studied parameters were the early warning signs for diagnosis, any unnecessary procedures done to the patients and any associated morbidity related to misdiagnosis of this association.

3. Results

Out of 446 cases with ARM only eleven (2.5%), 9 males and 2 female were diagnosed to have HD association. Their age at presentation ranged from 2 days to 10 years. Three cases had low ARM and eight cases had high ARM (four of them with rectourethral fistula) (Table 1). The diagnosis was suspected during neonatal period in 4

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Table 1
The demographic data, type of ARM, mode of presentation and associated anomalies of the eleven cases.

Case no.	Sex	Age at diagnosis	Type of ARM	Mode of presentation	Associated anomalies
1	Male	4 d	High without fistula	Intraoperative funnel	Down's syndrome
2	Male	10 y	High without fistula	Chronic constipation	
3	Male	9 mo	High without fistula	Fecal fistula after stomal closure	Down's syndrome and VSD
4	Male	1 y	High without fistula	Fecal fistula after stomal closure	
5	Male	5 d	High with rectourethral fistula	Nonfunctioning stoma	ASD
6	Female	3 y	Low (anal stenosis)	Chronic constipation	
7	Male	3 d	High with rectourethral fistula	Nonfunctioning stoma	
8	Male	2.5 y	Low (perineal fistula)	Chronic constipation	
9	Male	2 d	High with rectourethral fistula	Nonfunctioning stoma	
10	Female	2 y	Low (vestibular fistula)	Chronic constipation	
11	Male	1.2 y	High with rectourethral fistula	Chronic constipation	

cases (1, 5, 7 and 9) at the age of 4, 5, 3 and 2 days where; caliber change of bowel was evident in the rectosigmoid junction in one case (case 1); so proximal leveling colostomy and multiple full thickness biopsies were taken, proved later to be devoid of ganglion cells and by nonfunctioning stoma in three cases (cases 5, 7 and 9) drawn the attention for contrast study of the proximal colon where the discrepancy of the bowel caliber (transitional zone) was at splenic flexure of the colon in one case and the middle of descending colon in two (Table 2). Stomal biopsy also proved to be aganglionic. Regular stoma wash out was done for these 3 cases to relieve their bowel obstruction. All these four neonates underwent abdominosacroperineal pull-through (PT) later (Table 2). The diagnosis was a surprise in two cases (3 and 4) when fecal discharge developed on the 5th and 7th postoperative day after colostomy closure, failed to respond to conservative measures so stoma reconstruction was done and rectal biopsy was taken proved later to be aganglionic. The diagnosis was delayed in five cases (2, 6, 8, 10 and 11) because of atypical symptoms in the form of abdominal distention and severe progressive constipation that started after full ARM correction and were given medical treatment till the age of diagnosis. The gastrografin enema showed evident transitional zone in the rectosigmoid junction in three and short segment (rectal) in two. The histopathological examination of all specimens revealed absence of ganglion cells in the submucosa and muscle layers with hypertrophy of nerve bundles that ranged from 35 to 120 micron (mean 50 micron) (Fig. 1). This was confirmed by negative expression for chromogranin (Fig. 2). Transabdominal endorectal PT was the preferred surgical technique in all these seven cases (Table 2).

Eight cases were above 3 years of age after complete correction and according to Kelly's score [7] of continence 5 had fair and 3 had good score.

4. Discussion

Both HD and ARM are among the more frequent congenital anomalies encountered in pediatric surgery with incidence of 1: 5000 live births [8–10]. The association of both diseases is very rare with reported incidence to be 2.3%–3.4% [1,6,11]. In this series incidence of HD association with ARM cases was 2.5%. This incidence may reflect that the prevalence of HD among ARM population is higher than it is in general pediatric population.

The most common syndrome encountered with this association was Currarino syndrome (CS) followed by Down's syndrome [6]. The association of Down's syndrome and either HD or ARM is well known; 4.8% of Hirschsprung's patients had trisomy 21 [12,13]; where up to 2% of ARM cases had this syndrome [14]. Pena reported that high imperforate anus without a fistula was particularly common among patients with Down's syndrome [15]. In this series we report two males with high imperforate anus without fistula in association with Down's syndrome (cases 1 and 3).

The diagnosis of HD and ARM association was made on suspicion in four cases either because of well evident bowel caliber change that was noticed in attempting to do pelvic colostomy (case 1) or aganglionic stoma that did not function properly (cases 5, 7 and 9) without being stenosed or ischemic. Fortunately these three patients responded to stoma wash outs to relieve their obstruction which referred to long segment affected and distal stoma construction (in aganglionic segment); the reported incidence of which was 35% [6]. The diagnosis was a surprise in cases 3 and 4 where they developed fecal discharge after colostomy closure that necessitates refashioning of stoma and rectal biopsy proved to be devoid of ganglion cell. Diagnosis of this association sometimes may be difficult to make owing to the fact that the underlying ARM may be either masking the classical HD symptoms or these symptoms were misinterpreted as postoperative complications following ARM surgery [6]. Watanatittan et al [11] reported large series of this association and concluded that the diagnosis was delayed after full correction of ARM owing to atypical symptomatology and radiological findings. Five cases in this series had such delayed diagnosis where these patients developed abdominal distention and progressive constipation that were masked by the functioning stoma done as a first stage of ARM correction as in cases 2 and 11 or referred as a complication of ARM correction as in cases 6, 8 and 10 and were evident only after restoration of bowel continuity and full ARM correction.

Table 2
The extent of aganglionosis, morbidity, definitive procedure done, age at correction and the continence score of the eleven cases.

Case no.	Extent of aganglionosis	Morbidity	Operative procedure done	Age at correction	Continence score
1	Rectosigmoid	-	Abdominosacroperineal PT	9 mo	_
2	Rectosigmoid	-	Transabdominal PT	10 y	Fair
3	Rectosigmoid	Fecal fistula, wound dehiscence and incisional hernia	Transabdominal PT	1.3 y	Fair
4	Rectosigmoid	Fecal fistula and wound dehiscence	Transabdominal PT	1.6 y	Fair
5	Splenic flexure	Partial bowel obstruction	Abdominosacroperineal PT	6 mo	_
6	Rectal	-	Transabdominal PT	3 y	Good
7	Mid of descending colon	Partial bowel obstruction	Abdominosacroperineal PT	8 mo	_
8	Rectal		Transabdominal PT	2.5 y	Good
9	Mid of descending colon	Partial bowel obstruction	Abdominosacroperineal PT at 1 y	1 y	Fair
10	Rectosigmoid		Transabdominal PT	2 y	Good
11	Rectosigmoid		Transabdominal PT	1.4 y	Fair

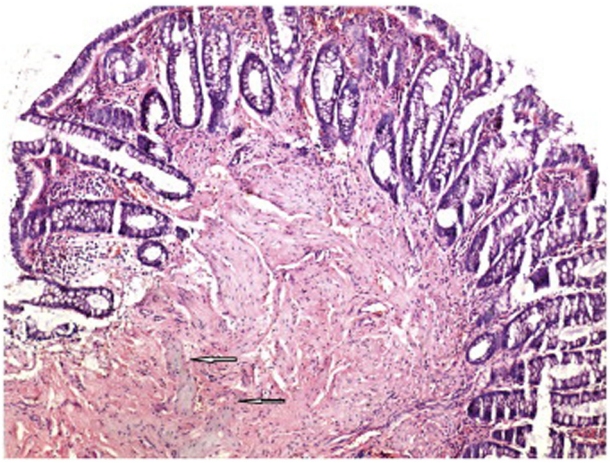

Fig. 1. Photomicrograph showing absence of ganglion cells in submucosal plexus with hypertrophic nerves (arrows). H&E ×100.

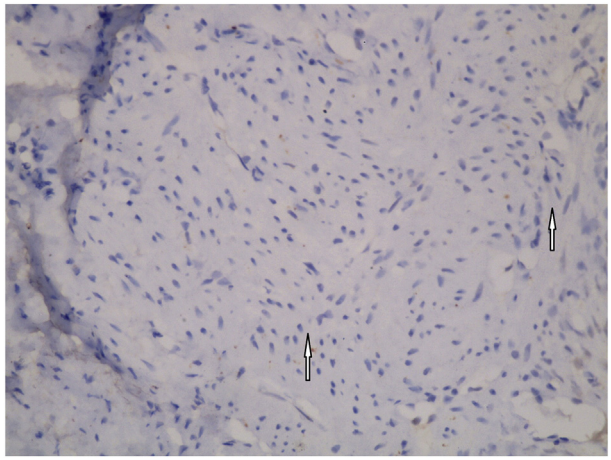

Fig. 2. Immunohistochemistry showing absence of staining for chromogranin in the submucosal plexus. (IHC ×400) IHC: Immunohistochemistry.

All the biopsies taken either from stoma or rectum were full thickness and examined by experienced pathologist reporting absence of parasympathetic nerve cells and hypertrophied nerve trunks.

The exact method of surgical correction for this association always depends on the extent of the affected bowel, localization of the disease and on the previous technique used for ARM correction [6]. As only the first stage of ARM correction (colostomy) was done for cases 1, 5, 7 and 9; the abdominosacroperineal (PT) approach was the preferred approach to avoid doing blind PT with its operative and postoperative sequel and to rap the sphincter around the centrally positioned rectum. This was not the approach for the remaining seven cases where the neorectum was already in place after ARM correction; so we choose to approach these patients via the endorectal plain "Soave's PT" to avoid the previously used extrarectal plain. This approach was commonly used and preferred by other authors as well [6,13].

In this study colostomy closures without diagnosis of distal bowel aganglionosis resulted in fecal fistula with wound infection and complete dehiscence in two cases; one of them developed incisional hernia later. These complications would be prevented if the diagnosis was made before attempting bowel recontinuity by rectal biopsy during the posterior sagittal anorectoplasty (PSARP). Also stoma construction in aganglionic segment resulted in bowel obstruction. Those patients were put on regular washouts to relieve their symptoms and distension.

Early diagnosis during the neonatal period or during ARM correction would save the patient the unnecessary technique (the patients would go directly for one major procedure (abdominosacroperineal PT) instead of two (PSARP followed by Soave's PT)).

5. Conclusions

Although the association of ARM and HD is rare; the incidence of HD among ARM cases seems to be higher than in general pediatric population. Nonfunctioning stoma or intraoperative caliber change of the bowel is early alarming signs to diagnose such association. Severe and progressive constipation after full correction of ARM without anal stricture should direct the attention for rectal biopsy.

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