A STUDY OF TOTAL COLONIC AGANGLIONOSIS

DISSERTATION

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CERTIFICATE

Certified that the dissertation entitled **"A Study of Total Colonic Aganglionosis"** is the original work undertaken by **Dr J Muthukumaran** under our guidance and supervision, in the Department of **Paediatric Surgery**, Institute of Child Health, Madras Medical College, Chennai, during the period of his postgraduate residency in MCh Paediatric Surgery from 2003 – 2006.

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INTRODUCTION

Intestinal Aganglionosis extending from anus to small bowel is called Total Colonic Aganglionosis (TCA) which may be present with or without small bowel involvement. It is an uncommon form, occurring in 5 to 15 % of all patients with Hirschsprung's Disease. Though this subgroup has difficulty in diagnosis and treatment, nowadays there is an increase in the reported incidence of Total Colonic Aganglionosis because of greater awareness of this entity, which has led on to improved survival by afforded definitive corrective surgery.

Though the Total Colonic Aganglionosis considered to be exceedingly rare, they are important subset because of the associated increased morbidity and mortality.

REVIEW OF LITERATURE

HISTORY

Harold Hirschsprung – senior Pediatrician at Queen Louise Childrem Hospital in Copenhagen in 1886 presented his classic description of disease entity that bears his name to The Pediatric Congress held at Berlin .Who described about two children who had classical and anatomical characteristics of the disease and died at the age of 8&11 months respectively duo to repeated Enterocolitis .

Hirschsprung's Disease of the colon was first reported in 1888 as an " Idiopathic dilatation and hypertrophy of large bowel " . It was only in 1948 that ***Swenson and Bill*** identified that ,it was actually the constricted segment of colon , which was at fault because of its inability to engage in peristaltic activity due to absence of ganglion cells, in the myentric plexuses.

In 1900 ***Fenwick*** putforward basic theories of HD

1 . MALFUNCTION THEORY	Hypertrophied colon is primary cause of defect
2 . OBSTRUCTIVE THEORY	Attributed the distal colon to the mechanical block caused by redundancy of colon or rectal valves .
3 . SPASTIC THEORY	Distal Colon Contract Spastically and cause

functional obstruction .

In 1901 ***Tittel*** Identified absense of Ganglion Cells in distal colon of Hirschsprung's Disease. Until 1940 there was confusion about the cause of disorder as the primary constipation cases were also included in the diagnosis of HD. In 1946 ***Ehrenpresis*** appreciated colon dilated proximally secondary to distal obstruction. In 1948 ***Whitehouse*** and ***Kenohan & Zuelser and Wilson*** documented the absence of ganglion cells of sympathetic plexuses in patient with Hirschsprung's Disease.

In 1949 ***Swenson etal*** has submitted a report on colonic peristaltic studies, which was conducted on two normal children and five children with congenital megacolon .Balloons were introduced through transverse colostomy and positioned at spleenic flexure, descending colon, and rectosigmoid. Normal patients exhibited High amplitude waves that progressed along the colon into rectum . Whereas in patients with megacolon irregular higher amplitude contractions than normal were recorded but they failed to progress through rectosigmoid into rectum . The resected aperistaltic segment were aganglionic . These findings were corroborated by ***Shipley***(1945) and later by ***Davidson etal*** (1955) . ***Bodian etal*** (1949) reported aganglionosis in resected distal segment .

The diagnosis of congenital megacolon was made by Barium enema as reported by ***Swenson etal*** (1948) which described narrow irregular distal segment with significant proximal dilatation. ***Bodian etal*** in 1951 reported that degree of aganglionosis could vary to great extent.

1 . Long segment cases involving the entire colon.

2 . Intestinal aganglionosis extending from the anus to small bowel (i.e) Total colonic aganglionosis (TCA).

In (1955) ***Swenson etal*** has described fullthickness rectal biopsy as a more prescribed diagnostic method and in 1972 ***Shandling*** described an improved technique called simple mucosal biopsy and later suction cup biopsy.

EMBRYOLOGY AND ETIOLOGY OF HD

In normal embryologic development , Neuroentric cells migrate from neuralcrest to upper end of alimentary tract and then proced to distal direction .

At 5^{th} week of gestation – First nerve cell arrive oesophagus

By 7 th week - they reach midgut

And by 12 th week - it reaches the distal colon

In these neuralcrest cells migration is actually guided by various Neural glycoprotiens or fibers (Fibronectin , hyaluranic acid , and laminin) Failure of neuroblast to achive distal migration occurs in HD, which was proved by transecting chick embryo at hindgut level, which showed Colonic aganlionosis

distal to transection, later it was demonstrated that implantation of Pigeon ganglion cells distal to transection allows normal incorporation of ganglion cells into the distal intestinal walls .

There are two basic theories exist regarding the Etiology of Hirschsprung Disease due to embryologic defect.

1 . FAILURE IN MIGRATION , HOSTILE ENVIRONMENT

2 . IMMUNOLOGIC THEORIES

Subsequently ***Tennyson*** etal and ***Gaillard*** etal demonstrated an abnormal distribution of fibronectin and laminin in extracellular space in patient with Hirschsprung disease which prevent the migration of ganglion cells into new environment

Langer, Betti and ***Blannerhassett*** proved the hostile environment, as the cause for HD, by demonstrating ganglion cells cultured with smooth muscle tissue from aganglionic colon, which showed decresed ability to adhere to smooth muscle cells .,suggesting lack of cell to cell adherence – NCAM (Neural cell adhesion molecule) positive nerve fibers were absent in myentric plexus of aganlionic segment .NCAM is important in neurocyte migration and localization of neurocytes to specific sites during embryogenesis. NCAM showed strong reactivity in submucosal plexus of the Aganglionic region but no reaction occurred in myentric plexus.

Immunologic theory suggest, In HD that there is an increased expression of Class II antigen in mucosa and sub mucosa, which causes immunologic response against neuro blast.

Colonic innervation by Autonomic nervous system consists of both intrinsic and extrinsic component. Extrinsic nerve supply consists of plexuses, ganglia , fibers from spinal cord to colon. Intrinsic system consist of Meissner's plexus (with in submucosal layer) and Auerbach's plexus (intramuscular layer) . Basic motor function seems tobe predominantly controlled by intrinsic nerve supply and the extrinsic supply modulates this function.

Cholinergic hyper innervations

Cholinergic nerve hyperplasia has been proposed as the cause of spasticity of aganglionic segment Histochemical staining demonstrate marked increase in acetylcholinestarase activity in aganglionic segment compared to ganglionic colon.

Histochemical studies: -

Kamijo etal in 1953, ***Koelle*** in (1954) comparing proximal innervated bowel and distal aganglionic portion, they were able to demonstrate Acetylcholinestrase activity in bowel wall of aganglionic portion which was 2 to 4 times greater than ganglionated portion.

Histological examination of bowel in Hirschsprung's disease reveals – total absence of Ganglioncells in the plexuses of Auerbach and Meissner in the distal segment.

In the aganglionic colon a normal arrangement of adrenergic fibers is impossible, the nerve fibers here are distributed through both muscle layers and increase in number towards the sphincter. ***Ehrenpreis*** demonsrated lack of adrenergic nerve fibers in aganglionic segment suggesting state of denervation hypersensity (based on Canons law) induced permanent contractions of smooth muscles in aganglionic segment. Normally the adrenergic fibers will cause relaxation of bowel.

According to ***Meier – Ruge*** (1968) the spasticity of aganglionic colon segment is due to continuous acetylcholine (Ach) release by the extra mural parasympathetics. The tissue concentration of nor-epinephrine (neuro transmitter) of adrenergic nerves, is nearly three times higher in the aganglionic segment than normal colon. Tyrosine hydroxylasc which regulates nor-epinephrine biosynthesis is also elevated which implies an increased sympathetic activity.

Non cholinergic, Non adrenergic automonic nerves are called **Peptidergic nerves**, as they contain different peptides, which act as neurotransmitter or neuromodulators.

- Decreased Vasoactive intestinal polypeptide (VIP)
- Decrease in nerve fibers containing substance P, matenkephalin, Gastrin releasing peptide are the cause for contracted state of segment due to abnormal peptidergic pattern of innervation.

Fibers containing Increased **Neuropeptide Y** (NPY) in aganglionic segments.

Substance – P : was found to be decreased in aganglionic segment and is the most important pathologic finding in HD as described by ***Ehrenpreis*** *and* ***Pernow*** (1952). On immunohistochemistry of HD. Activity of **NSE (Neuron Specific Enolase)** is intensely increased in hypertrophied nerve bundles. The absence of all 3 type of Ganglion cells (cholinergic neuron, interneurons, noradrenergic neurons), is the most important pathologic finding in HD. Because of this, the modulation of arriving impulses and their further transmission and distribution to smooth muscles does not take place

(EDNRB) Endothelin B receptor gene on chromosone 13 mediates activation of NO synthase in turn produces nitric oxide (NO), smooth muscle relaxant of GIT. Mutation of EDNRB leads to deficient NO Synthase reactivity in aganglionic segment of Hirschsprung Disease. Mutations of two other genes namely **Glial Cell line derived Neurotrophic factor** gene and **Endo thelin – 3** gene are involved in patho genesis of HD

Associated Anomoly

Chromosomal abnormality associated with HD

Down syndrome is more common

Interstitial deletion of distal 13 q

Partial deletion of 2 p and reciprocal translocation

Trisomy 18 mosaic

Unusual hereditary syndromes associate with HD

Waarden burg syndrome

Von recklinghausens syndrome

Type D brachydactyly syndrome

Smith – Lemli – Opitz syndrome

HD is associated with prematurity, congenital malformation which is higher than normal population association. Down syndrome with HD have other associated malformations like Congenital heart disease or Duodenal obstruction. Generally prematurity, Down syndrome, Urological malformation are more commonly associated in patient with HD. Urological systems will have VUR / UHN / disturbance of bladder function.

Sometimes Sacralagenesis is seen associated with HD, which has following significance like post-op urinary and stool incontinence. The later impotence observed may be mistaken as sequlae of HD surgery.

HD with Waarden Burg syndrome is rare, but this combination is interesting one because both have same pathogenetic mechanism. (Migration defect of neural crest) It is of interest that HD in association with WBS is usually of Long segment type or TCA.

In GIT – imperferate anus, or long segment Aganglionosis are seen with HD. Colonic atresia associated with HD is very rare, but whenever present, type 3 atresia is mostly seen. It occurs if the vascular accident occurs before 8th week of intra utrine life. Mostly type III atresia occurs with middle colic artery involvement. Vascular accident, not only result in atresia but also prevent the migration of entricneuroblast to distal segment and cause association of HD. ***Haffner*** and ***Sehistad*** state that it is advisable to do, rectal biopsy in all patients with colonic atresia. ***Hyde*** and ***de Lorimier*** proprosed that HD creates heavy dilated meconium impacted loop of bowel, which undergoes intra uterine volvulus, and infarction causing atresia.

HD is occasionally associated with Neuroblastoma.

Sex Incidence

According to ***Rickham*** (1978) 25% new born with HD are girls and according to ***Swensons*** (1973) 81 % are boys.

Familial Incidence

In ***Swenson's*** report of Hirschsprung's patients 7.8 % had one or more siblings with same disease. Whether the patient is boy or girl the risk of being of affected is 2.6 % and 7.2 % respectively for other siblings. The siblings of Hirschsprung's Disease patients are 130 times more at risk than general population if the affected child is boy and 360 times more if the patient is a girl. Hirschsprung's Disease more commonly transmitted by mother than by father,

the mode of inheritance is by autosomal resesive. In families with long segment type aganglionosis or in cases where both parents are affected by Hirschsprung's Disease it may be wiser to forego further offspring.

Risk of siblings involvement in HD is increased as the aganglionosis become more extensive.

CLASSIFICATION OF HD

Pathologic Anatomic criteria

Long segment aganglionosis	- Involvement of descending colon (15% to 20%)
Subtotal aganglionosis	- Extents to mid transverse colon
Total aganglionosis	- Entire large bowel involved (2% to 4%)
Total Colonic Aganglionosis	- With variable involvement of small bowel
Short segment HD	- Limited to rectum (60% to 70%)
Ultra short segment HD	- 2 to 3 cm of lower rectum involved

Clinical Criteria

Classic form	- Rectal, Recto sigmoid extending to splenic flexure
Ultra Short form	- Limited to distal 2 to 3 cm of rectum
Ultra long form	- More than half of colon

Zuelzer- Wilson syndrome - Colonic involvement with small bowel disease

Age Criteria

Disease of **new born**

Disease of **Infant**

Disease of **Toddler and school children**

Disease of **Adulthood**

CLINICAL PICTURE OF HD

1. Functional intestinal obstruction in HD can be acute, recurrent or chronic.
2. Vomiting - Mostly bilestained, progressed to feculant vomiting rarely Haematemesis
3. Reluctance to feed
4. 85% of cases present with delay in passage of meconium for more than 24 hours
5. Abdominal distension , develops gradually, become obvious after 3rd day of life.
6. Non tender until complication occurs, tenderness aggravated in enterocolitis and perforation.
7. Per-rectal examination – often empty, anus is tight. Explosive passage of flatus and meconium following per-rectal examination, and deflation occurs after rectal washouts.

BIOPSY

Rectal biopsy should be done at 2 cm above pectinate line as the length of hypoganglionosis ranges from 0.3 to 1.7 cm in normal infants. For ultrashort segment HD biopsy should be done at 1 to 1.5 cm length from pectinate line.

As a rule atleast 3 or 4 biopsy specimens should be taken at various levels in the rectum.

1. At dentate line (Anal mucosa junction with rectal mucosa)
2 2 cm above dentate line (ultra short segment identified)
3 2cm above anal ring
4 Biopsy with distances of 4, 8, 16 cm from anus

Optimum Biopsy specimen for dignosis is 3 to 5 mm in size with Mucosa and submucosa. Absence of ganglion cells and the presence of hypertrophied nerve fibers are seen in Histopathology.

In an aganglionic rectum all the parasympathetic nerve fibers show increased activity in muscle layer. Lamina propria, which are stained as intense brown yellow colour, Diffuse brown, cloudy, or Honey comb like staining of lamniapropria is the result of crushing of tissue with Biopsy forceps and bleeding into interstitium. In newborn, the parasympathetic nerves do not develop its

characteristic enzyme activity, so it cannot be visualized, and it is advisable to repeat biopsy after 2 to 3 weeks.

Myentric plexus can be very rapidly assessed with LDH stain or by Visualization of ganglion cells with the aid of an unspecific esterase reaction. LDH technique is much more expensive. Acetylcholinesterase can if necessary be stained satisfactorily upto 12 hours after biopsy, greater the delay the greater in the difficulty in identifying the sites of activity of the enzyme.

Histochemical staining is more sensitive than Histological study. The enzyme can be stained using Acetyl thiocholine Iodine on fresh specimen of bowel. Histochemical report shows Proliferation of acetyl choline estrase postive nerve fibers in lamina propria and muscularis mucosa, thickened nerve trunks if submucosa is included. Simultaneous estimation of Butyrylcholinestrase activity enhances the diagnostic accuracy. High serum choline estrase and erythrocyte acetyl choline estrase levels are demonstrated in HD.

In NID there is Hyperplastic ganglia with mild to moderate increase of Acetylcholinestrase.

MANOMETRIC STUDY

Principle of the Test: Internal Anal Sphincter normally relaxes with rectal distension. This is mediated through intramural ganglion cells. This reflex is not present in Hirschsprung's Disease as there is absent ganglion cells.

Technique : Infant or child is placed in lateral position, the test is to be done under sedation. 6 Fr foley catheter pushed into rectum for a distance of 4 to 6 cm, depending on the age of child it is used to inflate the rectum by air. A lubricated pressure probe is introduced into anal canal and its position adjusted so that balloon is just inside the anal orifice. Measuring of intraluminal pressure in the anus by means of water or air filled catheter. The recording of pressure done by a water column preferably or by more sophisticated electromanometer. When child is relaxed 5 to 10 ml of air instilled in the rectum and response of internal sphincter noted.

Normally there is a biphasic curve with deep relaxation of internal sphincter which is absent in Hirschsprung's Disease. Manomentric evaluation of internal sphincter relaxation considered as the proof of the presence of intramuralganglion cells in the most caudal segment of terminal rectum is useful to rule out HD (Ultra short segment)

Failure of relaxation of internal sphincter in response to rectal distention is a monometric finding of HD. In manometry, normally there should be a biphasic curve with deep relaxation of internal sphincter, this is absent in Aganglionosis. Normal reflex expected after 40th week of gestation, which is not possible if recorded within 14 days after delivery, babies delivered before 39 weeks of gestation or a pre mature baby or baby weighs less than 2.75 kgs

COMPLICATION

Enterocolitis

Classic clinical picture of enterocolitis consist of abdominal distension, fever, foul smelling, loose stools. ***Elharlaly etal*** described clinical grading system of Hirschsprung's Disease with enterocolitis.

Grade I	-	Mild explosive diarrhea, moderate abdominal distension, no systemic symptoms.
Grade II	-	Moderate abdominal distension, mild systemic symptoms
Grade III	-	severe explosive diarrhea, marked abdominal distension, shock or impending shock.

The cause of enterocolitis is multifactorial in nature. It depends on the length of residual colon, lack of mucous secretion leads to absence of protective mucous barrier, which allow bacteria a more ready entrance into the bowel wall and retention of fecal mass in a stenosed or too long segment causes

decomposition, irritation, inflammation and disruption of mucosa. Increase intraluminal pressure affects liquid absorption by disturbing mucosal microcirculation and causes foul smelling, watery diarrhea.

The following group is prone for developing Enterocolitis

- High incidence of Enterocolitis noted in post pull through procedures especially in Swenson procedure.
- Infant with Trisomy 21.
- Infant with delayed diagnosis of Hirschsprung's disease
- Infant with long segment of aganglionic bowel.

TOTAL COLONIC AGANGLIONOSIS

Total Colonic Aganglionosis accounts for 5 to 15% of infant with HD. TCA may be very difficult to diagnose. Even radiographic studies are diagnostic in only 20 to 30 % of all patients with TCA. The diagnosis is generally made at the time of laprotomy for suspected intestinal obstruction or perforation or when leveling colostomy is done for HD.

Familial incidence

According to ***Bodian and Carter*** patient with Total Colonic Aganglionosis will have upto 15 to 21 % of their siblings affected by the same disease, sometimes it may be raised to even 50 % in rare cases.

Male to female ratio is 1.3 : 1 which is much reduced to 0.8 : 1 in extensive small intestinal involvement.

In TCA, the aganglionic segment extends upto Ileum, the proximal levels ends at terminal Ileum 76%, Mid Ileum 19%, Jejunum 5%. The longer the extent of aganlionosis higher the mortality rate in absence of definitive procedures in Total Colonic Aganglionosis. More proximal extension of aganglionisis needs long term Total Parentral Nutrition because of dysfunctional intestine.

Biopsy

Frozen section of appendix is almost always diagnostic in TCA, showing absence of Ganglioncells in sub mucosal and myentric plexus level. Multiple biopsies from various parts of bowel (rectum, rectosigmoid, descending, transverse, ascending – colon, appendix and ileum) also show absence of Ganglioncells. In Total Colonic Aganglionosis full thickness biopsy may be required as there is occasional false negative results. Histochemical evaluation is by Acetylcholinestrase staining only on materials from recto sigmoid and distal part of descending colon. In the specimen from transverse colon, the diagnosis is based on presence or absence of ganglion cells in submucous myentricpluxes by LDH / SDH staining.

Investigation

TCA is diagnosed by radiology. Plain x-ray abdomen shows dilated bowel loops. Though the radiological findings were non specific in Total Colonic Aganglionosis the entity is very well diagnosed by Barium enema. In TCA the Barium enema picture shows fore shortened question mark colon due to rounded edges of spleenic and Hepatic flexure, no colonic transition zone, but occasionally TZ seen in the distal ileum.

24 hours Barium Enema shows retrograde reflux of Barium into mega ileum or retained contrast in colon. Radiographic finding of shortened colon of normal caliber or presence of "jejunalization" of colon suggest TCA in patient with suggestive history.

Barium Enema

In our Institute Barium powder mixed with lukewarm water and made as thin solution, about 10 to 20 ml is instilled into rectum via rectal catheter by a syringe or by allowing it to flow under gravitational force by keeping the container about 1 to 2 ft above the baby level. Anus is tightly closed by applying gentle

pressure on the buttocks. Films are taken while monitoring under fluoroscopy. Delayed films (24 hrs) also taken to note the retention of barium.

Enterocolitis

Once an infant has developed Enterocolitis there is a chance of developing the same in future also. The cases of Enterocolitis are treated with intra venous fluids, I.V antibiotics, I.V Metrogyl, and rectal washouts. If it does not improve diversion colostomy has to be done.

If repeated Enterocolitis occurs after pull through residual aganglionosis has to be ruled out by rectal biopsy or contrast enema has to be done to rule out mechanical obstruction. Neonatal perforation of appendix is seen in HD. Bowel perforation is a serious complication of HD with Enterocolitis. Perforation may be seen at transition zone or proximal to it due to distal obstruction in HD without Enterocolitis. There are cases of Pneumoperitoneum due to appendiceal rupture because of colonic obstruction related to Hirschsprung's disease. In Total Colonic Aganglionosis perforation is often seen in Aganglionic bowel. In Enterocolitis contrast enema is not performed due to risk of perforation and if performed enema shall show irregular mucosal line with saw tooth appearance.

TCA - SURGICAL PROCEDURES

Soave Endorectalpullthrough – ***Soave*** in 1960 described, in which circumferential incision is made all around about 2 inches above peritoneal reflection, incision made through serosa and muscular coat is extended upto submucosal level. Aganglionic bowel is dissected off the seromuscular coat and the dissection continued upto anal valves. Then the mucous membrane of the terminal bowel is pulledout through the anus until ganglionic proximal bowel is pulledout beyond anal verge. Then the excess bowel is amputated about 10 days after the surgery. Whereas in ***Boley's modification*** the end of ganglionic bowel is sutured to analmucosa at pectinate line.

Martins Modification of Duhamel Procedure: Proposed by ***Lemartin*** (1968) in which ganglianic bowel is pulled in presacral, retrorectal space and ileorectal anastamosis done, side to side anastamosis done between ileum and adjacent descending colon till splenic flexure, aganglianic colon proximal to splenic flexure is resected. Disadvantage is mainly the anterior aganglionic native rectum, which tends to collect fecal mass and present with constipation or enterocolitis. Patient undergoing very short (15 cm) Martin-Duhamel have the best outcome and the patient who had more extended operation landedup with complications and failed procedure.

Ileoanal Anastamosis (Swensons procedure) – The extent of aganglionisis is determined proximally by laprotomy, the bowel is divided in the ganglionated segment level, rectosigmoidectomy with coloanal anastamosis done after ganglionated bowel is pulled through the anus.

Kimura Procedure – in 1981 ***Ken Kimura*** proposed this. It is a staged procedure consisting of illeostomy in normal ganglianic ileum followed by Illeocolostomy (side to side anastomosis between ileum and aganglionic ascending colon), final operation includes pull through of Ileo colostomy segment and its anastomosis to the anal canal Right colon is used because of better absorption.

Stringel operation – pullthrough of normoganglionic ileum with anastomosis to left aganglionic colon and terminal Ileum.

Shanding Operation – Endorectalpullthrough of ileum using Soave technique, and anastomosis done between pulled down ileum and descending colon.

Double Barrel Ileostomy – is done as a primary procedure in almost all the Total Colonic Aganglionosis, while doing this proximal diversion the problem is managed temporarily by relieving the abdominal distension.

The definitive procedures are planned when the child is toilet trained for urine & for saline enema and when all signs of enteritis disappear.

The Definitive procedure most widely used are:-

Martins Modification of Duhamel Procedure or Endorectal pullthrough Procedures, which incorporate a common channel length of Aganglionic intestine, designed to improve fecal liquid absorption and thereby decreasing stool frequency or requires an anastomosis between ganglionic small intestine and anorectum respectively. Higher proportion of the patients experience episodes of Enterocolitis complication after surgery.

Holschineider has collected the results of commonly done operations and found that all the 3 operations (Swenson, Duhamel, Soave) resulted in small proportion of undesirable effects such as constipation, incontinence and Enterocolitis

Incidence of Encopresis seen after Soave (17.6%) and Swenson's (15.1%) procedures. Constipation was seen in patients who underwent Duhamel (41%) procedure

The mortality in TCA remains around 10 to 50 %

AIM

Aim of the study is to review our experience in the management of 19 patients of Total Colonic Aganglionosis over 7 years (July 1998 to June 2005)

MATERIALS AND METHODS

Retrospective review of 302 cases of Hirschsprung's Disease treated at the Institute of Child Health and Hospital for Children, Egmore, Chennai from July 1998 to June 2005. Showed 19 patients with Total Colonic Aganglionosis.

The medical records of the patients were analyzed with emphasis on age & sex incidence, presentation, type of operative procedures, complications of disease and therapy and follow up.

CASE REPORTS

1. 3 days old male child presented not having passed Meconium, bilious vomiting with associated anomaly of **Waarden Burg Syndrome** was found to have a perforation at the terminal ileum about 10 cm from ileocical junction. 15 cm of terminal ileum including perforation at the mesenteric aspect was excised, **Double Barrel Ileostomy** and appendecetomy were done. The HPE result came as absence of ganglion cells and on 3rd post-op day child went against medical advice.
2. Ileostomy done at the age of 1, **Martins procedure** done at the age of 3, there was a 2 years gap between ileostomy and definitive procedure in this patient. The child was admitted once for Enterocolitis (post procedure complication) about 10 months after the definitive procedure.
3. 2 months old male child under went **ileostomy** as a primary procedure after diagnosing it as a case of TCA, developed ostomy diarrhea (Enterocolitis) and seems to be the youngest age in which Enterocolitis developed in this study.
4. **Martins procedure** was done in a 2 ¾ years old male child who developed intestinal obstruction about 6 months after the definitive procedure, for whom laprotomy was done and was found to have multiple adhesions, attempted release made a perforation at ileum inadvertantly so ileostomy was done, which was closed subsequently after 3 months. Second episode of adhesive obstruction was treated conservatively one month after ileostomy closure. 4 months later 3rd episode of obstruction

developed, barium enema revealed dilated pulled through bowel up to anal verge. This time **posterior sphincterotomy** was done to relieve constipation as repeated **anal dilatations** did not help. Within one year period the child had 4 admissions and underwent 3 surgical procedures after the definitive surgery. 2 years was the interval between ileostomy and definitive procedure.

DIAGNOSTIC DILEMMA (case 5 & case 6)

5. Laprotomy was done on a 12 days old male child for bilious vomiting which revealed **Meckels Band obstruction** at ileum with multiple adhesions. Resection anastomosis and adhesion release was done, patient was reopened and **ileostomy** was done on 5th post-op day due to anastomotic leak and burst abdomen. HPE revealed absence of ganglion cells in the resected ileum. In this patient the meckels band obstruction caused confusion in diagnosis and masked the presence of TCA which was later confirmed by HPE result. Child was operated twice within 20 days and lost for follow up.

6. **Perterm Baby (38 weeks)**

   A male child presented at the age of 12 hours for abdominal distention, abdominal wall edema, a history of not having passed meconium with bilateral scrotal swelling revealed free fluid in the abdomen on examination. Antenatal USG done at the age of 8 months showed fetal ascites, frontal bossing with cardiomegaly. Postnatal USG revealed turbid fluid in the abdomen, plain X-ray abdomen showed ascites with the

centrally placed bowel loops, with an impression of **meconium peritonitis**. Findings at laprotomy were a. ileal perforation at 15 cm from IC junction, the distal ileum, caecun, ascending colon were unhealthy and found as a cord like structure with patent lumen. The distal colon appeared as unused microcolon. Resection of the unhealthy bowel with **end iliostomy** and transverse colon mucous fistula was designed. Child was on ventilator support and expired after 3 days. Biopsy of the resected portion revealed absence of ganglion cells. In this case meconium peritonitis caused confusion in diagnosis but at the same time the existence of TCA in a preterm baby, presence of meconium peritonitis in TCA due to perforation of bowel during antenatal period, poor prognosis with increased mortality of TCA in preterm baby with complications like perforation, quoted in the literature are proved. Surgery done in a very youngest age (15 hours old).

7. Primary ileoanal anastomosis **(Swenson)** with total proctocolectomy done on a 5 month old male child who got admitted thrice within a period of 6 months after the definitive procedure for the following complications.

   Adhesive obstruction – treated conservatively one month after surgery

   2 episodes of Enterocolitis treated conservatively with in 5 months of the surgery,

   The child had failure to thrive and it had a very poor weight gain of 1 kg over a period of 6 months.

On table during laprotomy the transition zone was found at terminal ileum (4 cm proximal to IC junction) but the barium enema picture of the baby showed the transition zone at the level of ascending colon.

8. **Double barrel Ileostomy** was done for an 8 hour old new born female child with **multiple congenital anomalies** (Rt club foot, Lt microtia, cleft palate, webbed neck, Anisocoria both eyes) who presented with abdominal distention. Laprotomy findings were microcolon extending up to terminal ileum, appendicetomy was done. The child expired on 6th post operative day and the biopsy suggested of TCA.

9. Barium enema picture of a 10 days old male child with a history of not having passed meconium after 48 hours showed transition zone near spleenic flexure. On laprotomy there were two constrictions, one at terminal ileum about 8 cm from IC junction and another at the left end of transverse colon. **Colostomy** designed at transverse colon followed by excision of membrane (**type 1 atresia**) through entrotomy Biopsy taken from ileal constriction level showed no ganglion cells, as the child presented with abdominal distention and dilated loops **ileostomy** was done after 1 month the distal portion from the ileostomy to colostomy site was also removed. **Soave pullthrough** procedure was done about 1 year after ileostomy, bowel trimming was done 15 days after the definitive procedure. The child is on regular follow up for the past 5 years. In this

case a TCA child presented with type 1 atresia, though the literature says the TCA usually present with type 3 atreasia. Child underwent 3 surgeries within a period of 13 months and the interval between ileostomy and definitive surgery was 1 year.

10. 2 months old female child admitted for Enterocolitis who was on **ileostomy** performed at the age of 20 days of its life. Lost follow up for 4 years

11. **Double barrel ileostomy** done on 1 month old male child for abdominal distension, fever, delayed passage of miconium, bilious vomiting, abdominal wall edema has lost follow up for 2 years. In this child the ileostomy was done as there was whole length of unused microcolon with a HPE suggestive of absent ganglion cells but the barium enema picture showed long segment HD.
12. **Double barrel ileostomy** done on a 16 days old male child for history of delayed and prolonged passage of meconium, bilious vomiting, and the barium enema suggestive of HD. Thyroid profile and blood investigations were normal. Laprotomy revealed marked dilatation of proximal small bowel with an abrupt narrowing of terminal ileum at 10 cm proximal to IC junction with distal microcolon. **Soave procedure** was done at 3 months since the biopsy showed absence of ganglion cells upto terminal ileum. The child is on follow up for the past 2 months .

13. **Ileostomy** was done on 10 days old male child who presented with abdominal distention, bilious vomiting and multiple congenital anomalies (Microtia, Heterochoromiairis) It was diagnosed as a case of TCA as the biopsies revealed absent ganglion cells in appendix and ileostomy site, though the barium enema revealed long segment HD. The terminal ileum was found to be abruptly narrowed at 15 cm from IC junction. Child lost follow up for 5 years.
14. **Ileostomy** and appendicectomy were done on a 3 days old female child for distended abdomen with bilious vomiting with barium picture suggestive of meconiumileus. Biopsies revealed absent ganglion cells.
15. **Double barrel Ileostomy** was done on a 2 month old female child, as barium enema suggested foreshortened colon. ***Duhamel type of pullthrough*** was done about one week after ileostomy as the biopsies revealed absent ganglion cells up to ascending colon. Child is on follow up for the past 2 years. Definitive procedure was done at the youngest age of 3 months.
16. **Ileostomy**, Appendicetomy and Multiple biopsies were done on a 7 days old male child who presented with multiple congenital anomalies with abdominal distension (White hair patch in the frontal region with alopecia- **Waarden Burg Syndrome**). On laprotomy small caliber terminal ileum with microcolon distally but barium enema was suggestive of malrotation. Biopsy revealed absent ganglion cells. The child expired 3rd post-op day.

17. **Loop Ilesotomy, Appendicetomy with multiple biopsies were done on one month old male child for prolonged passage of meconium, abdominal distention with visible loops and bilious vomiting.**

    Barium enema revealed fore shortened colon

    X-ray both Knees no evidence of Hypothyroidism.

    Manometry – no reflex inhibition on rectal stimuli

    Biopsies revealed absent ganglion cells.

    ***Martins modification of Duhamel Procedure* was done about 3 months after ileostomy**

    The child got admitted and treated conservatively 4 times with in a period of 1 year for entrocolotis. Child is on regular follow up for the past 4 years.

18. **7 months old male child with Double Barrel Ileostomy treated conservatively for adhesive obstruction, a known case of TCA proved by biopsy who actually underwent ileostomy on 3rd day of its life after barium enema for not passing meconium and abdominal distension. Child lost follow up for the past 6 years.**

19. **Double Barrel Ileostomy done on 1 ½ months old male child for abdominal distension and bilious vomiting.**

    Meconium history – delayed passage

    X-ray chest and knees – normal

    Barium picture suggestive of long segment HD

    Manometry – not suggestive of HD

    Laprotomy finding – Dilated small bowl loops narrowing in terminal ileum near IC junction. Collapsed colon filled with barium.

    Child lost follow up for the past 5 years

DISCUSSION

19 children with the TCA were treated between June 1998 and July 2005 at the Institute of Child Health and Hospital for Children, Chennai.

Age & Sex Incidence

Analysis of age at the time of diagnosis revealed that 10 (53%) cases were with in one month period, 7 (37%) cases were 1 to 6 months period. And 2 (11%) cases were between 6 to 12 months. Of whom 16 (84%) were boys. 3 (16%) were girls, with the ratio of 5:1.

All the cases were full term babies except one preterm baby.

Mean birth weight was 2.75 kg.

Familial Incidence

There was not even a single case with family history suggestive of Total Colonic Aganglionosis in this study.

Associated Anomoly

In this study there were 5 cases with associated anomalies in Total Colonic Aganglionosis they are as follows:

1. Waarden Burg Syndrome	– 2 cases	White hair follicle fore head, Alopecia
2. Multiple congenital	– 2 cases	Club foot , Cleft palate, Anomolies Microtia, Heterochromic Iris
3. Colonic atresia	– 1 case	Type 1 atresia – Lt . Tr. Colon

Presentation

14 (74%) cases presented with vomiting, of which 11 were bilious and 3 were non bilious in nature. 13 (68%) cases presented with abdominal distention. 10 (53%) cases presented with altered meconium history, in which 4 patients did not pass meconium for more than 48 hours in the neonatal period, 3 patients each presented with history of delayed and prolonged passage of meconium respectively. 5 (26%) cases presented with history of constipation. 5(26%) cases had refusal to take feeds. 4 cases presented with loose stools. Child with Fever, Scrotal Swelling, Abdominal wall edema each 1 case respectively.

Investigation

X-Ray Abdomen showed dilated bowel loops in most of the cases as an obstruction pattern. In 1 case X-Ray revealed ascites with centrally placed bowel loops suggestive of Meconium peritonitis. Which was later confirmed by Ultrasonogram. Laprotomy revealed perforation at terminal ileum level.

Barium Enema was done in almost 17 of 19 (89%) cases in which

5 (24%) cases were diagnosed as Total colinic Aganglionosis due to foreshorterned colon

5 (29%) cases were diagnosed as Hirschsprung's Disease

5 (29%) cases were diagnosed as long segment Hirschsprung's Disease as the Transition Zone at ascending and transverse colon,

2 (12%) cases were diagnosed as meconium ileus,

1 (6%) case was diagnosed as malrotation and for 1 case barium enema

was done post operatively as there was dilatation of pulled through bowel. X–Ray Knees and Serum T3, T4, TSH were done for 2 cases to rule out hypothyroidism causing constipation – which were negative.

Biopsy

Biopsies taken from multiple sites (rectum just above peritonial reflection, sigmoid, descending, transverse, ascending colon, appendix and terminal ileum) at the time of operation were submitted for HPE.

Ganglion cells absent in entire colon & appendix in 19(100%) cases.

Absent Ganglion cells in ileum and colon were found in 6(32%) cases.

Surgical procedures

About 18 of 19 (95%) cases underwent ***primary ileostomy*** following which **Definitive Procedure** was done for 7 (37%) cases. In which,

Martins – Duhamel procedure was done in – 4 cases (21%)

Soave pull through was done in – 2 cases (11%)

Ileo – anal anastomosis was done in – 1 case (5%)

Anal Dilatation &Posterior Sphincterotomy – 1 case

In this study 3 months old was the youngest age in which Duhamel and Soave procedure were done, Swenson's procedure was done at the age of 5 months, 3 years was the oldest age in which definitive procedure was done.

Stapler was used in two cases for doing ileocolonic anastomosis in Martins Procedure in the remaining two cases Anastomosis was done by

handsewn technique and Clamp was used to crush the colorectal septum in Duhamels

Interval between Procedures

The time interval between the primary ileostomy and definitive procedure varied from 1 week (earliest) to 2 years (longest).

Additional Surgeries

One child underwent enterotomy for excision of type I atresia membrane near left end of transverse colon and the same was designed as colostomy later. Ileostomy was done for the same patient as there was absence of ganglion cells at their constricted region in the terminal ileum.

3 of 19 (16%) underwent multiple surgeries other than definitive procedure, of which two had dilemma in diagnosis. The additional surgeries done between the primary and definitive surgery were enterotomy, adhesiolysis, ileostomy due to inadvertent rupture during adhesion release, and ileostomy closure, laprotomy for anastomotic leak following resection anastomosis.

Posterior sphincterotomy was done to relive constipation in a failed anal dilation case of Soave pullthrough.

Complications

Enterocolitis

7 (37%) cases presented with enterocolitis of which 3 of them had undergone Definitive procedure, (Soave, Martin's, Swenson's – each one case respectively) rest of the 4 (21%) cases were Ileostomy patients before undergoing definitive procedure. One child got admitted repeatedly (4 times) for enterocolitis within a period of 1 year.

Subacute Obstruction

A child got admitted twice for enterocolitis and adhesive obstruction within a period of 6 months. 2 cases who underwent Soave Procedure got admitted thrice for Subacute intestinal obstruction during postoperative period and managed conservatively

Constipation

One child had constipation followed by Martin's Procedure, and the child underwent Posterior sphincterotomy about 14 months after failure of several attempts made to relieve constipation by repeated anal dilatation.

Extent of Aganglionosis

Clinically 13 (68%) cases had distal microcolon with proximal megaileum, biopsy report showed absent ganglion cells of entire colon in 19 cases (100%), 13 cases (68%) showed absent ganglion cells in distal colon and terminal ileum. One child presented with perforation at terminal ileum on its mesenteric aspect at the time of birth itself, the other one presented with multiple adhesive obstruction with perforation and constriction at the level of terminal ileum due to Meckel's Band. In both the cases the leison at the terminal ileum were about 10 to 15 cm from Ileocolic junction.

Mortality

Mortality was 3 (16%) in this study. Longer the extent of Aganglionosis greater the Mortality, was proved by 2 cases in which transition zone was seen at terminal Ileum level. Death occurred in Total Colonic Aganglionosis with preterm babies, Multiple Congenital Anomolies & Complication like perforation are notable in this study.

2 of 3 cases presented with multiple congenital anomolies like Waarden Burg Syndrome and Club foot with cleft palate. A preterm baby presented as meconiumperitonitis with ascites.

One baby with WBS went against medical advice following Double barrel Ileostomy.

Follow Up

The follow up period is ranging from 2 months to 6 years duration after definitive procedure. Which is strictly maintained.

6 (32%) cases of

double barrel ileostomy last followup after ostomy was done as a primary procedure.

Outcome

Functional outcome of the operated cases were assessed by good stool pattern. In this study 75% of Martin's Procedure and 50% of Soave Procedure cases performed well, attained good stool pattern in the postoperative and follow up period.

3 cases with perineal excoriation were observed in the early postoperative period during follow up.(Soave, Martin's, Swenson's – each one case respectively)

CONCLUSION

- TCA is a severe form of HD, most commonly recognized in the Neonatal period.
- Male predominance was seen in this study.
- Martin's modification of Duhamel procedure results are better.
- Functional outcome were good in cases who underwent definitive procedure.
- Kimura Procedure was not done in this study
- Most of the cases in this study presented with bilious vomiting , Abdominal distension, Altered meconium history.
- Only 4 cases were diagnosed as Total Colonic Aganglionosis by Barium Enema Investigation.
- Acetyl choline sterase study was not done in any patient in this study.
- Manometric studies performed in two cases, in which only one case established the diagnosis, and the procedure was not repeated in any of the cases after definitive procedure.

- According to literature type III colonic atresia is more common than any other type though the presentation is very rare. In this study there was one case of type I atresia seen near the left end of transverse colon, which was associated with Total Colonic Aganglionosis. This was treated by Soave pullthrough and the child is alive and coming for follow up.

- There were no case of Down syndrome or genitourinary anomalies seen associated with Total Colonic Aganglionosis in this study.

- In no case Total Parentral Nutrition (TPN) was used in this study.

- In this study no case presented with a family history of HD or TCA

- Child with Total Colonic Aganglionosis admitted at 8 hours after birth was the youngest to present and 15 hours old was the earliest time at which surgery was performed in this study.

- The best time for pullthrough procedure would be around 6 months of age according to literature. In our Institute we have done pullthrough at the age of 3 months.

- Almost all the operated TCA children had poor weight gain.

- Total Colonic Aganglionosis associated with perforation of bowel near the proximal end of aganglionic segment were seen in two cases. As mentioned in the literature child presenting with perforation even at the time of birth was also seen in this study.

- Constipation- the postoperative complication of Soave pullthrough was relieved rather by posterior sphincterotomy than anal dilatation. The procedure in this study coincides with ***Elsen hamme*** (1974) description (he suggested immediate myectomy instead of sphincter dilatation as it causes laceration and fibrosis).

- Nearly one third of the TCA treated child (Ileostomy) has lost for follow up in this study.

- Mortality was seen in TCA with associated anomaly and in preterm baby with a complication of ileal perforation and peritonitis, otherwise the survival in TCA is good in operated cases. Morality rate of Total Colonic Aganglionosis in this study is similar to that of literature report.

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