

Case Series

Chronic Intestinal pseudo-obstruction : A case series

Study of a Big Iraqi Family

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Abstract

This is a retro-prospective case series study of a big Iraqi family consisting of 69 members, it was studied over more than 30 years. In all affected patients, multiple operations were done. Nineteen members were affected with the visceral type of intestinal pseudo-obstruction .Fifteen patients died at ages between (8-35) years. Four surviving patients are discussed .Fifty percent of the parents of the affected

patients were diabetics. The main clinical presentations were abdominal distention, abdominal pain, vomiting, constipation with occasional diarrhea .Radiological investigations showed variable dilatations and stenoses of the bowels ,megaduodenum was characteristic.

Keywords:- Intestinal Pseudo-obstruction, familial, Diabetes Mellitus

Introduction

Chronic intestinal pseudo-obstruction is a rare clinical disorder of abnormal intestinal motility characterized by a failure of the intestine to propel its contents through non-obstructed lumen (1,2) . The symptoms and signs can be very similar to mechanical bowel obstruction (1,2). The causes can be primary or secondary ;The primary form can be sporadic or familial and can be classified into neuronal or visceral types (2,3) . Any segment of the gastrointestinal tract can be involved. No signs or symptoms are diagnostic(1).In children ,the presentation is usually nausea, vomiting, abdominal distention, constipation.(4,5,6,7).In adults, dysphagia, abdominal pain and diarrhea are the commoner presentations (1).Diarrhea may be caused by abnormal motility, bacterial overgrowth or stagnant loop syndrome(1).The clinical picture may be similar to any other gastrointestinal tract

disorder, symptoms can overlap with non-ulcer dyspepsia, irritable bowel syndrome, cyclical vomiting. Extraintestinal manifestations include dilated bladder and ureter ,abnormal iris and uterine interia and autonomic nervous dysfunction (8,9,10).

The diagnosis should be suspected in the following situations:-

1. Co-existence of vomiting ,abdominal distention and constipation .
2. Chronic gastrointestinal symptoms and weight loss.
3. Succession splash.
4. Urinary symptoms (bladder distention , recurrent infections).
5. Positive family history for the disease.
6. Autonomic dysfunction (postural dizziness, sweating abnormalities).

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7. History of non-diagnostic laparotomies.
8. Radiological studies demonstrating no mechanical obstructions (1,2,4,5,8,9,10,11).

The principles of management of chronic intestinal pseudo obstruction are:-

- Nutritional support.
- Antibiotic.
- Prokinetic Drugs.
- Surgery.

Medical treatment:-

The goal is to restore the intestinal propulsion. Dietary measures include-frequent small liquid meals, low in fat and fiber in gastroparesis and esophageal hypomotility; prokinetic drugs are occasionally useful (1,2,3). Cisapride, metoclopramide, erythromycin, domperidone, misoprostol, octreotide, neostigmine, serotonin - 4 - receptor agonists were useful in selected cases (13,14,15). Endoscopic decompression is useful in some cases (1,16).

Surgical treatment:-

Bowel decompression by gastrostomy and jejunostomy with feeding through these openings are useful (venting enterostomy). Surgical bypass in cases of localized disease. Subtotal or total enterectomies may be needed; pacemaker implantation is investigational (17,18). Small bowel transplantation is the only definitive cure (17,18,19). In severe cases, parenteral nutrition is needed (1).

The aim of the study :-

To highlight the general features of chronic intestinal pseudo obstruction in this Iraqi family and increase awareness of the presence of condition with consequent results of reducing misdiagnosis and mismanagement for these patients.

Patients and Methods:-

The study is a retro-prospective analysis of data of this Iraqi family dated back to 1970, the family with 69 members, the data analysis included detailed history, thorough physical examination, investigations and review of operative reports.

The diagnosis of pseudo obstruction was made by a combination of suggestive presentation, laboratory tests and appropriate radiological examinations and after exclusion of any mechanical cause of obstruction.

The following investigation were done: complete blood count with blood picture, renal function test, liver function test, fasting blood sugar, electrolytes, thyroid function test, antinuclear antibody, plain abdomen, contrast studies of upper and lower gastrointestinal tract, upper endoscope, colonoscopy, diagnostic laparotomy with full thickness biopsy or bowel segmental resection.

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Results:-

✍ After discovering the first patient in 1984 by the Author, a detailed study of this family which consisted of 69 members was made.

✍ 19 members were affected.

✍ 15 members including the first patients died at ages between 8-35 years.

✍ All those who died had 2-5 operations for bowel obstruction.

✍ Over half parents of the affected patients were diabetics (8 from 15 members). All the members came from one great grand father who came from Balad near Samara in the middle of Iraq.

✍ After close intermarriages between families of the three sons of the above two were suspected to have the same disease, (with constipation and distention).

✍ Of the generations following this (third generation), four families with 15 members, 8 of them were diabetics, one is still alive at the age of 70 years, and 4 of his children are affected with pseudo obstruction.

✍ Close marriages between the four families (4th generation produced (41) members) 19 of them affected with pseudo obstruction.

✍ Of the 19 members, 15 died at ages (8-35y). The remaining 4 alive patients affected with bouts of distention, abdominal pain, constipation and occasionally diarrhea.

✍ The youngest patients was female age 13 years, diagnosed at the age of 2 years and had previous operations for intestinal obstruction who died with septicemia.

✍ The only patient who is still alive (at the age of 30) with no operations has now repeated distention and vomiting and investigation showed dilated small and large bowel.

✍ The other living relative with pseudo obstruction (case 15), had total colectomy with ileo-rectal anastomosis.

✍ The family works in their farm and practice herbal medicines for themselves & others, and eats refined diets rich in sugars & fats.

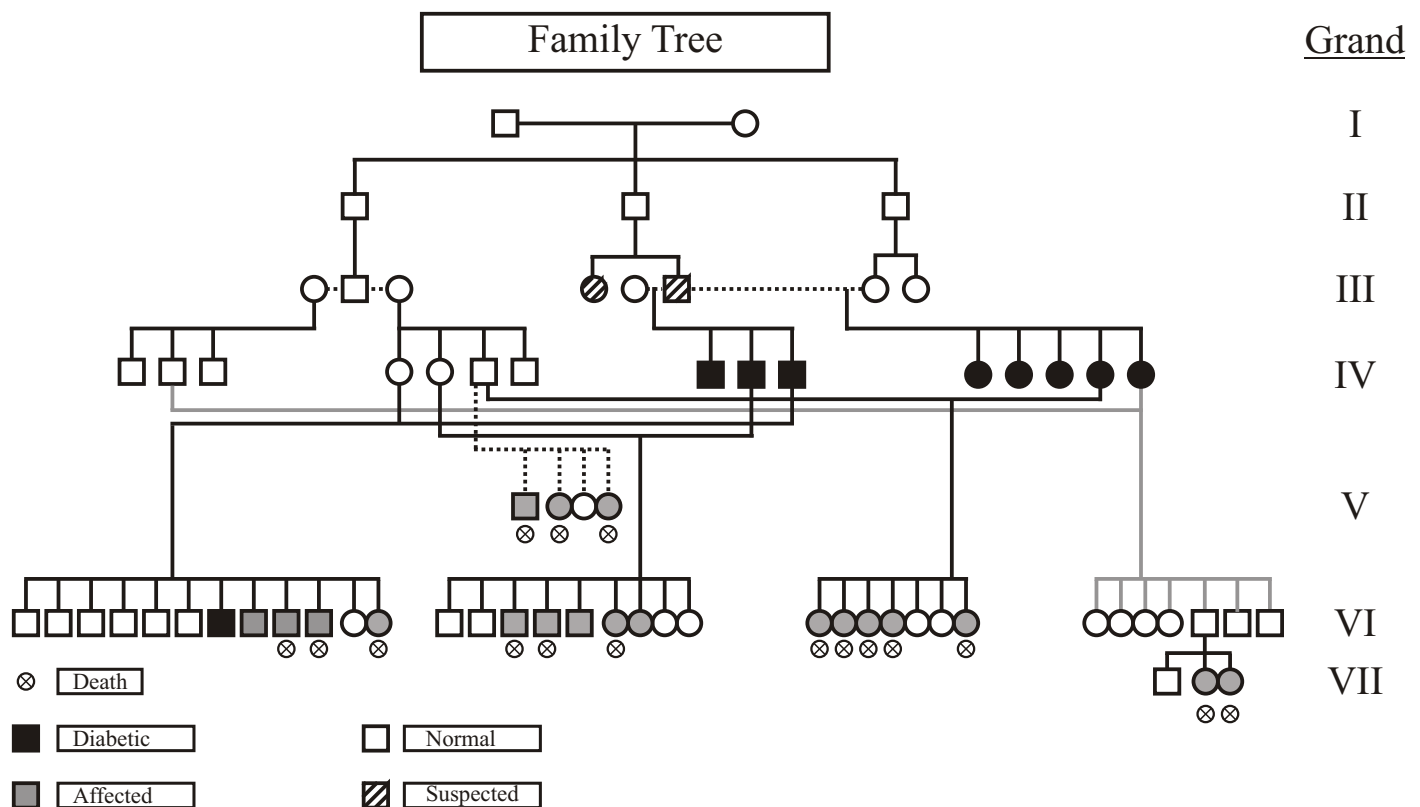
✍ Diagram:- Pedigree of the family.

Case series :

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✍ Diagram:- Pedigree of the family.



Case series :

Case 1:- Index patient

The first patient (S.A.A., male 28 years of age) was discovered in 1982 presented with recurrent abdominal pain since childhood associated with constipation, abdominal distention; occasional vomiting & diarrhea, with a history of urinary tract infection. Operation for intestinal obstruction at the age of 24 years was done followed by a big incisional hernia. He had severe proximal muscle weakness, severe abdominal distention.

Investigations:-

1. Chest x-ray: big gastric shadow.
2. Plain abdomen : gaseous distention.
3. Barium enema: dilated colon; featureless, localized stenotic segment in the rectum.
4. Barium meal and follow through: esophagus dilated, stomach dilated, duodenum "megaduodenum", massively dilated small bowel (saccules and diverticula) with very slow transit.

Bowel (saccules and diverticula) with very slow transit.

5. I.V.U. dilated atonic bladder.
6. Blood picture showed acanthocytosis.
7. Serum cholesterol decreased (90 mg/dl).
8. E.M.G. -myopathic form.

He gave a strong family history with 14 members affected. Nine of them died at a young age with the same disease . Because of the strong family history, he was labeled as (Familial intestinal pseudo-obstruction).He was treated conservatively with courses of antibiotics and prokinetic agents (prostigmine, metoclopramide). He was markedly improved on these measures . One year later , he was admitted in another hospital as intestinal obstruction & Laparotomy was done which resulted in death postoperatively.

The discovery of this patient and his family history has lead to the detailed study of his family. Because of the serious consequences of the disease in these

Because of the serious consequences of the disease in these families, we investigated all the living members and questioned in details their dietary habits and bowel motions.

Case 2:

I.D.A., 12 years old male, died in 1970 at the age of 12 years with 3 previous operations for intestinal obstruction.

Case 3:

H.D.A., 36 years old male. Operation was done to him in 1970 at the age of 8 years for suspected volvulus followed by multiple operations, in 1972 resection of small bowel, in 1974 right hemicolectomy, in 1980 for mal-rotation of the bowel & in 1981 for release of adhesions. Ever since, he was kept on medical follow up. Died 2001 with intestinal obstruction.

Case 4:-

M.D.A., 25 years old female, died postoperatively at the age of 25 years for bleeding gastric ulcer with huge dilatation of small and large bowel.

Cases 5,6,7,8,9,10,11,12,13 and 14 :-

Six males and 4 females, died at ages of 8-25 year with multiple operations. Four females died at the age of 17 and 18 years with multiple operations for intestinal obstruction.

Case 15 :-

S.A.A., 17 years old male was presented with minor complaints. He was an obese young patient. His bowel opens once every 1-3 days, sometimes every 1-2 weeks. He has never been to doctors. On clinical examination he had slight hyper-extensibility of the joints, neurological examination was normal, E.M.G. normal, Barium swallow was normal, Barium meal and follow-through showed a normal stomach and jejunum but the lower small bowel was very dilated with gross dilatation of the right side of the colon with long smooth narrow segments in the left colon.

Jejunal biopsy was normal. Blood examination was normal apart from mild indirect hyperbilirubinemia (Gilbert).

In 1986, he was sent and studied at the Hammersmith Hospital in London. Rectal biopsy showed strikingly abnormal muscles of the muscularis mucosa with multiple vacuolated muscle cells with normal ganglion cells. A diagnosis of familial intestinal myopathy was confirmed.

He underwent total colectomy with iliorectal anastomosis in U. K. in 1986. Since then he developed bouts of obstructions every 6/12 - 1 year. He is now

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Ever since 1986, four more members were seen.

Case 16 :-

24 year old female with multiple operations died post-operatively.

Case 17 :- 28 year old female with similar presentation, had total colectomy with ilio-rectal anastomosis. The biopsy showed possible hypoganglionosis. Died 3 years after the operation.

Cases 18 and 19 :- 2 children are followed up. One obstructed at the age of 6 months and had an operation for suspected mal-rotation and inguinal hernia, and now severely emaciated. An abdomen MRI was done because the family refused Barium examinations and the MRI showed massive dilatation of the bowel :-

The radiological features were :-

- I Megaduodenum.
- II Variable dilatation of small and large bowel.
- III Strictures.

Discussion:- This big Iraqi family was traced to 6 generations. Possible diagnosis of chronic intestinal pseudo obstruction was suspected in the 2nd generation. Over 50% of the 3rd generation were diabetics (maturity onset diabetes). Fifty percent of the children of the diabetic members had pseudo-obstruction which raises the possibility of a genetic mutations (12,20).

The disease looks like an autosomal recessive in the 4th generation and dominant in the last generation (1,5,8,21).

The main symptoms were Nausea, vomiting, weight loss, constipation and occasional diarrhea, the important radiological findings were variable dilatation and stenoses but mainly: Megaduodenum, dilated small and large bowel, long narrow segments, Dilated bladder in some (5).

The hematological investigations showed mainly anemia, aconthocytosis, low serum cholesterol which were attributed to malabsorption (1).

The biopsies from the bowel showed vacuolation of the smooth muscles in the early cases which confirmed visceral myopathy (1), and in late cases, (in one case) a decrease in nerve ganglia possibly

The hematological investigations showed mainly anemia, aconthocytosis, low serum cholesterol which were attributed to malabsorption(1).

The biopsies from the bowel showed vacuolation of the smooth muscles in the early cases which confirmed visceral myopathy (1), and in late cases, (in one case) a decrease in nerve ganglia possibly secondary to the massive dilatation of the affected segment (1).

The relationships to their dietary habits and the use of herbal medicines is striking which need detailed studies of the herbs used.

Gastroduodenal manometry is not available (as it's the situation at most medical centers) (1) ; but is rarely necessary for diagnosis in adults who have adequate radiographic examination (1).

Small bowel manometry does not always differentiate mechanical obstruction from pseudo-obstruction, and it's sensitivity and specificity are not known (1).

This study emphasizes the importance of early diagnosis of intestinal pseudo-obstruction and awareness of familial occurrence, the management should always be conservative and every effort should be used before trying surgery.

The relation to diabetes mellitus needs further studies to test the genetic linkage; the relation to the dietary habits and the use of herbal medicine need to be studied in detail. Pacing of the intestine, electrical stimulation of the stomach or intestine, and transplantation are considered experimental at this time. Bowel transplantation for patients with motility disorders has been performed infrequently, and the risk-benefit ratio is unclear (18).

However, intestinal transplantation may be life-saving in children.

In one report, for example, five of eight children who underwent transplantation were alive after a median follow-up of 26 years (22).

Reference :-

1. Anuras, S., Mitros, F., Nowak, T. et al. A familial visceral myopathy with external ophthalmoplegia and autosomal recessive transmission. *Gastroenterology* 84:346,1983.
2. Anuras, S., Mitros, F., Milano, A., et al. A familial viscus myopathy with dilatation of the entire gastrointestinal tract. *Gastroenterology* 90: 385,1986.
3. Camilleri, M., Disorders of gastrointestinal motility in neurologic diseases. *Mayo clin proc* 1990;65:825.
4. Camilleri, M., Brown, M., Malagelada, J. Impaired transit of chyme in chronic intestinal pseudo-obstruction: Correction by cisapride. *Gastroenterology* 91:610,1986.
5. Camilleri, M., Malagelada, J., Abell, T., et al. Effect of six weeks of treatment with cisapride in gastroparesis and intestinal pseudo-obstruction. *Gastroenterology* 96:704,1989.
6. Chokhavatia, S., Anuras, S. Neuromuscular disease of the gastrointestinal tract. *Am-J-Med-Sci*. 1999 Mar;301(3):201-14.
7. Farra, A., Rodriguez, G., Medina, S., et al. [trans-rectal endoscopic ileal decompression as treatment of small intestinal pseudo obstruction. Report of a case]. *Rev-Gastroenterol-Mex*. 1996 Jul-Sep;61(3):239-42.
8. Faulk, D., Anuras, S., and Christensen, J. chronic intestinal pseudo obstruction. *Gastroenterology* 74:922,1978
9. Goulet, O., Michel, J.L., Brousse, N. et al. [Can intestinal transplantation constitute treatment for intestinal failure] *Ann-Chir*-1999;53(5):412-21.
10. Higman, D., Peters, P., Stewart, M., familial hollow visceral myopathy with varying urological manifestation. *Br-J-urol*. 1992 Oct; 70(4):435-8.
11. Jones, S.C., Dixon, M.F., Linott, D.J., Axon, A.T. Familial visceral myopathy. A family with involvement of four generations. *Dig-Dis-Sci*. 1992 Mar;37(3):464-9.
12. Krishnamurthy, S., and Schuffler, M. pathology of neuromuscular disorders of the small intestine and colon. *Gastroenterology* 93:610,1987.
13. Lee, R.G., Nakamura, K., Tsamandas, A.C., et al. Pathology of human intestinal transplantation. *Gastroenterology* 1996;110:1820.
14. Quigley, E.M. Small intestinal transplantation: Reflections on an evolving approach to intestinal failure. *Gastroenterology* 1996; 110: 2009
15. Reyntjens, A., Verlinden, M., Schuerman, V. Cisapride in the treatment of chronic intestinal pseudo-obstruction. *Gastroenterology* 28(suppl 1): 79,1990.
16. Schuffler, M. D., chronic Intestinal pseudo-obstruction in Feldman M., Sleisenger M; *Gastrointestinal and liver disease* (6th edition) volume II, chapter 109, 1820-1830
17. Schuffler, M., Rohmann, C., Chaffee, R., et al.

- intestinal failure. *Gastroenterology* 1996; 110: 2009
15. Reyntjens, A., Verlinden, M., Schuerman, V. Cisapride in the treatment of chronic intestinal pseudo-obstruction. *Gastroenterology* 28(suppl 1): 79, 1990.
 16. Schuffler M. D, chronic Intestinal pseudo - obstruction in Feldman M., Sleisenger M; *Gastrointestinal and liver disease* (6th edition) volume II, chapter 109, 1820-1830
 17. Schuffler, M Rohmann, C., Chaffee, R., et al. Chronic intestinal pseudo obstruction : A report of 27 cases and review of the literature. *Medicine* 60:173, 1981.
 18. Schuffler, M., Pagon, R., Schwartz, R., et al. Visceral myopathy of the gastrointestinal and genitourinary tracts in infants. *Gastroenterology* 94:892, 1988.
 19. Schuffler, M., and Pope, C. Studies of idiopathic intestinal pseudo obstruction: II. Hereditary hollow visceral myopathy : Family studies. *Gastroenterology* 73: 339, 1977.
 20. Schuffler, M., Lowe, M., Bill, A. Studies of idiopathic intestinal pseudo-obstruction: 1. Hereditary hollow visceral myopathy clinical and pathological studies. *Gastroenterology* 73:327, 1977.
 21. Sigurdsson, L, Reyes, J, Kocoshis, SA, et al. Intestinal transplantation in children with chronic intestinal pseudo-obstruction. *Gut* 1999; 45:570.
 22. Stangellini, V., Camilleri, M., and Malageleda, J. Chronic idiopathic intestinal pseudo-obstruction: clinical and intestinal manometric findings. *Gut* 28:5, 1987.