Intestinal pseudo-obstruction in myotonic dystrophy

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Abstract

We describe four myotonic dystrophy (DM) patients who developed recurrent intestinal pseudo-obstruction. Some episodes were associated with gastroenteritis, while abdominal crowding may have occurred in one case during the third trimester of pregnancy. In most instances, however, no apparent cause could be identified. Intestinal pseudo-obstruction may occur at any stage of DM. In one of our cases intestinal pseudo-obstruction preceded significant muscle weakness by 15 years. Intestinal pseudo-obstruction is usually treated effectively with conservative measures. These include restriction of oral intake, intravenous fluids, and multiple enemas or colonoscopy. Improved intestinal function was noted in one case treated with the prokinetic agent cisapride. A partial sigmoid resection was performed in three cases with dolichomegacolon. No abnormalities were reported on histological examination. Since intestinal pseudo-obstruction is a rare complication of DM, it is of interest that two of our cases are sibs. Review of published reports showed several reports of familial occurrence of specific complications. These include cardiac conduction disturbances, focal myocarditis, mitral valve prolapse, pilomatrixomas, polyneuropathy, normal pressure hydrocephalus, and dilatation of the urinary tract. Myotonic dystrophy may show a tendency to familial clustering of organ specific involvement.

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In myotonic dystrophy (DM), smooth muscle involvement can be shown in most patients. Swallowing difficulties are a major concern and may lead to aspiration.[1] Symptomatic disturbance of colonic motility may occur with colicky abdominal pain similar to spastic colon. *X* ray studies may be normal or show frank megacolon. Occasionally patients develop a severe disturbance of intestinal motility such as volvulus or intestinal pseudo-obstruction.[2–6] We here report on four DM patients who developed this complication.

Case reports

CASE 1

This man was born in 1941. He first noted myotonia at the age of 15. He was a conscript in the army at 18, when he developed acute lower abdominal pain with abdominal distension. A temporary colostomy was performed. During the following year he experienced several episodes of abdominal pain. *X* ray studies showed a megasigmoid. On laparotomy, about 30 cm of sigmoid colon was resected. Microscopic examination showed normal ganglion cells without other abnormalities. At 34 years he presented with distal muscle weakness. Percussion myotonia of the thenar muscles and of the tongue was noted. EMG showed electrical myotonia and mild conduction delay. A diagnosis of myotonic dystrophy was made. At the age of 42, he developed fever, abdominal distension, and pain. Plain abdominal *x* ray showed marked dilatation of many small bowel loops and the patient was admitted to hospital. The erythrocyte sedimentation rate increased from 12 to 42 mm. Cultures of peripheral blood and faeces were negative. The patient improved with conservative measures. At the age of 43 he was again admitted with vomiting, abdominal distension, and bowel dilatation. The clinical picture again resolved with conservative measures. A contrast barium enema showed loss of haustra throughout the colon. Several subsequent episodes of constipation and crampy abdominal pain have led to two more admissions to hospital. No further abdominal surgery has been necessary.

CASE 2

This woman was born in 1947. She is the sister of case 1. Her first pregnancy was complicated by polyhydramnios. A son was born who died of respiratory insufficiency. A cardiac defect was suspected, but no abnormality was identified at necropsy. The patient became pregnant again and delivered a normal daughter. At the age of 28, myotonic dystrophy was diagnosed during family studies. During her third pregnancy at the age of 29, she developed acute ileus at 28 weeks, believed to be owing to pressure of the uterus against the rectosigmoid. A temporary colostomy was performed and she delivered a healthy girl on the same evening. The child weighed 1880 g and subsequently did well. The colostomy was closed two weeks after delivery. At the age of 30 years, she was admitted with crampy abdominal pain, constipation, and vomiting, which resolved spontaneously. *X* ray studies showed megacolon. A rectal biopsy showed no evidence of Hirschsprung's disease. Two years later, she was readmitted with ileus thought to result from volvulus of the sigmoid. A laparotomy was performed during which the obstruction was relieved. *X* ray studies two

months after operation showed an elongated sigmoid and a sigmoid resection was performed. The resected segment showed normal anatomy, with ganglion cells in both Auerbach's and Meissner's plexuses. At the age of 37, the patient was again admitted because of subileus. Plain abdominal *x* ray showed dilatation of multiple small bowel loops with air-fluid levels. She was treated with intravenous fluids and multiple enemas. At 39 years, an episode of gastroenteritis necessitated another admission for intestinal pseudo-obstruction. At 41 years, she experienced her sixth episode of intestinal pseudo-obstruction, which again resolved with conservative measures.

CASE 3

This man was born in 1963. At the age of 14, myotonic dystrophy was diagnosed on the basis of myotonia and positive family history. Both his father and paternal aunt have classical myotonic dystrophy. His paternal grandfather is mildly affected. The patient works in a sheltered environment. At the age of 19 years, he experienced several periods of abdominal pain and evaluation at 20 years showed reduced oesophageal motility and gastritis. Oesophageal manometry did not register a high pressure zone at the level of the lower oesophageal sphincter. Abdominal ultrasound studies were reported to be normal. No diagnosis was made. At the age of 25 years the patient was admitted because of abdominal pain and constipation of one week's duration. The abdomen was distended with high pitched bowel sounds. Plain abdominal *x* ray showed a dilated descending colon. Colonoscopy showed a distended rectum and colon, connected by a collapsed segment of approximately 10 cm. After endoscopy, normal intestinal motility was restored. *X* ray studies of the colon showed dilatation and elongation of the sigmoid. Pressure recording of the anal sphincter was normal. Rectal biopsy showed presence of ganglion cells. A partial sigmoid resection was performed six months later and no abnormalities were noted on histological examination.

CASE 4

This woman was first diagnosed as having myotonic dystrophy at 20 years of age during family studies. She had been admitted as an infant because of hypotonia, respiratory insufficiency, and swallowing difficulties. Her motor and mental development were delayed and she did not learn to read and write during 12 years of special schooling. She is considered to have the congenital form of DM. Since the age of 9 years she has had alternating diarrhoea and constipation with abdominal cramps. No cause was identified during a paediatric examination. At the age of 21 she was admitted to the surgical department because of bilious vomiting and abdominal pains for three days. The abdomen was distended with high pitched bowel sounds. A diagnosis of ileus was made. After 24 hours of conservative treatment, a laparotomy was performed. Both the small and large bowels were distended. No obstruction was found. Her postoperative course was complicated by pneumonia, necessitating artifical respiration for eight days. She was discharged from hospital after four weeks. With cisapride medication, there has been normal daily defecation for six months.

Discussion

In DM, abnormal motility of the oesophagus, stomach, small intestine, colon, and anal sphincter has been reported.[7] Swallowing difficulties are common, as well as disturbances of oesophageal motility which put these patients at increased risk of aspiration.[1] Also common are attacks of abdominal pain accompanied by constipation or diarrhoea caused by reduced colonic motility.[1] However, only a few reports exist of major abdominal problems in DM patients. The patients reported here developed signs and symptoms of intestinal obstruction as a complication of myotonic dystrophy. In case 1, intestinal problems predated significant muscle weakness by 15 years. Reduced intestinal motility is a likely factor that leads to this complication. Furthermore, elongation and distension of the sigmoid colon may have predisposed our patients to volvulus and invagination, and thus contributed to the risk of ileus. Other predisposing factors in our patients were bacterial gastroenteritis and pregnancy. Routine histological examination of resected colon showed no abnormalities in our patients, but special studies were not performed. Yoshida *et al*[8] reported pathological studies in a DM patient in whom a hemicolectomy was performed because of a megacolon. They found normal smooth muscle but marked abnormalities of the myenteric plexus, indicating a possible neuropathic origin of the intestinal motility. However, smooth muscle abnormalities of small and large intestine have been reported by others.[9]

Conservative measures were usually successful in the treatment of episodes of intestinal pseudo-obstruction in our cases. Treatment consisted of restriction of oral intake, intravenous fluids, and multiple enemas or colonoscopy. If abdominal surgery cannot be avoided, care should be taken to prevent the possible complications of general anaesthesia in DM patients,[10] as exemplified by our case 4. Maintenance therapy with prokinetic agents may be considered. Cisapride has been shown to stimulate gastric and colonic motility in DM patients,[11] and was effective in our case 4.

Intestinal pseudo-obstruction appears to be a rare complication of DM but a few published case reports can be found.[1-6] We have seen this complication in three out of 130 patients (2·3%) in the course of genetic linkage studies. In view of the low frequency of this complication it is striking that our cases 1 and 2 are sibs. Another sib pair with prominent gastrointestinal involvement has been described.[6] An interesting model that may explain such clustering of apparently rare complications was recently proposed by Beggs *et al*,[12] who found deletions in the dystrophin gene in three out of 23 patients with a clinical diagnosis of Fukuyama

Complications that have been reported in multiple relatives with DM.

Feature	Family relation	Reference	Frequency in DM
Intestinal pseudo-obstruction	Brother and sister	This report	Low
Dilatation of ureters	2 brothers	19	Unknown
Cardiac conduction disturbance (CCD)	8 affected in 4 DM families with CCD. 22 unaffected in 14 DM families without CCD	23	High[29]
Neuropathy	14/14 members of a single pedigree	20, 21	Common, but less severe[20]
Mitral valve prolapse	9/11 members of a single pedigree	22	30%[32]
Pilomatrixoma	2 sisters, mother, and son	26	At least 4%[26]
	Brother and sister	27	
	4 affected in single pedigree	28	
	Brother and sister	Personal observation	
Normal pressure hydrocephalus	Brother and sister	25	Low[30]
Focal myocarditis	Mother and son	24	Probably low[31]

congenital muscular dystrophy (FCMD). They suggested that the FCMD phenotype in these patients could be explained on the basis of an interaction of heterozygosity for FCMD and hemizygosity for the dystrophin mutation. Similarly, our cases could have a specific genetic susceptibility to intestinal pseudo-obstruction, which is only uncovered by the additional presence of the DM mutation. Interaction of a major gene mutation and the genetic background may explain familial clustering of specific phenotypes in several other disorders,[13-18] and could well turn out to be an important determinant of variable expressivity in inherited disease.

Familial occurrence of specific complications of DM has been reported before[19-28] (table). However, a number of these reports concerned features that may be more common in DM than was originally realised. This is certainly the case for mitral valve prolapse[22 32] and for cardiac conduction abnormalities,[29] and could even apply to pilomatrixomas and ureteral dilatation, since their prevalence in DM patients is not known. The sibs with normal pressure hydrocephalus reported by Christensen[25] were incompletely documented, while a report of focal myocarditis in a mother and son[24] could represent a relatively non-specific inflammatory reaction owing to many possible causes including infection. On the other hand, the finding of markedly decreased conduction velocities in a large family with otherwise classical DM[20 21] may represent an unusual allelic mutation, since all 14 carriers of the DM mutation in this family also had a polyneuropathy.

In conclusion, both allelic mutations of the DM gene proper and unlinked modifying genes may influence the clinical picture in persons with DM. It may be worthwhile to be aware not only of the many possible complications of DM in general, but also to document unusual complications in a given pedigree. Such complications may show a tendency to recur, especially in close relatives.

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