Case report

Disorganised electrical activity in a child with idiopathic intestinal pseudo-obstruction*

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SUMMARY This report presents the findings of investigation of a child with idiopathic intestinal pseudo-obstruction (IIP). Functional abnormalities of the smooth muscle of the gastrointestinal tract were disclosed by electrical recordings from the gut obtained after laparotomy. In vitro analysis of tissue and ultrastructure were undertaken and a possible aetiology of the disorder in this patient based on these findings is presented.

The clinical syndrome of chronic IIP comprises a spectrum of diseases which have in common intestinal obstruction without mechanical occlusion. This functional anomaly may occur secondary to a variety of diseases such as myxoedema, amyloidosis, and scleroderma, but the primary form, termed idiopathic, has no known aetiology. This idiopathic group is itself far from homogeneous. Characteristically there is a primary motor disorder with evident involvement of the small bowel. However motor abnormalities resembling those in achalasia may occur in the oesophagus. Gastric fundal receptive relaxation has been shown to be abnormal in one patient. The myoelectrical activity of the duodenum and colon in four patients with IIP has been reported as normal by one group, but a detailed study of one patient in this laboratory demonstrated absence of electrical control activity in the small intestine except when it was stimulated or during a migrating myoelectrical complex. Hyper-tension in the internal anal sphincter was reported in one patient and another case described had involvement of the colon and rectum only. The smooth muscle abnormality in the gastrointestinal tract may extend to the urinary collecting system with hydroureter and hydronephrosis. It seems likely that the abnormality in both systems is the same, causing a functional disorder of smooth muscles. A corresponding structural disorder of smooth muscle primarily involving the circular muscle coat has been reported. Two cases have been presented in which neurological disease with partial degeneration of neurones in the ganglia of the oesophagus, stomach, and small bowel was demonstrated. In several of the previously mentioned studies, pathology of the neurones was not excluded.

Case history

This report presents the findings of investigation of a child aged 12 months with IIP. The patient was delivered per vaginam to a prima gravida at full term. There was no family history of urogenital or gastrointestinal disease. Hydramnios was present and the urinary tract was investigated in the neonatal period. Hydrenephrosis and hydroureter were demonstrated radiologically but no obstructive lesion identified. Bilateral nephrostomy was performed for relief of oliguria and these spontaneously closed at about 5 months of age. Though urine flowed via the regular route, urecholine was given by mouth and manual expression used to empty the bladder. There was no neurological deficit detected by conventional clinical examination and there were no biochemical abnormalities.

By 6 months of age the child’s weight had reached only 7.5 kg from a birth weight of 5.5 kg. There was a corresponding failure of development

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together with the impaired physical growth. Nausea, vomiting, and constipation were the presenting gastrointestinal symptoms and over the previous two months the child had refused solids.

Examination disclosed gross abdominal distension and weight and length below the third percentile.

INVESTIGATIONS

Barium swallow
The primary peristaltic wave pattered out in mid-oesophagus and the lower oesophagus emptied only occasionally by a peristaltic wave.

Barium meal
The stomach was normal in size but no gastric contractions were present. The stomach emptied by gravity when the patient was turned on his right side.

Small bowel meal
In the duodenum the contractions appeared to be normal in the sense that they propelled barium distally. In the proximal jejunum the contractions were erratic—sometimes they were orad and sometimes caudad. The meal, however, did not seem to go past mid-jejenum. Over a 30 minute period it appeared as if the mid-jejenum were in spasm and acting as an obstruction to the distal movement of contents.

Barium enema
There was a uniform dilatation of the colon without evidence of stricture or distal narrowing to suggest Hirschsprung's disease. Rectal biopsy showed ganglion cells in usual numbers.

IVP
Hydronephrosis, megacystis, and megaureter were demonstrated.

Cystogram
There was a residual urine of 450 ml and no vesicoureteric reflux was demonstrated.

Radionuclide gastric emptying
Eight gastric emptying studies using Coates' method were performed using 113I indium in pineapple juice, which the patient enjoyed. Each study was performed on a separate day and two of the studies, one at the beginning and one at the end, were controls. In the other six tests a single drug was given. The agents used and effects on gastric emptying are summarised in Table 1.

INTERIM MANAGEMENT
During this period of study the clinical management of the child, with which the investigators were not involved, was maintained by the paediatric surgical unit. Nutrition was attempted intravenously via a central venous catheter, but it was evident that this provided inadequate input to allow for growth and development.

A laparotomy was arranged to perform gastrostomy and feeding jejunostomy. At surgery the stomach was of normal size as was the duodenum and proximal 10 cm of jejunum. The remainder of the small bowel was dilated to five times the normal diameter. The distention was gaseous, only a small amount of fluid being present in the small bowel. The colon was similarly distended by gas. The surgeon plicated all the distended small bowel hoping to increase the propulsive effects of peristalsis (Fig. 1). A 50% overlap of the bowel wall was produced reducing the lumen to approximately normal size. A gastrostomy and jejunostomy were fashioned and a piece of stomach and macroscopically normal jejunum provided for histology, electron microscopy, and in vitro study of muscle strips. A caecostomy was performed to decompress the large bowel. Teflon-coated stainless steel bipolar electrodes were placed suberosally on the stomach (three pairs) and on the duodenum and proximal jejunum (seven pairs) and led out of the abdomen via a Penrose drain. The duodenal pair of electrodes, and the first two pairs of jejunal electrodes were placed on macroscopically normal, uniplicated bowel (Fig. 1). This procedure was undertaken with informed consent from the parents and without implied therapeutic intent and in an attempt to elucidate the mechanism of this child's motility disorder. During the postoperative period electrical records were obtained from the smooth muscle of the stomach and small bowel under resting conditions after food and with drugs. On the 10th postoperative day the electrodes were removed with the drain.

POSTOPERATIVE INVESTIGATIONS
Recordings were made during recovery from anaesthesia (in which atropine and prostigmin were used) and for an additional nine days. The timing of

Table 1 Gastric emptying studies using 113I indium labelled pineapple juice

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose</th>
<th>Gastric emptying at 60 minutes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (saline)</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Tension</td>
<td>80 mg/kg IV</td>
<td>50</td>
</tr>
<tr>
<td>Urecholine</td>
<td>2 mg SC</td>
<td>28</td>
</tr>
<tr>
<td>Metaclopramide</td>
<td>2-5 mg IV</td>
<td>0</td>
</tr>
<tr>
<td>Pentagastrin</td>
<td>6 μg/kg IV</td>
<td>20</td>
</tr>
<tr>
<td>Cerulein</td>
<td>600 ng IV</td>
<td>0</td>
</tr>
<tr>
<td>Control (saline)</td>
<td></td>
<td>10</td>
</tr>
</tbody>
</table>
recordings during the initial period and later when drugs were given was adjusted to minimise interference with the medical and nursing care with which the investigators were not involved. In considering small bowel electrical recordings readings from normal calibre bowel—that is, duodenum and jejunal sites 1 and 2—are compared with those from the dilated bowel—that is, jejunal sites 3 through 6—which was surgically plicated.

**ELECTRICAL ACTIVITY**

Electrical activity was present continuously in the stomach, duodenum, and jejunum in the immediate postoperative period during recovery from anaesthesia and each day thereafter for 10 days. Recordings lasted a minimum of one hour, maximum eight hours.

**Stomach**

Electrical control waves were present at all three stomach electrode sites with identical frequencies of 3-8 cpm. The gastric control waves were phase locked with a distal direction of phase lag. Response potentials were not seen at any time even after food or drugs.

**Duodenum and jejunum**

Electrical control activity (ECA) was present at all electrode sites in the duodenum and the jejunum. The mean ECA frequency decreased from the duodenal electrode site to jejunal electrode site 4 and then increased up to jejunal electrode site 6 as shown in Fig. 2.

Two different patterns of ERA were observed. At the duodenal electrode and at the proximal jejunal electrodes B₁ the ERA was intermittently present only on a part of the control wave cycle and lasting less than 50% of its duration; this was similar finding to that in normal adults.

At the jejunal electrodes B₃ to B₆ the ERA appeared as a continuous burst lasting throughout the control wave cycle for periods ranging from eight seconds to 40 minutes with no recognisable patterns.

At electrode site B₂ ERA patterns were similar to B₁ but occasional prolonged patterns were observed as on electrodes B₃ to B₆.

**Drugs**

When ileus had resolved clinically drugs were given (four to 10 days postoperatively) each on a different

**Fig. 1** Summary of operative techniques. The siting of electrodes in stomach, S₁, S₂, S₃, duodenum, and jejunum B₁—B₆ is shown. The plicated small bowel distal to the second jejunal electrode is illustrated and the nature of the plication. Biopsies for in vitro analysis were taken from the jejunostomy and gastrostomy sites. S₃ was 3 cm and the single pair of duodenal electrodes 4 cm from the pylorus. In the jejunum the siting of electrodes B₃ in centimetres distal to the jejunostomy is indicated by numbers enclosed with ellipses. Inter-electrode distances are similarly indicated. The biopsies used for in vitro analysis were taken from the T shape to ensure orientation so that longitudinal and circular muscle strips could be investigated for their properties so avoiding spiral strips of muscle.
day (except antagonists and meperidine given for pain). None of the following agents had any noticeable effect on ECA or ERA, meperidine 10 mg intramuscularly, prostaglandin F₂=30, 60, 90 µg/h, Buscopan 2 mg intravenously × 2, Tensilon 80 µg/kg, noradrenaline 1-0-2-4 µg/min and indomethacin 6-5 mg suppository, atropine 100 µg/kg intravenously, except possibly urecholine 2 mg subcutaneously, which might have provoked ERA but this was given within one hour after meperidine (for analgesia). Urecholine given alone on another occasion did not alter the above described patterns and ERA or ECA frequencies.

ELECTRICAL PACING
On the sixth postoperative day, electrical pacing of the stomach and small bowel was attempted.

Stomach
Pacing the middle pair of electrodes at a frequency of 5/min, 200 ms pulse duration, and pulse strength 12 V had no effect.

Small bowel
Similar pacing applied to the pair of electrodes on the first part of the duodenum at a frequency of 12-5 cpm, pulse strength 12 V, and 100 ms pulse duration did not change the frequency of the electrical control wave in the jejunum (Fig. 3). However, with a pulse duration of 200 ms there was entrainment of the frequencies of the first and second jejunal electrodes to the stimulating frequency of 12-5 cpm from undriven frequencies of 11-4 and 11-0 respectively. Pacing at the third jejunal electrode site was ineffective. No changes were noted in response potentials during electrical stimulation.

In vitro studies
Methods
Pieces of antrum and jejunum were placed in oxygenated Krebs-Ringer solution at 21°C. Strips of tissue (approximately 2 cm × 0-5 cm) were removed immediately and, after 24 hours of oxygenation at 20°C, used for in vitro analysis. Strips of circular and longitudinal muscle were studied in duplicate. A piece of jejunum was placed in Krebs-Ringer solution at 20°C and from this piece two circular and two longitudinal strips were studied immediately. All strips were mounted vertically under 1-0 g tension in a bath containing 20 ml of oxygenated (95% O₂, 5% CO₂) Krebs-Ringer solution at 37°C with field stimulation (40 V, 10 Hz, 0-1 to 5 ms), an arrangement similar to that of Molnar et al. Normal stomach, jejunum, and ileum removed at operation were studied using the same technique. Effects of agents on contractions were assessed semi-quantitatively by summing the amplitudes of contractions over a representative period of one minute before and after drug administration. Drugs were added to the bath and concentrations were expressed as micrograms of the salt per millilitre of bath.

Results
SPONTANEOUS ACTIVITY
Gastric antral strips showed no spontaneous activity, whereas all circular and longitudinal muscle strips from jejunum contracted spontaneously (0-1-0-6 g). The average frequency over five minutes of contraction of the jejunal muscle strips was 9-6 ± 0-6 SE, while the maximum frequency over 30 second intervals was 13-5 ± 0-7 SE. Absence of spontaneous activity was seen in normal gastric antral muscle (removed at partial gastrec-
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tomy). Spontaneous contractions of slightly lower frequency were seen both from normal adult jejunum and ileum.

**RESPONSES TO STIMULANTS, RELAXANTS, AND TRANSMURAL FIELD STIMULATION**

These are summarised in Table 2.

The responses obtained from the patient's tissue were qualitatively the same as those obtained from normal adults previously reported by us and by Bennett and Stockley. Structurally (including EM) the smooth muscle was normal.

**Discussion**

The motility disorders in this patient with IIP can be summarised as follows: (1) poor oesophageal peristalsis; (2) poor gastric emptying, coupled with absence of normal electrical response activity (ERA), but gastric muscle was capable of some response to an anticholinesterase (edrophonium); (3) normal frequency gradient as far as electrode 4 distal to which frequency gradient is reversed—consistent with the radiological observation of both oral and caudal contractions; (4) a prolonged occurrence of ERA throughout the control wave cycle on many control wave cycles in mid-jejunum; (5) no migrating myoelectric complexes.

Some of the above disorders have been shown in other cases of IIP—for example, the oesophageal peristalsis and slow gastric emptying. But other disorders of ECA and ERA are peculiar to this patient and are even in contrast with those we have reported in another patient. That patient showed complete absence of ECA and hence ERA, except during a migrating myoelectric complex, when an ECA was present along with a normal ERA pattern. However, the symptoms of pseudo-obstruction in the present case can be explained by the disordered motility we observed. Radiological studies indicated the presence of normal propulsive contractions in the duodenum. In the proximal jejunum, contractions occurred but they propagated in both directions and also they were not effective in moving the contents beyond a certain point in mid-jejunum which seemed to act as an obstruction. The contents were propelled to this point and then retropelled as if often seen in the antrum shortly after a meal. The mid-jejunum showed no mechanical obstruction but there were long duration sustained contractions. Our recordings with serosal electrodes can explain both of these disorders. The retrograde contractions occurred because of the presence of high frequency control waves in the jejunum which were driving proximal lower frequency control waves. As the control wave determines the frequency of contractions these would occur from distal to proximal and luminal contents would tend to move in the oral direction.

The presence of response potentials through most of the control wave cycle in mid-jejunum could explain functional obstruction if tonic contractions of the gut are the result. Normally, the response potentials are present over only a part of the control wave cycle—that is, during the depolarised state. Thus, the muscle has time to relax in between two successive depolarisations. But if the response potentials persist throughout the cycle, then the muscle will remain in the contracted state resulting in a non-propagating segmental contraction. This sustained contraction would act as an obstruction blocking transit, even if there were normal distally moving contractions proximal to it. We have observed a similar pattern of prolonged ERA in the adult human colon and called this the continuous electrical response activity. We have also shown that in the

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**Table 2** Results of in vitro responses to stimulants, relaxants, and effect of transmural field stimulation

<table>
<thead>
<tr>
<th>Stimulants*</th>
<th>Stomach</th>
<th>Normal adult</th>
<th>Jejunum</th>
<th>Normal adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylcholine</td>
<td>Contraction</td>
<td>Inhibition</td>
<td>Contraction</td>
<td>Inhibition</td>
</tr>
<tr>
<td>Carbamoylcholine</td>
<td>Contraction</td>
<td>Inhibition</td>
<td>Contraction</td>
<td>Inhibition</td>
</tr>
<tr>
<td>Serotonin</td>
<td>Contraction</td>
<td>Inhibition</td>
<td>Contraction</td>
<td>Inhibition</td>
</tr>
<tr>
<td>DMPP</td>
<td>Contraction</td>
<td>Inhibition</td>
<td>Contraction</td>
<td>Inhibition</td>
</tr>
<tr>
<td>Noradrenaline (1–5 µg/ml)</td>
<td>Inhibition</td>
<td>Inhibition</td>
<td>Inhibition</td>
<td>Inhibition</td>
</tr>
<tr>
<td>Isopropyl noradrenaline (0.1–1 µg/ml)</td>
<td>Inhibition</td>
<td>Inhibition</td>
<td>Inhibition</td>
<td>Inhibition</td>
</tr>
<tr>
<td>Transmural field stimulation (0.2 – 1.0 ms, 2–10 Hz)</td>
<td>On contraction and small off or on relaxations no off response</td>
<td>Same</td>
<td>On contraction and small off or on relaxations no off response</td>
<td>Same</td>
</tr>
<tr>
<td>40V for 10–15 s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*All blocked by atropine except serotonin which was partly blocked.
human colon this type of activity results in a tonic segmental contraction. In this patient, the pattern of excessive response potentials was frequently present but the site varied. Sometimes this pattern occurred over one electrode and at others over several electrodes. Thus the length of segmental contractions and the location of the obstruction varied. Although impaired gastric emptying may have contributed to the symptoms of pseudo-obstruction it is uncertain whether this was a primary event or secondary to jejunal obstruction. The impaired oesophageal function would appear to be a primary phenomenon common to patients with IIP. The absence of MMCs may have been due to excessive and almost continuous presence of ERA in jejunum, simulating the fed condition.

No single mechanism can account for these events. Inadequate vagal cholinergic input could account for the poor activity of oesophagus and stomach. Since cholinergic agonists were not very effective in restoring gastric emptying there may have been failure of the muscle to respond rather than failure of neuronal activity. However, in vitro studies showed that both gastric and jejunal strips of longitudinal and circular muscle were pharmacologically normal. This suggests that the site of pathophysiology is proximal to the muscle and to the efferent nerves activated in vitro.

While essential in vitro control data are lacking, the results suggest a neurogenic rather than myogenic abnormality. A neural disorder which could involve failure of the non-adrenergic inhibition is suggested, as additional and excessive ERA might result from such a failure.

The disorders of electrical activities in this patient are in contrast with those of another IIP patient on whom we have reported earlier. In our previous patient IIP resulted from a small bowel the hypo-activity of which was due to the complete absence of ECA except during an MMC or after a cholinergic stimulant. In this patient the pseudo-obstruction resulted from a hyperactive bowel resulting in non-propagating segmental contractions and antiperistaltic contractions.

Idiopathic intestinal pseudo-obstruction has been shown to result from a diverse number of causes. Our studies show that these causes could manifest in a diverse number of ways resulting in a motility disorder. The clinical intervention in these cases is limited by our understanding of the functioning of myogenic, neurogenic, and hormonal control systems and the interactions between them. In view of recent reports that pathological changes in IIP may involve destruction of circular muscle or neuronal damage it is important to emphasise that smooth muscle in this patient was normal both by light microscopy and by electron microscopy with no evidence of neuronal damage. Thus it may not be safe to assume that the functional failures are always secondary to the structural changes observed to date.

We gratefully acknowledge gift of cerulein from Adria Laboratories USA.

References


