SHORT REPORTS

Presentation and incidence of Hirschsprung’s disease

Hirschsprung’s disease is a well recognised cause of obstruction in neonates, but considerable delay may still occur in diagnosing it in older children. In south east Scotland (Lothians, Borders, and Fife) all children noted to have constipation from the first year of life who fail to respond to conventional treatment are now investigated by anorectal manometry and rectal mucosal biopsies. Thus 17% of these patients have been found to have Hirschsprung’s disease, which is a dramatic increase in the incidence of diagnosis, particularly in older children and those with ultrashort segment disease.1 As the exact incidence and pattern of presentation of Hirschsprung’s disease in the United Kingdom are unknown2 these findings prompted a study of the local population to establish the incidence of the disease, its familial occurrence, and its pattern of presentation within the community.

Patients, methods, and results

We reviewed the case records of 103 patients with Hirschsprung’s disease born in south east Scotland during the 30 years 1953-82. We obtained additional information from the patients’ families and their general practitioners. The length of aganglionic segment was described as ultrashort (distal third of rectum or less) in 15 patients; short (rectum or rectum and sigmoid colon) in 69; and long (proximal colonic disease) in 19. There were 82 male and 21 female patients, a ratio of 4:1. Apart from five patients with total colonic aganglionosis, in whom the sex ratio was 1:5:1, there was no variation in the sex incidence with varying lengths of aganglionic bowel. The table shows the age at diagnosis.

<table>
<thead>
<tr>
<th>Age at diagnosis of Hirschsprung’s disease</th>
<th>Year of birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis</td>
<td>Total</td>
</tr>
<tr>
<td>1953-67</td>
<td>27 28 55</td>
</tr>
<tr>
<td>1967-82</td>
<td>6 16 24</td>
</tr>
<tr>
<td>5-14 years</td>
<td>6 18 24</td>
</tr>
<tr>
<td>Total</td>
<td>40 63 103</td>
</tr>
</tbody>
</table>

The 103 patients came from 98 families, giving a family incidence of 6%. Of 238 siblings traced, five had the disease, giving an incidence of 2%. From the reports of the Registrar General in Scotland for the first 25 years of the study we established the incidence of the disease in this geographical area as being one in 4500 live births (99/445 000).

Comment

This is the first regional study of Hirschsprung’s disease in the United Kingdom. Previous genetic studies have recorded information on patients drawn from a wide area with poorly defined populations.3 We had an advantage in that patients were referred to a single surgeon (WGS) from a well defined geographical area; this offered the ideal basis from which to study the pattern and incidence of a disease. With an established incidence of one in 4500 live births, 140 new cases of Hirschsprung’s disease may be expected each year in the United Kingdom. With an established family incidence of 6%, it is essential that at the time of diagnosis an accurate family history is obtained so that potential patients may be traced.

In 1964 Bentley first described ultrashort segment Hirschsprung’s disease,4 which is often diagnosed late in older children who have previously been described as encopretic or suffering from psychological problems.5 Indeed, almost half of the patients in this series in whom the disease was diagnosed late had ultrashort segment disease. Awareness that some of these patients may have a surgically correctible lesion permits referral for initial investigation by anorectal manometry and if indicated rectal mucosal punch biopsy. Histochemical analysis of the biopsy sample for acetyl cholinesterase yields rapid confirmation of the diagnosis.6 After the introduction of these measures the disease will be diagnosed in an increased number of patients, but the table shows that this increase will occur mainly in older children. Most patients should still be diagnosed as neonates, but an awareness of the problem in older children allows earlier referral for diagnosis and treatment.


(Accepted 31 August 1983)

Intestinal perforation associated with osmotic slow release indomethacin capsules

Patients presenting with bleeding or perforation due to a peptic ulcer have often recently taken non-steroidal anti-inflammatory drugs.1 The introduction of a new formulation of indomethacin (Osimosin) designed to release the drug in the small intestine should decrease the risk of these complications, but it may result in complications affecting the small bowel and colon. We describe two patients who suffered such complications.

Case reports

Case 1—A 70 year old man had been taking ordinary indomethacin tablets 25 mg three times daily for 10 years. Two weeks before admission with severe diarrhoea he had been changed to slow release indomethacin trihydrate 105 mg twice daily. He had had a gastrectomy for duodenal ulcer in 1957. On admission he was found to be mildly dehydrated, and was initially diagnosed as having infective diarrhoea. Faecal cultures, however, were negative for pathogens, sigmoidoscopic appearances were normal, and his condition appeared to resolve with rehydration. Three days after admission he became confused. He did not complain of abdominal pain but his abdomen was found to be rigid. He was pyrexial, not shocked, and maintained a constant pulse rate of 110 beats/minute. X ray examinations of the abdomen showed copious free gas. At operation he was found to have multiple haemorrhagic perforating ulcers of the terminal ileum. Adjacent to the perforation were two capsules of slow release indomethacin. A further capsule in the ascending colon was adjacent to a small area of ulceration. Cultures of faeces and mesenteric lymph nodes were negative for Salmonella spp. After operation he developed further ulceration and perforation of the ileum and colon, from which he died two days later. At necropsy a further capsule of slow release indomethacin was recovered from the abdominal cavity.

Case 2—A 79 year old woman with a longstanding history of diverticular disease was admitted with an exacerbation of abdominal pain. She had been taking benorylate 4 g twice daily for osteoarthritis, and two weeks before admission this had been supplemented by slow release indomethacin trihydrate 105 mg twice daily. On examination she was pyrexial with a pulse rate of 90 beats/minute and a blood pressure of 140/90 mm Hg. Her abdomen was diffusely tender and almost rigid. Bowel sounds were absent. Laboratory findings were: haemoglobin 12·1 g/dl, while blood cell count 6·7 x 1012/l, and serum amylase 105 IU/l (normal 70-300 IU/l). X ray examination of the chest and abdomen showed nothing abnormal. Abdominal paracentesis showed a purulent peritonitis. Metronidazole 500 mg and cephalizin sodium 1 g were instilled via the paracentesis catheter, and she was rehydrated with intravenous fluids. At operation she had faecal peritonitis. There was a 4 mm
Convolusions after self poisoning with zimeldine

Zimeldine is a new antidepressant that is chemically unrelated to the tricyclic and tetracyclic antidepressants. Information on its effects in acute overdose in humans is scanty. We report on two patients in whom zimeldine overdose caused grand mal convulsions.

Case reports

Case 1—A healthy 32 year old man was admitted to hospital four hours after ingesting about 2.5 g zimeldine and six pints of beer. He denied any specific complaints and was fully conscious with no neurological abnormalities. His pulse rate was 100 beats/minute and blood pressure 110/65 mm Hg. He refused gastric lavage, and emesis was induced with ipecac syrup. Four and a half hours after taking the tablets he had a generalised convulsion. Diazepam (5 mg) was given intravenously, and thereafter his recovery was uneventful.

Case 2—A 37 year old woman presented four hours after ingesting about 2 g zimeldine. She had not ingested any other drugs or alcohol. She had been treated with 100 mg zimeldine daily for several months for depression. The overdose made her feel sleepy, but on examination she was fully conscious and orientated. Fine jerky nystagmus was noted on lateral gaze, but she showed no other neurological abnormalities. Her pulse rate was 92 beats/minute and blood pressure 120/75 mm Hg. Gastric lavage was carried out, and five hours after ingestion she had a generalised convulsion lasting 45 seconds associated with incontinence of urine. No treatment was given, and her subsequent recovery was uneventful.

Neither patient had a personal or family history of epilepsy. On admission plasma electrolyte concentrations and results of liver function tests were normal. Electrocardiograms in both patients showed prominent U waves but were otherwise unremarkable. The figure shows serial plasma concentrations of zimeldine and norzimeldine, measured by gas liquid chromatography.

The peak zimeldine concentrations of 4.8 mg/l in case 1 and 4.7 mg/l in case 2 were seen on admission and declined thereafter with half lives of 3.6 and 4.4 hours respectively. Norzimeldine disappeared from the plasma much more slowly. One patient (case 1) had plasma ethanol concentration of 1.9 g/l of admission, but screening for anticonvulsants, benzodiazepines, barbiturates, paracetamol, salicylates, and tricyclic antidepressants yielded negative results in both patients.

Comment

Zimeldine is a derivative of the antihistamine pheniramine and appears to act by selectively inhibiting uptake of serotonin (5-hydroxytryptamine) in the central nervous system. The demethylated metabolite, norzimeldine, is responsible for at least part of its pharmacological activity. Therapeutic doses seem to cause only minor anticholinergic effects, but attention has recently been drawn to serious adverse reactions including liver damage, neurotoxicity, and convulsions.

Zimeldine overdose in man has been reported on only three occasions. One patient with a family history of epilepsy had a grand mal convulsion after ingesting 1.7 g together with alcohol; and drowsiness and vomiting were the only abnormalities noted in a patient who ingested 2.8 g zimeldine together with alcohol. A third patient showed no toxic features after taking 1.75 g zimeldine together with deoxypropoxyphene and alcohol.

The maximum plasma zimeldine concentrations after a single dose of 200 mg are about 0.2-0.4 mg/l. The peak concentrations in our patients were at least 10 times higher, confirming substantial overdoses. Despite this, convulsions were the only complication noted.

The manufacturers are aware of 27 possible cases of zimeldine overdose, but most were not confirmed by laboratory analysis and other drugs were not excluded. Three patients had tremor or twitching, and two had convulsions, but coma seemed to develop only with concomitant ingestion of depressants of the central nervous system. One patient developed ventricular tachycardia, which could reasonably be attributed to thioridazine rather than zimeldine. Five patients regularly taking zimeldine and other drugs died outside hospital. Three had taken zimeldine overdoses, but the data are insufficient for death to be attributed to zimeldine alone. In the two other patients there was no evidence of an overdose of any drug. The limited reliable information

Comment

Indomethacin is a potent inhibitor of prostaglandin synthesis, and it can cause gastrointestinal disturbances including haemorrhage. The incidence of haemorrhage, and its severity, seems to be related to the dose. In our patient, who had a perforation at the time of admission, indomethacin was stopped and she recovered without sequelae.