SHORT REPORTS

Peptic ulcer in Reye's syndrome

The clinical and pathological features of Reye's syndrome are well known,[1] but to our knowledge neither gastric nor duodenal ulcers have been reported as a complication. In two recent cases of the syndrome at this hospital a perforated gastric and a perforated duodenal ulcer were found at necropsy. The ulcers were not suspected and may have contributed to the deaths of both children.

Case reports

Case 1—A 6 six month old baby girl presented with tachypnoea after a flu-like illness lasting five days that had been treated with salicylates. On admission she was fully conscious and had a generalised purpuric rash. Meningococcal septicaemia was suspected initially, but 19 hours after admission she developed generalised convulsions with episodes of decerebrate rigidity. Reye's syndrome was suspected and this was confirmed by results of investigations. She had raised serum transaminase activities (alanine transaminase 300 IU/l, aspartate transaminase 104 IU/l, and creatine phosphokinase 600 IU/l) and raised blood ammonia concentration (158 μmol/l (927 pg/100 ml). Blood and cerebrospinal fluid glucose concentrations were low (1·6 mmol/l (29 mg/100 ml) and 0·6 mmol/l (11 mg/100 ml) respectively). Haemoglobin concentration was 12·4 g/dl with 538 v 10^9/l platelets. Prothrombin time was raised at 1·7 seconds (control 1 second) as was cephalin-kaolin time at 120 seconds (normal range 38-48 seconds). Computed tomography showed cerebral oedema. She was treated with dexamethasone, mannitol, intermittent positive pressure ventilation, and high doses of phenobarbitone. She had frank bleeding from both upper and lower gastrointestinal tract and oozing from venepuncture sites. She needed repeated administrations of clotting factors concentrate. Renal failure was treated by continuous peritoneal dialysis. She died from cardiac arrest after nine days in coma. At necropsy she had enlarged fatty liver, cerebral oedema, bronchopneumonia, perforated gastric ulcer, and renal vein thrombosis.

Histological examination showed widespread microvesicular fatty change of the liver and acute mucosal erosion of the stomach with inflammatory debris and blood forming the floor; adjacent submucosal blood vessels were dilated. Appearances were in keeping with acute stress erosion of gastric mucosa.

Case 2—A 9 year old boy presented to another hospital with severe abdominal pain, weakness, and lethargy after a flu-like illness lasting three days. He was treated with intravenous fluids, salicylate suppositories, and intramuscular diazepam. He was transferred the following day as results of investigations suggested Reye's syndrome. Blood ammonia concentration was raised (288 μmol/l (1690 pg/100 ml)), haemoglobin concentration was 13·4 g/dl with 370×10^9/l platelets. Glucose concentration was 1·5 mmol/l (27 mg/100 ml) in blood, and 1·8 mmol/l (32·4 mg/100 ml) in cerebrospinal fluid. Prothrombin time was raised (2·3 seconds) as was cephalin-kaolin time (60 seconds). On admission to this hospital he was drowsy, confused, and irritable. He did not have any gastrointestinal bleeding. Computed tomography confirmed cerebral oedema and an intracranial pressure monitor was inserted. He was treated with intravenous Mannitol and intermittent positive pressure ventilation was started to induce hypocapnia. Clinical brain death occurred 14 hours after admission when intracranial pressure suddenly spiked from 10 to 40 cm of water pressure. He died from cardiac arrest 36 hours after admission. Necropsy showed an enlarged pale fatty liver, left sided lobar pneumonia, cerebral oedema, large perforated ulcer in the first part of the duodenum anteriorly with secondary peritonitis. Histological examination showed hepatic appearances in keeping with Reye's syndrome, and examination of sections of the duodenum confirmed acute peptic ulceration.

Comment

Gastrointestinal bleeding is a recognised complication of Reye's syndrome and has been attributed to the associated bleeding diathesis,[2] but in view of these cases bleeding ulcers must also be considered. Peritonitis from an unsuspected perforated ulcer, may have contributed to death in case 2. Recognition of this complication is difficult in the presence of coma.

Peptic ulcers in Reye's syndrome may have many causes and it is difficult to evaluate their relative importance. Raised intracranial pressure, which is a feature of Reye's syndrome, can cause secondary peptic ulcers. Both steroids and salicylates are ulcerogenic and may have been important in these cases. Breheny *et al*[3] advocated the use of cimetidine to prevent stress ulcers in Reye's syndrome but cimetidine has not been shown to prevent the development of peptic ulceration in stressed patients. Furthermore, the use of cimetidine may be harmful as it has been implicated as a cause of interstitial nephritis and polymyositis.[4] Ranitidine, a newer H_2 antagonist, has shown some promise in preventing stress ulcers and may be a better alternative.

The value of Dexamethasone in controlling raised intracranial pressure must be weighed against its possible ulcerogenic role, as the cases reported suggest an association between Reye's syndrome and peptic ulceration. We recommend prophylactic antacids[5] in the routine management of Reye's syndrome, and suggest that doctors should be alert for clinical signs of peptic ulceration.

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Treatment of cutaneous leishmaniasis by curettage

No particular method of treating cutaneous leishmaniasis has been established as indisputably superior to the many others. Treatment has included local infiltration of emetine hydrochloride, mepacrine hydrochloride, and berberine sulphate; oral dehydroemetine or metronidazole; coned infrared irradiation of lesions; topical solid carbon dioxide; diathermy; parenteral pentavalent antimonials; and old fashioned scraping.[1-3]

Cutaneous leishmaniasis due to *Leishmania tropica* occurs widely in the tropical and subtropical areas of Europe, Asia Minor, and Asia. The increased population of irrigated desert areas and the presence of large numbers of expatriate workers in affected regions increase the immediate importance of the disease to a wider range of physicians, and the problem is compounded by the unsatisfactory nature or toxicity of some of the recommended treatments. The skin lesions, granulomatous nodules developing central necrotic ulcers that become secondarily infected with pyogenic bacteria, result from bites by infected sandflies or the transference of Leishman-Donovan bodies from an established sore to a different site by scratching or other contact. Neglected ulcers commonly grow to 0·5-3 cm in diameter and, after an interval of months to years, heal with considerable scarring, which is particularly noticeable on the face. I have assessed the efficacy of simple surgical curettage as the sole treatment for this disease.

Patients, methods, and results

Curettage was performed in 50 patients (39 male, 11 female; estimated age range three to 70 years, mean 28) with a total of 120 lesions who attended this hospital, near the Afghan border of Pakistan, between October 1982 and March 1983. Most lesions (67) occurred on the lower leg, the rest being scattered over the face, neck, arms, and thighs. Forty four of the 50 patients were Afghans, who are a minority group in the area. This confirmed the impression that they are more susceptible to cutaneous leishmaniasis than

the indigenous Pathans are. Diagnosis was made clinically and by examination of Giemsa stained smears of exudate.

Sores were cleaned, infiltrated with 2% lignocaine, and then curetted with removal of all raised inflamed edges. This was a rapid procedure (total procedure time four to 10 minutes, mean 6·8 minutes) and well tolerated, with only three patients complaining of pain. The 10 inpatients and 40 outpatients had their dressings changed daily after cleaning with calcium hypochlorite solution. The outpatients' wounds were assessed weekly, though this assessment was reliable in only 20 outpatients. This gave a total of 30 patients (78 lesions) in whom healing time was recorded accurately. The table shows healing times of the 78 lesions, taken as the time to complete re-epithelialisation of the granulating curetted wound.

Time taken for healing after curettage

Size of lesion	No of sores healing within:				Total
	2 weeks	3 weeks	4 weeks	>4 weeks	
Any size	12	34	27	5	78
Up to 1·5 cm diameter	12	27	6		45

Comment

This small study showed that after simple curettage alone 73 out of 78 adequately observed lesions healed within four weeks. Thirty nine out of 45 smaller sores (up to 1·5 cm diameter) healed within three weeks. These results are comparable with those achieved using any other method of treatment. This definitive treatment is rapid and requires only one attendance, which is a distinct advantage in an unreliable population. The cosmetic result, particularly for facial sores, is remarkably good, with none of the disfigurement that ensues from chronic, self limiting tissue destruction. Cutaneous leishmaniasis is becoming an increasingly important problem, particularly throughout the Middle East and wherever more widespread habitation within desert areas is promoted by irrigation schemes. With increasing ease of travel, and with many expatriates working in such areas, patients with this condition are likely to be seen in Britain. Curettage, an old and simple treatment that is effective, may be preferable to using the toxic parenteral pentavalent antimonials recommended in standard modern textbooks.[4]

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Implications of diagnostic delay in Duchenne muscular dystrophy

Duchenne muscular dystrophy is the commonest of the childhood muscular dystrophies. Inheritance is X linked. Progressive proximal muscle weakness in early childhood leads to loss of ambulation between 8 and 12 years and death in the late teens or early 20s. Newborn screening programmes have been undertaken elsewhere[1] to ensure early diagnosis of sporadic cases and counselling of families at risk. British paediatricians, however, have largely taken the view that preclinical detection of an incurable disease is not justified.[2 3]

The greater availability of genetic counselling together with more precise methods of detection of carriers[4] will in the future greatly reduce the number of second cases in known Duchenne families. Where second cases do occur they will increasingly be due to births before the diagnosis of the first affected boy.

We report a study of 34 boys with the disease from 16 families, each with two or more affected boys and none with a diagnosed case in an earlier generation.

Methods and results

The families were drawn from 35 kindreds seen throughout Britain as part of a genetic linkage analysis using DNA restriction fragment length polymorphisms to study the disease locus[5] and develop more accurate methods of carrier detection.[4] For each affected boy details of age at onset, presentation and diagnosis were collected.

Of 18 families with two or more affected boys in a sibship and no known case in a previous generation, clinical details were available in 16. The table gives the results for 34 affected boys from the 16 sibships. Among the 16 families, 10 had been incorrectly diagnosed, one mother had not been counselled, and five had not sought medical attention at the time of conception of the affected brothers.

Clinical details of 34 affected boys from 16 sibships

Family	Sib	Date of birth	Mode and age of presentation (years)	Age at diagnosis (years)
1	1	15/5/66	1-2, toe walking, Achilles tendon lengthening age 5	8
	2	29/8/67	Waddle*	7
	3	11/5/73	Raised CK activity*†	1-2
2	1	1965	Abnormal gait, unable to run age 4	9
	2	1973	*†	Raised CK activity at age 1
3	1	27/3/71	Gait problems, unable to run age 4½	7
	2	5/5/76	*	Raised CK activity age 2
4	1	11/2/68	Walking on toe age 2, clumsy, orthopaedic referral age 4	>3 (two weeks before birth of 2nd child)
	2	3/1/72	*†	1 month
5	Twins‡	13/7/65	Excessive falling, abnormal gait, age 4	6
	2	30/7/70	*†	1, raised CK activity
6	1	7/9/72	Delay in walking age 2	5
	2	2/2/75	*	1-2, raised CK activity
7	1	2/2/60	Tightening Achilles tendon age 4-5	10
	2	25/10/62	Abnormal gait, unable to climb age 4	7-8
8	1	28/4/65	Gait problems age 2	3
	2	7/11/68	*†	6 months, raised CK activity
9	1	4/9/63	Falling excessively, flat footed age 4	9
	2	10/1/69	Uncertain†	4, raised CK activity
	3	20/10/71	Uncertain†	6, raised CK activity
10	1	1974	Walking poorly, falling age 4-5	4½
	2	1976	*	2, raised CK activity
11	1	27/12/61	Psychomotor retardation age 2½	9
	2	5/6/63	Psychomotor retardation, gait problems age 3-4	7
12	1	8/11/65	Psychomotor retardation age 2	7
	2	2/12/68	Gait problems age 3†	4
13	1	29/8/75	Delayed motor development age 1-1½	3
	2	16/12/79	*†	Raised CK activity 1st year of life
14	1	14/1/67	Not sitting up at 9 months, delayed motor development age 1-2	6
	2	2/5/70	*†	3
15	1	14/8/75	Delayed walking age 1½	>4
	2	4/2/80	*†	Raised CK activity at 6 months
16	1	11/6/56	Abnormal gait and walking poorly age 1½	3½-4
	2	7/2/61	*†	3

CK = Creatine kinase.
*Screened because of family history.
†Conceived after misdiagnosis in older affected sibling.
‡Twin boys analysed as one.

Comment

The 16 families studied were representative of those in whom neonatal screening could have prevented the birth of a second affected boy. Nevertheless, 10 of the 16 index patients had been medically examined but not correctly diagnosed and one other mother had not been informed of the genetic implications of the disease, resulting in the conception of 12 further affected boys; hence increased awareness of the disease by practitioners would have a considerable effect. Similarly, Gardner-Medwin[3] reported that in 15 of 24 first cases symptoms developed before the second affected boy was conceived, though it is uncertain how many in that series had been brought to medical attention.