Congenital stenosis and atresia of the jejunum and ileum

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SYNOPSIS The macroscopic and microscopic findings in 12 cases of stenosis and/or atresia of the jejunum and ileum are presented. There was considerable uniformity within the series with overlapping of cases of atresia, stenosis, and gut infarction. An analysis of associated lesions in cases coming to necropsy suggests that the infants were suffering from shock. In nine out of the 12 cases there was evidence of intrapartum asphyxia and in eight cases evidence of retardation of intrauterine growth. It is argued that, since many of the associated complications of pregnancy are known to be of importance in the aetiology of gut infarction in the neonatal period, they are likely to be of aetiological significance in the development of atresia and stenosis of the gut. A review of perinatal deaths shows that gut ischaemia of varying degrees of severity is a common finding at necropsy, being noted in 19 out of 56 cases studied. It is suggested that stenosis and atresia are sequelae of previous gut ischaemia.

There is controversy regarding the pathogenesis of congenital stenosis and atresia of the small bowel. The traditional explanation favoured by Stowens (1966) and Morison (1970) is that atresia and stenosis are caused by a failure of recanalization of the bowel lumen following a developmental stage of obliterative epithelial proliferation. Alternatively, Louw and Barnard (1955) have led the opposing school who suggest that the development of stenosis and/or atresia is secondary to a vascular insult. What may be interpreted as a refinement of the latter proposition is the view that intestinal stenosis/atresia may develop as a consequence of intussusception (Parkkulainen, 1958).

This paper presents the findings in cases of congenital stenosis/atresia of the jejunum and ileum occurring in the United Oxford Hospitals during the 10 years 1962-71. From the changes seen the possible pathogenesis will be suggested.

Material and Methods

The records of the Department of Pathology at the Radcliffe Infirmary, Oxford, were searched for cases of intestinal obstruction in stillbirths and neonatal infants. Those cases where intestinal obstruction was due to volvulus, herniae, intussusception, paralytic ileus, or meconium ileus were excluded.

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Sixteen cases of stenosis or atresia were traced but attention was concentrated on the 12 cases where histological material was available. The older slides were reassessed, fresh sections cut where necessary and stained as thought to be most appropriate.

Details of age, sex, birth weight, gestation, obstetrical history, postnatal progress, age at which symptoms presented, and associated malformations were extracted from the clinical notes and, where applicable, the necropsy reports.

In view of the apparent clinical associations further neonatal necropsy material was studied. This included sections of small bowel from 15 cases associated with preeclamptic toxemia, 12 associated with maternal antepartum haemorrhage, 21 cases with intrapartum asphyxia, and eight cases where congenital cardiac malformations were associated with neonatal death.

Results

A summary of the main findings in the 12 cases is shown in Table I.

MACROSCOPIC FEATURES

Single lesions of the bowel were found in eight of the 12 cases, and multiple lesions were seen in the four remaining cases.

Atresia

In two cases there was at least one site of complete

Case No.	Sex	Gestation (wk)	Birth Weight (g)	Birth Weight Score	Age at Onset of Symptoms	Types of Lesion	Pathology of Gut Lesions	Associated Vascular Lesions (Necropsy Cases Only)	Associated Clinical Findings
1	Male (M)	38	2890	0	2 days	Multiple lesions; atresia with mesenteric defect and multiple stenoses	(1) Fibrous cord with haemosiderin macrophages (2) Granulation tissue and simple mucosa	Intraventricular haemorrhage, bilateral, capillary thrombi	Threatened abortion, old retroplacental clot noted on delivery
2	M	38	3380	0	3 days	Solitary stenotic lesion, discoloured serosal surface	Granulation tissue, haemosiderin simple mucosa	—	Marked foetal bradycardia, meconium in liquor (intrapartum asphyxia)
3	Female (F)	39	2910	0	4 days	Solitary stenotic lesion, discoloured serosa	Simple flattened mucosa, numerous haemosiderin macrophages	—	Rhesus isoimmunization
4	F	40	3360	0	1 day	Collapsed segment preceded by vascular constricting bands proximally	Collapsed segment normal histologically; extensive mucosal ulceration with regenerating mucosa proximally	—	Severe foetal bradycardia (intrapartum asphyxia)
5	F	32	1200	-1	1 day	Diaphragm across jejunum (solitary lesion)	Fibrous tissue in diaphragm	Capillary thrombi; bilateral segmental necrosis of adrenal glands	Preeclamptic toxemia; foetal bradycardia
6	F	36	1800	-1	2 days	Multiple stenoses	Varying pattern; mostly simple mucosa and scarring in stenotic segments	Capillary thrombi	Antepartum haemorrhage; foetal bradycardia
7	M	37	2300	-1	3 days	Solitary stenotic segment near terminal ileum	Granulation tissue and marked scarring of muscularis in stenotic segment	Extensive bilateral segmental necrosis in adrenal glands	Preeclamptic toxemia; foetal bradycardia
8	M	39	2670	-1	1 day	Solitary stenotic lesion with patch of acute necrosis proximally	(1) Granulation tissue and early scarring in stenotic segment (2) Acute full-thickness necrosis	Capillary thrombi Bilateral intra-ventricular haemorrhages Capillary thrombi	Severe foetal bradycardia (intrapartum asphyxia)
9	F	41	2640	-1	1 day	Solitary stenotic lesion	Extensive scarring of muscularis and simple mucosa; arterial intimal plaques	None seen	Foetal bradycardia (intrapartum asphyxia)
10	M	38	2520	-1	3 days	Solitary stenotic lesion; discoloured serosa	Scarred stenotic segment, simple mucosa, numerous haemosiderin macrophages, splitting of muscularis mucosa	—	Foetal bradycardia (Placenta said to be extensively 'infarcted')
11	F	43	2560	-1	1 day	Solitary stenotic segment	Mucosal ulceration and granulation tissue replacement; early scarring	None seen	Transposition of great vessels; ventricular septal defect
12	M	39	1480	-2	2 days	Multiple stenotic segments	Variable pattern (as in case 6)	Scattered capillary thrombi	Preeclamptic toxemia; foetal bradycardia

Table I Summary of main features in cases with atresia and/or stenosis

obliteration of the lumen. The first case (case 1) was associated with a deficiency of the mesentery and the bowel at this point was represented by a fibrous cord. In this case there were other areas of apparent atresia of the small bowel but on histological examination a small lumen could be identified in each of these zones. In the second case the lumen was occluded by a thin diaphragm.

Stenosis

In the remaining 10 cases the bowel appeared narrowed but a lumen could be traced. These lesions were classified as 'stenoses'. In one infant (case 4) two congested, band-like vascular constrictions could be seen proximal to a collapsed, presumably stenotic, segment of bowel (Fig. 1). On opening the bowel it was apparent that the constrictions corresponded

to sharply demarcated, circumferential ulcers, and the adjacent mucosa was granular and oedematous (Fig. 2). In three other cases (2, 3, 10) the stenotic segment and the adjacent bowel wall were noted to be congested and discoloured. In 11 of the 12 cases meconium was noted both proximal and distal to the atretic or stenotic segment of bowel. In one infant (case 8) in addition to an area of stenosis, a zone of complete necrosis of a segment of proximal bowel was present.

Fig. 1 Loop of bowel showing collapsed bowel distally with congested vascular band-like constrictions proximally (arrowed) (case 4).

Fig. 2 Same case as in Figure 1. The vascular constricting bands correspond to circumferential ulcers. Note the collapsed segment of bowel distally (on left) and the coarse rough appearance of the mucosa near the ulcers.

MICROSCOPIC FINDINGS

Atretic segments

The diaphragm noted in case 5 was seen to be made up of loose fibrous tissue with scattered vascular channels, but at necropsy no epithelium was seen. The atretic segment in case 1 was made up of vascular fibrous tissue but abundant haemosiderin-laden macrophages were present.

Stenotic segments

In case 4 (Figs. 1 and 2) the collapsed segment was histologically normal, though the lumen was small. However, as seen in Figs. 1 and 2, areas of ulceration of the mucosa could be seen proximally. The histological features in the ulcerated areas of this case and in the stenosed segments of the other cases were similar with many overlapping features. The changes will be described together as they appeared to belong to a common pattern of lesions related to mucosal destruction and cicatricial repair.

There was extensive ulceration of the mucosa with loss of the lamina propria and its replacement by granulation tissue containing haemosiderin-laden macrophages (Fig. 3). These areas became continuous with others covered by a regenerating flattened cuboidal epithelium spreading over the granulation tissue, producing a mucosal layer devoid of villi and with simple glands (Fig. 4). The muscularis mucosa was scarred and in its most extreme form it was split into two component layers (Fig. 5). Fibrosis of the submucosa spreading into the muscularis propria was seen in all cases but extensive scarring of the muscle coat was a feature in only two

Fig. 3 Case 4: ulcerated area of mucosa corresponding to a vascular constriction. Note the mucosal loss and destruction of the muscularis mucosa and the oedema of the adjacent mucosa (cf Fig. 2). Haematoxylin and eosin (H & E) $\times 160$.

Fig. 4 Case 6: the mucosa in this stenotic segment is extremely simplified. Note the regenerating unilayered epithelium on the right, and the extensive scarring of all layers of the bowel wall. Lendrum's Martius Scarlet Blue (MSB) $\times 128$.

Fig. 5 Case 10: extensive scarring of the muscularis mucosa is seen with splitting of the structure into two component layers. Note the haemorrhage in the lamina propria, and the simple mucosal pattern. Masson's trichrome $\times 120$.

cases in this series. In three cases (6, 8, 12), zones of mucosa devoid of villi were seen in otherwise normal segments of bowel (Fig. 6) suggesting previous minor episodes of mucosal loss.

In four of the specimens removed at laparotomy patchy areas of acute haemorrhage into the lamina propria were seen (Fig. 5). It is possible that this represents the earliest stage in the evolution of the lesions described, though the probability of operative trauma could not be excluded.

In only one infant (case 9) was there any definite structural abnormality of the vessels in the bowel wall. Here there was obvious intimal thickening of several muscular arteries in the submucosa (Fig. 7), suggesting previous thromboembolism.

Lesions of other organs at necropsy

Eight of the 12 patients died and at necropsy segmental necrosis of the adrenal glands (deSa and Nicholls, 1972) was demonstrable in two cases (5 and 7). In a further two cases (1 and 8) bilateral intra-ventricular haemorrhages were found. In a re-assessment of the slides of all eight cases scattered capillary thrombi were demonstrable in six (cases 1, 5, 6, 7, 8, 12), with the adrenal cortical capillaries, hepatic sinusoids, vasa rectae, and peritubular capillaries of the kidney, being the commonest sites.

ASSOCIATED CLINICAL FACTORS

Birth weight score

Only four infants had a birth weight score (Butler and Alberman, 1969) of 0 (within 1 standard deviation).

Fig. 6 Case 12: an area of mucosa devoid of villi (arrows) in bowel near zone of stenosis. This may indicate previous mucosal loss. H & E $\times 120$.

Fig. 7 Case 9: intimal plaques are clearly shown in this muscular artery in the submucosa near a stenotic segment. Picro-Mallory, $\times 600$.

tion of the mean for gestation). Seven had a score of -1 (between 1 and 2 standard deviations below the mean for gestation), and the remaining infant had a birth weight score of -2 (greater than 2 standard deviations below the mean for gestation). Table I suggests a high mortality in infants of a low birth weight for gestation.

Sex distribution

There were equal numbers of males and females in this series.

Intrapartum asphyxia

This was considered to be present if there was evidence of sustained foetal bradycardia. (In one case the amniotic fluid was said to be meconium-stained.) Nine of the cases in this series were adjudged to have suffered from intrapartum anoxia. In three infants (cases 5, 7, 12) this was associated with maternal preeclamptic toxemia and in a further infant with accidental antepartum haemorrhage (case 6). The cause of the asphyxia in the five

remaining cases (2, 4, 8, 9, 10) was undetermined or uncertain.

Other associated features

The clinical history in case 1 was of considerable interest. While the latter months of the pregnancy had been uneventful, examination of the clinical records showed that between 12 weeks' and 16 weeks' gestation there had been several episodes of maternal vaginal bleeding.

There was one infant suffering from rhesus iso-immunization (case 3) and another infant where stenosis of the bowel was associated with transposition of the great vessels and a ventricular septal defect (case 11).

Age at onset of symptoms

No clear pattern emerged (Table I).

Bowel ischaemia in neonatal deaths

This material was studied for evidence of bowel ischaemia and the results are shown in Table II.

	No. of Cases	Full-thickness Necrosis	Mucosal Ischaemia	Total
Preeclamptic toxemia	15	—	4	4
Antepartum haemorrhage	12	1	4	5
Intrapartum asphyxia	21	2	5	7
Congenital heart disease	8	1	2	3
Total	56	4	15	19

Table II Bowel ischaemia in neonatal deaths

Necrosis of the entire thickness of the bowel was noted in four cases, two of which had a perforation of the necrotic bowel. The characteristics of mucosal ischaemia have been described elsewhere (deSa, Mucklow, and Gough, 1970) and comprise a combination of several if not all of the following features: capillary dilatation and sludging with or without fibrin deposition, interstitial haemorrhage and oedema of the lamina propria and submucosa, necrosis and sloughing of the mucosal epithelium, and destruction of the muscularis mucosa. A total of 15 cases were noted. In 19 of the 56 cases, therefore, there was evidence of bowel ischaemia.

Discussion

In this small series the overlap between atresia, stenosis, and infarction of the bowel indicates that they are related conditions and that the obstructive lesions are secondary to ischaemia. Ischaemia may be related to embolism, as suggested in the infant with arterial intimal thickening (case 9), but in most cases it is likely to be related to splanchnic shunting in relation to intrapartum asphyxia as suggested

earlier (deSa *et al.*, 1970). This would place most cases of neonatal and congenital stenosis of the bowel as an end-stage in the spectrum of gut ischaemia affecting this age group. It is of interest that case 5 of deSa *et al.* (1970) developed a stricture of the large bowel following a previous perforation, and that case 7 in the same series showed evidence of regeneration. Further, the mucosal changes seen in the stenotic segments are extremely similar to the persistent mucosal changes in the colon following the ischaemic phenomena associated with Hirschsprung's disease (Berry, 1969).

The aetiological importance of the complications of pregnancy noted in this series is suggested by the study of the morphology of the small bowel in the neonatal deaths not associated with stenosis (Table II), where it can be seen that ischaemic bowel lesions are a frequent finding in babies suffering from intrapartum asphyxia. The case for the importance of intrapartum asphyxia, and in particular the complications noted in this series, in the aetiology of ischaemia of the gastrointestinal tract has been clearly stated by Lloyd (1969).

It would be unrealistic to suppose that the complications of pregnancy listed in this small series of cases were of importance as acute phenomena only. In an examination of placentae from a large number of pregnancies complicated by the same abnormalities, a high proportion were found to have organizing thrombi of varying age in their foetal chorionic veins (deSa, 1971). These venous thrombi were the starting point in the development of intimal cushions in the affected veins and are commonest in infants of low birth weight score, a point noted earlier by other observers (Gruenwald, 1963; Blanc, 1968). The importance of the placental changes is that they indicate longstanding damage occurring within an important part of the foetal circulation. It is regrettable that the placenta was not available for histological examination in any of the cases of the present series. The relatively large number of infants of low birth weight score in the present series, however, is notable, and the apparently high mortality among these infants has been remarked upon.

Table II demonstrates further that ischaemic lesions of the small bowel are not uncommon in congenital heart disease, a situation that finds a parallel in adults with cardiovascular disease and bowel ischaemia (Marston, Pheils, Thomas, and Morson, 1966; McKinnell and Kearney, 1967).

The presence of other ischaemic lesions and scattered fibrin thrombi in infants with stenosis or atresia suggests that the affected infants were suffering from shock (McGovern, 1971), and provides further support for the aetiological role of the complications of pregnancy noted in this series. The

presence of scattered ischaemic lesions and fibrin thrombi in other organs would tend to suggest that an incidental intussusception was not of major importance in the cases studied.

If an episode (or episodes) of ischaemia is the basic aetiological factor in the development of stenosis of the bowel it is easy to understand why lanugo, squames, and meconium may be present distal to an atretic segment (Santulli and Blanc, 1961) or why segments of atretic bowel may be separated by relatively normal bowel lined by normal intestinal mucosa and containing meconium (Schultz and Lawrence, 1960). Such findings are incapable of being explained by a failure of recanalization during the organogenesis of the bowel, and it seems appropriate to suggest that this traditional theory should be discarded. In any case, a phase of obliterative epithelial proliferation has never been seen in the small bowel below the duodenum (Johnson, 1910), and it seems inappropriate that it was ever advanced as an explanation of stenosis/atresia of the small or large bowel.

The overlap between frank necrosis and obliterative scarring, the high incidence of complications of pregnancy, and the evidence of necrotic and thrombotic phenomena in other organs all point in the same direction and the uniformity in this small series is striking. There is nothing new in suggesting that ischaemia can produce scarring, and the example of myocardial infarction is familiar to every pathologist. Strictures are an accepted complication of ischaemic colitis in adults (Marston *et al.*, 1966) and it would appear that ischaemic episodes are of primary importance in the development of the homologous complications in the small bowel of the newborn.

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