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Clinical features of rotavirus gastroenteritis*

J. G. McCormack†

Summary

Five hundred and eighteen children under the age of five years admitted to hospital with a diagnosis of gastroenteritis over a twelve-month period were studied prospectively. Rotaviruses were demonstrated by stool electron microscopy (EM) in 132 of these cases (25·4 per cent), but in none of 108 age- and sex-matched controls. Non-specific cases, where no potentially pathogenic organism could be demonstrated in stools submitted for EM, viral and bacterial culture accounted for 46 per cent of cases. If EM of the stools had not been performed the proportion of non-specific cases would have risen to 85 per cent, thus demonstrating the importance of this technique in diagnosis.

Rotaviruses were most commonly found in winter and between the ages of six and eighteen months. A history of contact with an adult with diarrheoa, vomiting occuring before diarrhoea, accompanying upper respiratory tract infection (URTI), otitis media and pyrexia and the need for administration of intravenous fluids were all significantly more prominent features of the rotavirus than the non-specific cases of gastroenteritis, and are suggested as pointers to such a diagnosis. Pneumonia is described in three patients as an accompanying illness with rotavirus gastroenteritis.

Introduction

Rotaviruses were first described in the duodenal mocosa of six infants with acute gastroenteritis in 1973,[1] and they are now considered the commonest agents responsible for such an illness.[2–6] Acquired infection with rotaviruses in the pre-school child is usually followed by a gastroenteritic illness with the interesting exception of the neonatal period when such infection is often symptomless, presumably due to maternally-derived immunity.[7] Infection in children over the age of five and in adults usually produces mild symptoms or is symptomless, probably due to acquired immunity.[6, 8] Diagnosis of rotavirus gastroenteritis is usually made by electron microscopy (EM) of stools although techniques of immune EM[9] and various serological methods are also available.[6, 10, 11] Culture of the virus has not so far been universally successful,[3, 4, 9] although more definite progress in this respect seems imminent.[12, 13]

The laboratory facilities for the diagnosis of this condition are, as yet, not widely available, and it would seem desirable for clinicians and epidemiologists to appreciate any clinical features that might distinguish rotaviral from other forms of gastroenteritis. This study was embarked upon in an attempt to identify any such features.

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† Present address: Tawam Hospital, Abu Dhabi UAE.

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Methods

The children in the study were those under the age of five years referred to a large infectious diseases unit over a twelve-month period from May 1978 to April 1979 inclusive, because of acute diarrhoea regardless of any other factors. They were studied prospectively. A detailed history, which included data on feeding, contact and past history, was taken and examination was performed with special reference to the temperature, ears, nose, and throat, chest, weight and state of hydration. Haemoglobin, white-cell count, sedimentation rate, urea, electrolytes and bicarbonate values in the blood were estimated. Notes were made of treatment, feeding requirements and progress.

Three bacterial cultures of the patients' faeces were prepared, each using McConkey's agar, desoxycholate agar, selenite selective broth, mannitol salt agar and latterly, Skirrow's medium. Potentially pathogenic strains of *Escherichia coli* were identified for the following serotypes: 018ac, 026, 044, 055, 086, 0111, 0112ac, 0114, 0119, 0124, 0125, 0126, 0127, 0128 and 0142. Viral cultures of the faeces using rhesus monkey or baboon kidney, green monkey kidney and HEP 2 tissue cultures were instituted.

Stool specimens for EM were prepared by suspension with phosphate-buffered saline, differential centrifugation, deposition on to standard copper grids pre-coated with formvar and carbon and stained with phosphotungstic acid. EM scanning was performed for 30 minutes on each specimen, mostly at a magnification of 40000. All stool specimens were, if not immediately transported to the laboratories, stored at 4 °C.

As an adjunct study, stool specimens were collected from 108 controls with other illnesses but without diarrhoea. EM and viral cultures as described above were performed on these.

Results

A total of 518 patients were studied and the isolation rates for the various organisms are outlined in Table I. The adenoviruses were predominantly found on EM rather than culture. The largest single group was made up of non-specific cases which amounted to 238 patients (46 per cent). The contribution of EM to the diagnosis can be measured by the fact that if this procedure had not been employed, 440 patients (85 per cent) would have fallen into the nonspecific category. Picornaviruses were defined as small round particles of about 28 mm diameter seen on EM, but not cultured. Of the 132 rotavirus cases, 23 were associated with other organisms: 11 type-specific *Esch. coli*, five ECHO viruses, four adenoviruses, two picornaviruses and one coxsackie B_2. The identification rate for rotaviruses was higher in winter than in summer; a reversal of this pattern was noted for adenoviruses (Table II).

The control group comprised a total of 108 cases, 59 males and 49 females, with a mean age of 11·6 months and a range of four days to five years. The adenovirus was less commonly found compared to the study group and in all five cases was cultured. No rotaviruses were identified in this group (Table III).

In the study group the isolation rate for rotaviruses was relatively higher in the 6–18 month age group (35·8 per cent) and lower in infants of less than six months (16·4 per cent).

Table I *Details of organisms identified in stools of* 518 *patients with acute gastroenteritis*

Organism	No. of cases	Percentage of total
Rotavirus	132	25·5
Adenovirus	68	13·1
E. coli	32	6·2
ECHO	31	6·0
Salmonella	15	2·9
Shigella	9	1·7
Picornavirus	8	1·6
Coxsackievirus	8	1·6
Poliovirus*	6	1·2
Staph. aureus	3	0·6
Campylobacter	3	0·6
Threadworm	3	0·6
Giardia lamblia	2	0·4
Mixed (> 1 organism)	42	8·1
Non-specific (no organism)	238	46·0

* Vaccine-like strains.

Table II *Monthly variation of rotavirus and adenovirus identification in* 518 *patients with acute gastroenteritis*

Month	Total no. of cases	Percentage of Rotaviruses	Percentage of Adenoviruses
May	40	42·5	7·5
June	62	27·4	21·0
July	37	10·8	24·3
Aug.	36	11·1	16·7
Sept.	48	12·5	10·4
Oct.	31	19·4	22·6
Nov.	48	18·8	18·8
Dec.	44	43·2	2·3
Jan.	51	31·4	3·9
Feb.	39	30·8	5·1
Mar.	55	27·3	12·7
Apr.	27	26·0	14·8

Comparison of the rotavirus and non-specific groups yielded many results outlined below (Tables IV, V and VI). Pyrexia was significantly commoner in the rotavirus cases ($P < 0{\cdot}002$) and maximum temperatures recorded in hospital tended to be higher in this group (Table IV). Minor differences were observed in mean age, sex distribution, hospital stay, duration of diarrhoea, previous history of gastroenteritis and the incidence of vomiting, but these differences were not statistically significant ($P > 0{\cdot}05$). The reporting of vomiting occurring before diarrhoea was significantly commoner in the rotavirus group ($P < 0{\cdot}01$). Although a history of contact with another case of gastroenteritis was found more commonly in the rotavirus group, the

Table III *Diagnoses and virus identifications in stools of* 108 *control patients*

Diagnosis		Viruses	
Pertussis	33	Picornavirus	6
URTI	17	Adenovirus	5
Pneumonia	14	ECHO	4
Measles	7	Poliovirus*	4
Meningitis	6	Coxsackie B2	1
Others	31	Reovirus	1
		Coronavirus	1
		None	86

* Vaccine-like strains.

Table IV *Comparison of incidence and pattern of pyrexia between* 132 *rotavirus and* 238 *non-specific gastroenteritis patients*

	Rotavirus cases (%)	Non-specific cases (%)
Pyrexia		
Incidence	60·6	29·4
> 39 °C	21·2	12·0
38–39 °C	43·8	30·0
37–38 °C	35·8	58·0

Table V *Comparison of various clinical data in* 132 *rotavirus and* 238 *non-specific cases of gastroenteritis*

	Rotavirus cases	Non-specific cases
Age (mean, months)	13·0	10·6
Sex ratio (M:F)	1·8:1	1·2:1
Hospital stay (mean, days)	8·3	8·4
Past history of gastroenteritis	9·1%	13·0%
Vomiting	93·2%	84·0%
Vomiting before diarrhoea	15·9%	2·3%
Contact history	41·0%	24·8%
Contact history – adults	12·1%	2·9%
Breast-fed cases	2	4
URTI	31·1%	12·6%
Otitis media	8·3%	2·9%
Pneumonia (cases)	3	0
Bronchitis (cases)	2	0
Blood in stool (cases)	2	1
Macular rash (cases)	4	5
Conjunctivitis (cases)	1	4
Meningism (cases)	0	1
Febrile convulsions (cases)	1	4

Table VI *Further data on* 132 *rotavirus and* 238 *non-specific cases of gastroenteritis*

	Rotavirus cases	Non-specific cases
IV fluids used	28·5%	12·6%
Weight		
< 50th centile	72·7%	70·7%
< 3rd centile	17·4%	14·3%
ESR (mean mm/hour)	10·2	15·9
HCO_3 (mean mmol/l)	16·3	19·8
$Na^+ > 160$	0	1
(mmol/l) > 155	4	5
(cases) < 130	2	5

difference between the two groups did not reach statistical significance ($0{\cdot}10 > P > 0{\cdot}05$); however, when such a history was confined to contact with adult cases, the difference was more pronounced and was statistically significant ($P < 0{\cdot}05$). A significantly larger proportion of the rotavirus cases had symptoms or signs of an upper respiratory tract infection (URTI) ($P < 0{\cdot}01$) and a similar difference was noted for patients with visibly inflamed tympanic membranes ($P < 0{\cdot}001$). Three cases with pneumonia, diagnosed on both clinical and radiological criteria, and two of bronchitis, were observed amongst the rotavirus group; no such features were encountered in the non-specific group. Rectal bleeding, rashes, conjunctivitis, meningism and febrile convulsions were noted in a small number of cases and, interestingly, in none of the cases with a rash was there evidence of an enteroviral infection. The necessity to use intravenous fluids was significantly higher in the rotavirus group ($P < 0{\cdot}001$). The gastroenteritis patients as a whole tended to be of lower weight than normal on admission although the skewing of these figures may be partly accounted for by dehydration. Small differences in haemoglobin, ESR, urea, electrolytes and bicarbonate levels in the blood were noted, but none of these reached statistical significance. Hypernatraemic dehydration, a condition seen less frequently nowadays in association with gastroenteritis, was not significantly commoner in any group of patients.

Discussion

Isolation rates for rotaviruses in acute gastroenteritis in children less than six years old have varied within the range 18 per cent to 60 per cent.[2, 5, 6, 14, 15] The rate for this study of 25·5 per cent would have been higher if we had excluded cases which did not appear to be infective, e.g. feeding and social problems and drug-induced diarrhoea, but such differentiation can be very arbitrary and indefinite. Similar patterns of seasonal variation in rotavirus and adenovirus identification in faeces have been documented,[5, 7] and one report suggests that this variation for rotaviruses may be lost in tropical climates.[17] The failure in this study to find rotaviruses in the stools of control patients without diarrhoea

correlates with other similar reports.[4, 5, 15, 16] A similar age distribution to that shown in this study has been previously described for rotavirus gastroenteritis, the relatively lower incidence in the under six months age group being explained by maternally-derived antibody.[18, 19]

The male predominance in gastroenteritis, a well-documented but poorly understood feature, was reproduced in both rotavirus and non-specific groups in this study. Pyrexia has been said to occur in 50–60 per cent of cases of rotavirus gastroenteritis,[9, 20] although one group in Romford noted fever as a feature of all 100 of their cases.[14] In this study, pyrexia is seen to be significantly commoner and generally more severe in the rotavirus than in the non-specific cases. The incidence of vomiting in this survey of 93·2 per cent in the rotavirus cases correlates well with other reports,[2, 18] and although one of these studies suggested that vomiting was commoner in rotavirus than in other forms of gastroenteritis,[2] this study, based on larger numbers of patients and statistical analysis, cannot confirm this finding. However, this study does show that vomiting occurring prior to the onset of diarrhoea is a significant feature of the rotavirus infection. As the study year went by, an impression was formed that a definite history of contact was obtainable more often in the rotavirus cases than in other groups, and although there was a difference in this respect between the rotavirus and non-specific groups, this difference did not qualify for statistical significance. Although an outbreak of rotavirus gastroenteritis has been described involving adults without the known infection of children,[8] the finding of rotaviruses in adult stools has usually been acompanied by no intestinal symptoms.[21] The finding in this study of a significantly higher incidence of a history of contact with an adult with gastroenteritis in the rotavirus than in the non-specific cases would suggest that adults may represent a reservoir for potential rotavirus infection in infants.

Upper respiratory tract infection (URTI) as a preceding or accompanying event in rotavirus gastroenteritis has been previously described in 29–42 per cent of cases;[2, 6, 14] in one survey of gastroenteritis cases, patients with URTI were excluded.[12] The current study shows that URTI is a significantly commoner event in rotavirus than in non-specific gastroenteritis. The frequency of otitis media in rotavirus gastroenteritis in this study was lower than in two other reports,[21, 14] but this series demonstrates it as a significant feature of this illness. The finding of three cases with pneumonia and two with bronchitis amongst the rotavirus group without any such cases in other groups was surprising. These findings suggest that when gastroenteritic symptoms occur in a patient with URTI, otitis media, pneumonia or bronchitis, rotaviruses should be sought in the stools rather than accepting the diarrhoea or vomiting as being secondary to the respiratory or ear infection. The failure to find rotaviruses in the stools of any control patients with similar infections, but without diarrhoea, would support the role of the rotavirus as being responsible for the intestinal features of such illnesses. What role rotaviruses play, if any, in the non-intestinal features of such illnesses is not known; there is no record of demonstration of these viruses from throat, bronchial or aural secretions of such cases.

Although one report showed clinically apparent passage of blood in the stools in six out of sixty patients with rotavirus gastroenteritis,[20] this study suggests that this is an infrequent complication.

The requirement for intravenous fluids in rotavirus gastroenteritis has been reported as between 3 and 34 per cent:[2, 14, 21] such variation probably represents varying indications for this form of therapy in different hospitals. This study, where similar criteria were applied to all cases in this regard, showed that intravenous fluids were considered necessary in a significantly higher proportion of patients with the rotavirus rather than the non-specific form of gastroenteritis, and under such conditions these former cases would probably be said to be more severely dehydrated than the non-specific cases.

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Abstract of literature

RAPID DIAGNOSIS OF PURULENT MENINGITIS BY INDIRECT PASSIVE LATEX AGGLUTINATION AND COUNTER IMMUNOELECTROPHORESIS: INVESTIGATION AND APPLICATION

Denis F, Saulnier M, Chiron JP. *Bull WHO* 1981; **59**: 143–151. (In French)

Difficulties with transport, handling and culture of cerebrospinal fluid (CSF) in Dakar, where they were working, led the authors to investigate serological methods of diagnosis in bacterial meningitis.

They studied 1030 CSF samples, taken on the day of hospital admission, from patients with purulent meningitis, and compared the efficacy of Gram-staining, standard culture techniques, latex agglutination (LA) and counter immunoelectrophoresis (CIE) in providing a diagnosis.

Of 1030 cases, 212 defied diagnosis by any means. It is of interest to consider the diagnosis in the remaining 818 cases. They included: pneumococcal, 345; *Haemophilus influenzae*, 297; meningococcal, 81; *Staphylococcus aureus*, 19; *Salmonella* spp., 18; other streptococcal, 17; *Escherichia coli*, 10.

The techniques of LA and CIE were used to seek cases of pneumococcal, meningococcal and *H. influenzae* meningites. Gram-staining provided 80 per cent of diagnosis, Gram-staining and culture together, 85 per cent. CIE alone provided 90 per cent of diagnosis, LA alone, 82 per cent (but meningococcal cases were not so well detected, being 72·5 per cent by CIE and 71·2 per cent by LA). The best combination of tests was Gram-staining plus CIE which provided a 95 per cent successful diagnosis.

Difficulties were encountered in that *H. influenzae* and tuberculous meningitis sometimes produced false-positive pneumococcal CIE, and some pneumococcal and meningococcal types produced cross reactions with LA. Some of the undiagnosed cases had epidemiological features of meningococcal meningitis.

The authors concluded that serological and Gram-stain diagnosis of the three common types of bacterial meningitis might avoid the need for expensive cultural techniques, which require a good standard of laboratory facilities. These simple techniques can be performed on CSF samples which have been stored at low temperatures, or transported long distances, and so lend themselves particularly to use in developing countries.