Original article

Severe infectious colitis in non-immunocompromised patients: confusion with Crohn's disease

Erminia Matrella, Maria Tzardi[1], C. Leontidis, E.A. Kouroumalis

SUMMARY

Objective: **Despite a significant progress in diagnostic facilities infectious colitis may present considerable diagnostic problems. The *aim* of the present prospective study was to establish criteria for clinical and endoscopic diagnosis and delineate problems of differential diagnosis. *Design:* 57 cases of severe infectious colitis admitted to a referral Gastroenterology Department over the last 3 years were prospectively studied with stool cultures, total colonoscopy and histological examination. *Results:* Salmonella species were isolated from stools of 77% of patients. A peak during spring time was identified. 22% of patients presented with severe diarrhoea of more than 10 days' duration while leucocytosis was present in only 39% of cases. Reactive arthritis was not found in our patients. These clinical presentation caused considerable confusion and resulted in inappropriate antibiotic administration in the majority of patients. Histology was not useful with many false negative and positive results, in as many as 30% of cases. Skip lesions and typical apthous ulcers reminiscent of Crohn's disease were found in many cases at colonoscopy, indicating a consideration of both diseases when such findings are established. Severe lesions of the left colon, contrasting with a mild endoscopic picture of the right colon is, according to our experience, a very useful diagnostic endoscopic finding. *Conclusions:* A typical clinical presentation with endoscopic and histological confusion with Crohn's disease is a common finding in severe infectious colitis.**

Departments of Gastroenterology and Pathology[1], University Hospital of Crete, Heraklion, Crete, Greece

Address for correspondence:

Erminia Matrella MD, Dept. of Gastroenterology, University Hospital Heraklion P.O. Box 1352, 71110 Heraklion, Crete, Greece, Tel. 0030-2810-392355, Fax: 0030-2810-542085

Severe endoscopic lesions of the left colon and mild lesions of the right colon is a valuable aid in diagnosis.

Keywords: Infectious diarrhoea, endoscopy, salmonellosis

INTRODUCTION

Differential diagnosis of infectious diarrhoea is difficult both clinically and endoscopically. This is particularly true in areas of high endemicity of various pathogens causing infectious diarrhoea. There have been descriptions of various endoscopic appearances particularly after Salmonella or Shigella infection[1-5].

An additional problem for a correct endoscopic diagnosis is the fact that very often the rectum remains intact while endoscopic findings are encountered in other parts of the large bowel[6], as a result, making ordinary sigmoidoscopy of limited value.

The purpose of the present investigation was to prospectively study 57 patients with proven infectious diarrhoea, in an effort to establish endoscopic and clinical criteria for diagnosis.

PATIENTS

57 patients (35 men, 22 women, age 14-82 years - median 48 years), requiring hospitalization because of severe infectious diarrhoea, underwent total colonoscopy within 24 hours of admission. None of the patients was HIV positive or had any other indication of immune-mediated disease. Colonoscopy was done without purgative preparation. A liquid diet was the only bowel preparation. Number of bowel movements, body temperature, presence of abdominal pain, duration of disease and presence of blood in the stools were the clinical parameters recorded.

In addition routine haematology and biochemistry and blood and stool cultures were included in the routine investigation. Microscopic presence of white and red blood cells in stool was also recorded.

RESULTS

A. Seasonal variation: A spring peak was identified. 39% (22/57 patients) were admitted during the 3 spring months (March, April, May). The remaining cases had an equal distribution over the other three seasons.

B. Clinical presentation: All patients had more than 8 bowel movements a day, on the day of admission. 53 out of 57 had fever over 38°C. Only 6/57 patients had intense abdominal cramps. 45/57 described mild to moderate abdominal pain. Interestingly, 62% of cases had macroscopic blood in the stools. Contrary to common belief, 12/57 patients presented with a serious syndrome (more than 8 bowel movements a day) for more than 10 days before admission. 41/57 patients had serious diarrhoea for 4 to 10 days before admission and in only 4 patients was the syndrome of less than 4 days' duration.

C. Laboratoty investigations: Stool cultures identified a candidate pathogen in 88% of cases (49/57 patients). In 77% of patients (43 cases) the causative agent was Salmonella species (S. enteritidis 33 cases, S. typhimurium 7 cases and S. ajonas, S. infantis and S. newport, 1 case each).

Campylobacter jejuni was identified in 4 patients and Shigella flexneri in two patients.

In 7 patients no pathogen was identified. It should be noted, however, that pathogenic E. coli are not specifically identified in our laboratory. In these patients diagnosis of infectious colitis was confirmed by the favourable outcome of the patients, without any drug prescription. Moreover, no recurrence was noted after one year of follow up.

No parasites were identified in any of the patients.

Peripheral leukocytosis was of no help, since only 39% (22 cases) had abnormally high white blood count and in only 9 patients was a prominent leukocytosis (over 20 $10^3/mm^3$) noted.

D. Endoscopic findings: All but one patient had significant endoscopic abnormalities, classified into one of the following 3 categories:

Serious (severe oedema, excessive friability of the mucosa, overtblood oozing and presence of irregular ulcers). Moderate (mild oedema, congestion of the mucosa with haemorrhagic infiltrations and superficial ulceration). Mild (only oedema and presence of a congestive mucosa). 10 patients were classified as severe, 34 as moderate and 12 as mild.

Most importantly, aphthous ulcers similar to those described in Crohn's disease were found in 9 patients. 37 patients had continuous lesions of the mucosa, while in 19 patients, the lesions were intermittent with normal mucosa between areas of inflammation.

One important finding was that in all cases with continuous lesions of the mucosa, the left part of the bowel (ascending colon) was more seriously damaged than the right part (descending colon and sigmoid).

E. Histology: All 57 patients had a mild derrangement of crypt architecture with lamina propria oedema and polymorhonuclear infiltration.

Crypt abcesses were found in 36 patients. In 39 patients a diagnosis compatible with infectious colitis was made but none was considered as diagnostic or pathognomonic. Inflammatory bowel disease was diagnosed in 8 patients while non-specific colitis was diagnosed in 10 patients.

F. Treatment: 41 patients received antibiotics (either ampicilline-clavoulanic acid or Co-trimoxazol). 16 patients received no specific treatment. No difference was found in either time of recovery from diarrhoea or in days of hospitalization between those who received antibiotics and those not treated.

DISCUSSION

Certain findings require further commendation. A relatively large number of patients appeared with protracted, serious diarrhoea of more than 10 days' duration, in contrast to the common belief that infectious diarrhoea in the Western World is a mild disease self limiting within a few days.

Moreover, reactive arthritis, commonly associated with Salmonella or Campylobacter[16,18] - Yersinia infections were not found in our series. Only 3 patients exhibited a mild self-limiting arthralgia.[17-22]

Common symptoms usually associated with infectious colitis, like abdominal pain and fever, were absent in 10% of patients.

Leucocytosis, another finding usually associated with infectious colitis, was present in only 39% of patients.

No correlation was noted between the presence of blood in stools microscopically and the reported blood by the patients. Many patients reported blood in stools which could not be verified by microscopic examination. This finding indicates that either patient and/or hospital staff falsely report blood in stools or, most probably, there is a delay in stool examination with a destruction of red blood cells which might result in false negative examination.[23]

Histology is also mostly non-diagnostic. In 33% of cases there was a false exclusion of infectious colitis, while inflammatory bowel disease was falsely diagnosed in 13% of cases. Similar problems have been previously reported[7-10].

In the majority of our cases, Salmonella species was the offending organism. These microbiological results are different from those reported elsewhere[11-13]. Most probably, consumption of fresh vegetables from local gardens and not from commercially organized large farms, a characteristic of our area, is responsible for this discrepancy. Endoscopic findings are of particular interest. Severe lesions were most often localized in the left bowel while the right bowel usually had only mild lesions. We believe that this observation may be a useful indicator of the correct diagnosis. In a significant number of cases an endoscopic false diagnosis of Crohn's disease could have been made. 19 out of 56 patients were found to have skip lesions with normal mucosa alternating with inflammatory lesions, while in 9 cases (16%) apthous ulcers considered to be specific to Crohn's disease were identified.[25]

This large number of Crohn's like lesions, suggest that both diseases should be included in the differential diagnosis of either Crohn's disease or infectious colitis.

Antibiotic administration has been reported to be without any therapeutic value in the treatment of infectious colitis including salmonellosis[14,15]. These findings were also verified in our study.[26]

However, in view of the severe clinical presentation of the disease in this study, administration of antibiotics before a positive diagnosis could be established, is probably partly justified.

REFERENCES

1. Speelman P, Kabir I, Islam H. Distribution and spread of colonic lesions in Shigellosis: A colonoscopy study. J Infec Dis, 1984; 150:899-903.
2. Anand BS, Malhotra V, Bhattacharya SK, et al. Rectal histology in acute bacillary dysentery. Gastroenterology, 1986; 90:654-660.
3. Mandal BK, Mani V. Colonic involvement in salmonellosis. Lancet, 1976; 1:887-889.
4. Appelbaum PC, Scragg J, Schönland MM. Colonic involvement in salmonellosis. Lancet, 1976; 2:102.
5. Radsel-Madvescek A, Zargi R, Acko M, et al. Colonic involvement in salmonellosis. Lancet 1977; 1:601.
6. Farthing MJG. Infective diarrhoea. In: Inflammatory Bowel Diseases. G. Jarnerot (ed). Corona Astra publ. Malmo Sweden 1992; p.p. 174-195.
7. Dronfield HW, Fletcher J, Langman MJS. Coincident Salmonella infections and ulcerative colitis: problems of recognition and management. Br Med J 1974; 1:99-100.
8. Lindeman RJ, Weinstein L, Levitan R, et al. Ulcerative Colitis and intestinal salmonellosis. Am J Med Sci 1967; 254:855-861.
9. Day DW, Mandal BK, Morson BC. The rectal biopsy apearance in salmonella colitis. Histopathology, 1978; 2:117-131.
10. Allison MC, Hamilton-Dutoit SJ, Dhillon AP, Pounoles RE. The value of rectal biopsy in distinguishing self-limited colitis from early inflammatory bowel disease. Quant J Med 1987; 65:985-995.
11. Hook EW. Salmonella species (including typhoid fever). In: Mandell G.L., Douglas R.G. Jr., Bennet J.E. eds. Principles and practice of infectious diseases. 3rd ed. New York Churchill Livingstone, 1990; 1700-1716.
12. Cloalker RB, Blasu MJ. A review of human salmonellosis. III. Magnitude of Salmonella infection in the United States. Rev Infec Dis 1988; 10:111-124.
13. Cohen ML, Potter M, Pollard R, et al. Turtle associated Salmonellosis in the United States. JAMA 1980; 243:1247-1249.
14. C.O. Record. Colonic Infections and Infestations in Diseases of the Gut and Pancreas. J.J. Misiewicz (eds), C.W. Venables Blackewell Sc. Publ. Oxford 1994; p.p. 784-804.
15. David C, Wolf MD, Ralph A, Giannella MD. Antibiotic Therapy for Bacterial Enterocolitis: A Comprehensive Review. Am J Gastroenterol Copyright 1993 by Am Coll of Gastroenterology vol. 88 No 10 p.p. 1667-1683.
16. NachamkinI. Chronic effects of Campylobacter infection. Microbes Infect. 2002; 4:399-403. Review. PMID: 11932190.
17. Locht H, Krogfelt KA. Comparison of reumatological and gastrointestinal symptoms after inection with Campylobacter jejuni/coli and enterotoxigenic Escherichia coli. Ann Rheum Dis 2002; 61:448-452.
18. Hannu T, Mattila L, Rautelin H, Pelkonen P, Lahdenne P, Siitonen A, Leirisalo-Repo M. Campylobacter-triggered reactive arthritis: a population-based study. Rheumatology (Oxford). 2002; 41:312-318.
19. Chaudhuri A,Bekdash BA. Toxic megacolon due to Salmonella: a case report and review of the literature. Int J Colorectal Dis 2002; 17:275-279.
20. Jimenez-Saenz M, Gomez-Rodriguez BJ, Carmona I, Rebollo J, Torres Y, Rodriguez-Banos J, Herrerias-Gutierrez JM. Salmonella dublin infection: a rare cause of spontaneous bacrterial peritonitis and chronic colitis in

alcoholic liver cirrhosis.
21. Chao HC, Chiu CH, Kong MS, Chang LY, Huang YC, Lin TY, Lou CC. Factors associated with intestinal perforation in children's non-typhi Salmonella toxic megacolon. Pediatr Infect Dis J 2000; 19:1158-1162.
22. Cross E, Engelhard D, Katz S. Large obstruction: an unusual presentation of salmonella enterocolitis in infancy. Pediatr Surg Int 2000; 16:525-526.
23. Sodd A, Midha V, Sood N. Massive hemorrhage from colonic ulcers in typical in typhoid fever. Indian J Gastroenterol. 2001; 20:80.
24. Shigeno T, akamatsu T, Fujimori K, Nakatsuji Y, Nagatab A. The clinical significance of colonoscopy in hemorrhagic colitis due to enterohemorrhagic Escherichia coli 0157:h7 infection. Endoscopy 2002; 34:311-314.
25. Dassopoulos T. Diagnostic methodologies: serology, endoscopy, and radiology. Curr Gastroenterol Rep. 2001; 3:491-502.
26. Madsen K, Gornish A, Soper P, McKaigney C, Jijon H, Yachimec C, Doyle J, Jewell L, De Simone C. Probiotic bacteria enhance murine and human intestinal epithelial barrier function Gastroenterology. 2001; 121:580-591.