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Lecture

Endoscopic diagnosis of infectious colitis

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The colon has a limited ability to react to noxious stimuli. Therefore, irrespective of the nature of the original insult, be that, chemical, ischemic, or of unknown nature, it may cause various degrees of colonic inflammation manifesting itself with variable degrees of oedema, erythema, friability, ulceration, and bleeding.[1] The intensity of colonic inflammation depends greatly on the magnitude and strength of the original insult and the 'readiness' and ability of the colonic wall constituents (epithelium, lamina propria, immune cells, neuronal network, vascular supply, etc) to counterbalance and down-regulate this attack. Therefore, clinical manifestations of colitis, such as abdominal pain, diarrhoea, rectal bleeding, bloody diarrhoea, localized or generalized abdominal tenderness, rebound tenderness, etc may show a remarkable variability and may be graded as mild, moderate or severe depending on their severity. As a consequence, the medical history is an essential and crucial part of the diagnostic procedure; diagnostic tests should be directed accordingly, and should not be applied indiscriminately.

The predominant clinical manifestation of gastroenteritis is diarrhoea. Diarrhoea can be subdivided into two main categories, namely non-inflammatory, watery, non bloody diarrhoea and inflammatory, bloody diarrhoea.[2] These two conditions differ in the underlying causative factors, the site of intestinal involvement and the management and outcome. The former manifests itself as large volume watery diarrhoea, occasionally associated with nausea, vomiting, and abdominal cramps and the small intestine is the site of inflammation. The causative agents are usually *viruses*, *vibrio*, *Giardia lamblia*, Enterotoxigenic *E. Coli*, enterotoxin producing bacteria, or food-borne agents, and the faecal leucocyte count test is negative. The latter is small volume, bloody diarrhoea associated with left lower quadrant pain or cramps and the patient may be febrile or even toxic. *Shigella*, *Salmonella*, *Campylobacter* species, *Yersinia enterocolitica*, invasive *E. coli*, and *Clostridium difficile* are usually identified as causative agents. The site of inflammation is usually the colon with or without terminal ileitis and the faecal leukocyte count test is positive.

Traditionally, the diagnosis of infectious colitis is based on a combination of positive stool tests [faecal leukocyte counts (FLC), culture for common pathogens, parasitology, and toxin tests], and/or serological and molecular tests and characteristic histological abnormalities on rectal biopsies. However, even with most sophisticated methods a positive stool culture is found in no more than 80% of the patients with true infectious colitis whereas common pathogens may initiate a first attack of UC.[3,4] Furthermore, the value of sigmoidoscopy in the differential diagnosis of acute bloody diarrhoea of unknown cause has been questioned. This underlies the necessity for early, cautious colonoscopy as a useful procedure to identify, characterize and grade mucosal lesions,[3, 5-9] and obtain multiple regional colonic biopsies that would allow the timely differential diagnosis between type and various other forms of colitis, especially when they are manifested clinically as acute bloody diarrhoea.[3,5,10,11] In addition, examination of intestinal fluid aspirated during colonoscopy may provide useful information as to the diagnosis of colitis.[12] Thus, the main indications for colonoscopy in suspected ulcerative colitis are inflammatory, bloody diarrhoea of unknown cause, non-bloody diarrhoea with a positive FLC test but negative stool culture, parasitology and *Clostridium difficile*-toxin A as well as in the HIV positive or AIDS patient. In contrast, colonoscopy has a very limited role for acute, watery, non-bloody (non-inflammatory) diarrhea especially when faecal leukocytes are not detected in the stools. On some occasions, gastroduodenoscopy with biopsies and intestinal fluid aspiration may give some clues to some diagnosis of some diseases such as *giardia lamblia*, intestinal tuberculosis, Whipple's disease, etc. Absolute contrain-

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dications for colonoscopy in infectious colitis are proven or suspected perforation and major co-morbidity; relative contraindicatons are acute, fulminant colitis and impeding toxic megacolon. Under these circumstances colonoscopy is an invaluable clinical and research tool, because it is relatively inexpensive, widely and readily available, allows rapid, full inspection and selective biopsies from mucosal lesions, inflamed and healthy mucosa, and it is safe, in experience hands.[2-5]

Colonoscopy should be performed early, preferably within the first 4-5 days after initiation of symptoms.[3,10,11] The reasons are that lesions tend to migrate distally and become coalescent with time lapsing from the onset of disease: the rectum may be intact early in the course of infectious colitis but severely infected in later stages and patchy lesions may become confluent. Therefore, the differential diagnosis between infectious and idiopathic ulcerative colitis may be more apparent if colonoscopy is performed soon after the onset of haemorrhagic diarrhea. Another important reason is that histology may aid in the differential diagnosis of acute self-limited colitis and infectious colitis if biopsies are obtained within the first 4-5 days of the onset of symptoms. [3,5,10,11]

If feasible, colonoscopy should be performed in an unprepared colon. If not, very mild cleansing agents should be used in enema rather than oral form. Strong laxatives and/or purging agents should be avoided. Anti-spasmodic agents are contraindicated. Unnecessary stretching and looping should be avoided. The endoscopist must describe the nature, severity, and distribution of the lesions in the colon. Mucosal biopsies must be taken from inflamed and 'healthy-looking' mucosa.

Some infectious agents (such as *yersinia enterocolitica*, *amoeba histolytic*a, *C. difficile*, *CMV*) may cause typical mucosal lesions. However, this is the exception to the general rule and it is not uncommon to encounter a pattern of polymorphic mucosal lesions, even with the aforementioned agents. Prominent endoscopic features in infectious colitis are patchy or diffuse mucosal oedema and mucosal erythema, focal or coalescent haemorrhagic spots, a variety of ulcerations [superficial erosions, pinpoint (microaphthoid) ulcers, small aphthoid ulcers surrounded by red halos, typical aphthae, irregular ulcers (star-shaped, angular, transverse, longitudinal) occasionally with cobblestone appearance], and spontaneous bleeding (occasionally oozing blood). Another characteristic feature in some forms of IC is the presence of a mucopurulent exudate strictly adherent to the underlying mucosa.

Shigellosis may be manifested clinically as acute, dysenteric syndrome, which may render colonoscopy extremely uncomfortable because of the intense involvement of the rectosigmoid. The disease extends proximally to involve various parts of the colon and pancolitis is found in approximately 15% of these cases. Prominent endoscopic findings are erythema, severe oedema, irregular (stellate, serpiginous, well-like ulcers) and spontaneous bleeding. Alternatively, the disease may show a subacute presentation which is clinically and endoscopically indistinguishable from ulcerative colitis but a positive stool culture and response to appropriate treatment establish the correct diagnosis.[14,15]

Campylobacter jejunii is responsible for 98% of the infectious colitis caused by *campylobacter* species. Usual presentation is with abdominal cramps and bloody diarrhoea. Colonoscopy reveals mucosal inflammation (erythema, oedema, usually continuous), erosions and ulcers (aphthoid, large, or flat). The endoscopic appearance in the rectosigmoid area may be indistinguishable from ulcerative colitis, but proximal involvement is not uncommon.[16]

Salmonellosis may cause various forms of gastroenteritis including inflammatory, bloody colitis. Salmonella colitis may be the trigger for subsequent development, or exaggerate pre-existing quiescent ulcerative colitis, and be the cause for toxic complications, such as toxic megacolon.[1,4,17,18] Colonoscopy reveals mucosal inflammation with erythema, oedema, granularity and loss of the normal vascular pattern. In more severe cases there is diffuse erythema, pitting oedema and ulceration (punctuate, aphthoid, aphthae, irregular (stellate), deep). Occasional, extensive areas of colonic mucosa may be denuded.[17,18]

Yersinia enterocolitica may cause various forms of syndromes depending on the age of the affected individual, including enterocolitis, mesenteric adenitis, upper respiratory tract infections, bacteraemia, and post-infectious extraintestinal manifestations, such as erythema nodosum, reactive arthritis, and Reiter's syndrome. Endoscopically, erosions and various forms of ulcerations (usually punctuate ulcers) are seen in the right side of the colon, which mimics Crohn's disease. On other occasions, a continuous pattern of inflammation with erythema, blurred vascular pattern, and friability which mimics ulcerative colitis is seen.[19]

Cytomegalovirus colitis is a rare entity in a normal, immunocompetent individual. However, it may cause exacerbations of UC and may be responsible for failure of intensive treatment regimens in patients with severe UC, especially when they are immunosuppressed. Clinically,

it is manifested with chronic watery diarrhea, abdominal pain, and, rarely, haematochezia. The endoscopic appearance is usually non-specific but includes discrete ulcerations, varying from punctate and superficial erosions to deep ulcers, on occasion only granularity and friability indistinguishable from UC. Histology may reveal typical inclusions which confirm the diagnosis.[20]

Intestinal *tuberculosis* may mimic Crohn's disease. Endoscopic lesions are very similar in the two diseases but a recent study has shown that anorectal lesions, longitudinal ulcers, aphthous ulcers and cobblestone pattern are more commonly encountered in Crohn's disease. In contrast, involvement of less than 4 segments, a patoulous ileocaecal valve, transverse ulcers, and scars or pseudopolyps are more common in tubesrculosis.[21]

Acute *amebic* colitis is manifested endoscopically with diffuse erythema, granularity, friability resembling ulcerative colitis. In its chronic form, discrete or localized mucosal ulcers with a characteristic pounched-out appearance (rolled edges) helps the differential diagnosis from Crohn's disease. [22]

Pseudomembranes are usually found in *C. difficile* colitis.[23]

The severity of endoscopic lesions in infectious colitis depends as has already been mentioned on the nature and the infectious strength of the responsible agent and the defensive mechanisms of the immunocompetent host. The lesions characteristically spare the rectum in the early phases of infectious colitis but may involve the entire rectum as a late event. Unlike ulcerative colitis, friability and granularity are rare endoscopic features of infectious colitis. Lesions are focally and unevenly distributed in the colon with the sigmoid colon and the flexures being more severely affected unless the causative agent has a predilection for the ileocolonic area, as is the case in yersiniosis and intestinal tuberculosis. Areas of normal mucosa which may contain normal faeces may intervene between involved areas. This pattern makes infectious colitis look much more like Crohn's colitis rather than ulcerative colitis.[3] Mucosal bridging, pseudopolyps, extensive denuded areas of colonic mucosa are only very exceptionally encountered in cases of acute infectious colitis. However, in some cases endoscopic discrimination between ulcerative colitis and infectious colitis is virtually impossible.[5]

Some agents, such as *neisseria gonorrhoeae*, *Chlamydia trachomatis*, *herpex simplex*, *treponima pallidum*, and human *papilloma virus* show a predilection for the anal canal or perianal tissues, or affect the distal colon and the rectum. These are more commonly seen in highly promiscuous homosexual men as well as in AIDS patients. Symptoms include local pain, diarrhoea, anal discharge, perianal discomfort. Endoscopic appearances may in part depend on the causative agent but they are usually non specific.

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