Clinical feature of a small intestinal mucosal injury in chronic NSAID users in Japan

To the Editor,

The damage of gastric and duodenal mucosa caused by NSAIDs is well established, and there has been increasing recognition of the damage of mucosa of the small intestine caused by NSAID treatment [1-4]. Recent reports have indicated that low-dose aspirin (LDA) causes not only gastroduodenal mucosal injury, but also small bowel injury with high frequency [5, 6].

A total of 201 patients who underwent capsule endoscopy (CE) or double balloon endoscopy (DBE) for overt gastrointestinal bleeding (OGIB) were included in this study. Based on the clinical records, laboratory data such as hemoglobin levels, major symptoms, underlying diseases, the types and duration of NSAID consumption, and the endoscopic characteristics of CE or DBE were reviewed. In the present study, the erosions included the redspots, small erosion and large erosions in CE results. In cases examined by DBE, we defined erosions as a small mucosal superficial mucosal defect (<3mm in diameter) and an ulcer as a large mucosal defect (≥ 3mm in diameter). In the CE cases, the small bowel was equally divided into two segments (proximal and distal) on the basis of each subject's small bowel transit time and in the DBE cases, the location of the lesion was determined radiographically.

The results of CE and DBE are shown in Table I and the clinical characteristics of ulcerative or erosive lesion of chronic NSAID users are summarized in Table II. The mean diameter of the ulcerative lesion was 9.8±3.2 mm. The percentage of chronic LDA users was significantly higher in the erosion cases than in the ulcer cases (P<0.05). The ulcerative lesions were predominantly located in the ileum, while the erosive lesions were predominantly found in the jejunum (P<0.05). In 5 of 9 ulceration cases, NSAIDs, were withdrawn. In 4 patients who had continued the NSAID therapy, 2 cases used prostaglandin, 1 used rebamipide (a drug stimulating the endogenous production

Table I. The ulcerative or erosive lesions of small intestine in OGIB cases

	DBE (n=73)	CE (n=128)	CE+DBE (n=201)
Ulcer	7 (9.6%)	9 (7.0)	16 (8.0%)
NSAID	3 (4.1%)	4 (3.1%)	7 (3.5%)
Non-aspirin NSAID	2 (2.7%)	4 (3.1%)	6 (3.0%)
LDA	2 (2.7%)	1 (0.8%)	3 (1.5)
Erosion	6 (8.2%)	20 (15.6%)	26 (12.9%)
NSAID (-)	3 (4.1%)	10 (7.8%)	13 (6.5%)
Non-aspirin NSAID	1 (1.4%)	2 (1.6%)	3 (1.5%)
LDA	2 (2.7%)	8 (6.3%)	10 (5.0%)

*DBE: double balloon endoscopy; CE: capsule; LDA: low-dose aspirin

Table II. The clinical characteristics of ulcerative or erosive lesions in chronic NSAID users

	Erosions	Ulcer	p
Cases (no)	13	9	
Gender (Male/Female)	8 / 5	5 / 4	N.S.
Age (years)	71.1±8	68.5±13.6	N.S.
Types of OGIB	1		
Ongoin overt / Previous overt / Occult	1 / 5 / 7	0 / 3 / 6	N.S.
Clinical symptoms			
Abdominal pain	1	1	N.S.
Hemoglobin level (g/dl)	10.2±1.2	9.9±1.0	N.S.
NSAID			
LDA	10	2	p<0.05
Non-aspirin NSAID	3	7	
Location			
Jejunum	4	0	
Jejunum and ileum	6	2	p<0.05
Ileum	3	7	
Lesions including jejunum	10	2	p<0.05

of prostaglandin) and one used prostaglandin and rebamipide concomitantly; these 4 cases showed improvement in the re-CE study. In 3 of 13 erosion cases, NSAIDs were withdrawn. In 10 patients who had continued the NSAIDs, 3 cases used prostaglandin concomitantly. All 13 cases demonstrated a good clinical course.

A previous study investigated the distribution and types of small intestinal injury due to NSAID, and it was shown that most of the denuded areas were located in the proximal part, erosions were found throughout the small intestine, and all ulcers in the distal part, suggesting that the distribution differed according to the types of mucosal injury in the short-term NSAID medication [7].

Our results demonstrate the contrasting distribution of ulcers and erosions in the long-term NSAID users having OGIB, indicating the possibility that distribution of NSAID-induced small intestinal lesion differ according to the types of mucosal injury.

Junichi Iwamoto[1] , Yoshifumi Saito[1], Akira Honda[1], Tadashi Ikegami[1], Yuji Mizokami[2], Yasushi Matsuzaki[1]
1) Tokyo Medical University Ibaraki Medical Center, Tokyo; 2) University of Tsukuba, Tokyo, Japan

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Hepatic arteriovenous malformation in Rendu-Osler-Weber syndrome

To the Editor,

We read with interest the recent article by Takafumi Taguchi et al entitled “Hepatic arteriovenous malformation with hyperammonemia in Rendu-Osler-Weber syndrome” [1]. We are not in disagreement with any of the excellent imaging findings. However, initial and follow-up diagnostic approach of liver involvement in Hereditary Hemorrhagic Telangiectasia (HHT), or Osler-Weber-Rendu disease can be also performed with ultrasonography. We would like to present an additional useful imaging tool: ultrasonographic findings of hepatic arteriovenous malformations (VMs) in a case of HHT presented in our department.

The patient illustrated below, a 66-year-old Caucasian man, with known history of Osler-Weber-Rendu disease, was referred for further investigation and possible interventional management of recurrent episodes of epistaxis. The preoperative ultrasound examination revealed hepatomegaly with relatively abnormal echogenicity. This abnormality of liver parenchyma was consistent with hepatic nodular changes (Fig. 1) and vascular alterations. More specific the prominent imaging findings of these alterations included hepatic artery dilatation associated with tubular structures parallel to the portal branches representing dilated arterial branches (Fig. 2a). The diameter of the proper hepatic artery was 8mm, with normal measurements in healthy population referred up to 2.61±0.64. A dilated diameter of the hepatic artery represents a very sensitive diagnostic parameter for hepatic VMs in HHT, without an overlap between HHT patients with liver involvement or patients with HHT without liver involvement as well as patients with cirrhosis and healthy subjects. Color Doppler Sonography (CDS) revealed prominent and tortuous arterial branches with high-velocity (peak systolic velocity PSV: 177 cm/sec, end diastolic velocity EDV: 63, 5 cm/sec, resistivity index RI: 0.64) (Fig. 2b). In our patient the portal vein had normal sonographic aspect and the size of spleen was normal. In general sonographic findings of the HHT are severe dilation of the hepatic artery (>7mm) and its branches which are the primary diagnostic criteria are included. Additional sonography reveals dilated celiac and hepatic arteries and tortuous intrahepatic tubular structures.

Color Doppler Sonography is helpful as a noninvasive method for examining the hepatic vasculature of patients with HHT and assists in the confirmation of the arterial nature of the intrahepatic tubular structures [2]. Moreover, abnormal Doppler waveforms with increased flow velocities are suggestive for this condition. RI usually is normal due

Fig 1. B-Mode ultrasound para-axial image of liver (right lobe): hyperechoic micronodular changes throughout liver parenchyma. Vascular alterations also present.

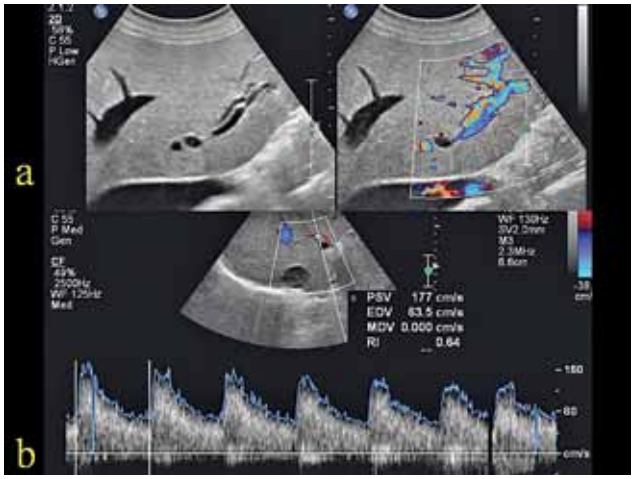

Fig 2. Color Doppler Sonography: a) prominent and tortuous arterial branches (hepatic artery dilatation associated with tubular structures parallel to the portal branches representing dilated arterial branches) with b) high-velocities (PSV and EDV).

to both PSV and EDV increase (high EDV due to low parenchymal resistances). Hepatic involvement in Osler – Rendu – Weber disease can not only be detected with US and Color Doppler Sonography, but it also can be graded according to the severity of the hepatic vascular malformations[3].

Savas Deftereos, Eugenia Vranou, Eleftheria Michailidou, Panos Prassopoulos
Radiology Department, Democritus University of Thrace, Alexandroupolis, Greece

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Clostridium difficile infection in gastroenterology settings: more frequent or better diagnosed?

To the Edtor,

Clostridium difficile (*Cl. Diff.*) is recognized as a cause of infectious colitis usually occuring as a complication of antibiotic therapy in elderly hospitalized patients. The reported incidence of *Cl. Diff.* infection remained stable at a rate of 30-40 cases per 100,000 admissions until the latter 1990s but has risen in the last years, with an alarming increase of severe and fatal cases, as demonstrated in recent studies [1, 2]. In the Western world, *Cl. Diff.* infection predominantly affects elderly patients but the risk of infection has been recognized by the CDC in populations not previously considered at risk, such as young and previously healthy persons [3].

Little is known about *Cl. Diff.* prevalence, severity and risk factors in gastroenterology units. In the Quiz HQ 61 published in the last issue of JGLD, Cojocariu et al warns of the risk of *Cl. Diff.* infection in gastroenterology settings [4] and comments on its diagnosis, risk factors and therapy. Six years ago, we reported a case of *Cl. Diff.* infection in a healthy immunocompetent 56-year-old male patient, previously exposed to antibiotics as an outpatient [5].

These two cases brought about the following comments, which we would like to share with the authors.

1) We have observed an increasing incidence of *Cl. Diff.* infection as a cause of nosocomial diarrhea in gastroenterology settings. In 2011, in a 12-months interval, we diagnosed 27 cases (mean age 63.55 yrs; F/M: 14/13) per approximately 12,000 admissions. This figure is more than 20-fold higher than our previous data (2005), although still 10-fold lower than in recent papers from North America [6]. Diagnosis of *Cl. Diff.* infection was made in the presence of diarrhea and a positive fecal cytotoxin assay or a pathognomonic endoscopic appearance of pseudomembranous colitis, or a pathological diagnosis of *Cl. Diff.* infection (volcano-like exudate).

2) Although the vast majority of infected patients were still at risk individuals (elderly, neutropenic/immunosuppressed) we would like to stress the cases of *Cl. Diff.* infection diagnosed in young, healthy outpatients, previously exposed to antibiotics (4 patients).

3) Despite the reduced number of *Cl. Diff.* infection in IBD patients in our experience (2 cases), we emphasise that endoscopy was not helpful in diagnosing *Cl. Diff.* infection in these particular patients.

4) As *Cl. Diff.* is the most common cause of nosocomial diarrhea, adequate measures should be taken to prevent and control infection since *Cl. Diff.* causes heavy contamination of the patient's environment and spores can survive on dry surfaces for up to several months! Patients should be assigned single rooms with a private bathroom; hypochlorite based solutions are indicated for cleaning. Antibiotic (clindamycin, fluoroquinolones, cephalosporins, macrolides) restriction/avoidance and patient education are recommended [7].

Conclusions: Gastroenterologists should be aware of the increasing number and severity of *Cl. difficile* infection in patients with chronic diarrhea admitted for gastroenterological examination. A high index of suspicion in all patients presenting with moderate-to-severe watery diarrhea is essential for the diagnosis. Antibiotics (metronidazole/vancomycin) and a variety of interventions destinated to prevent and control spreading of infection should be rigorously applied in gastroenterology settings.

Liana Gheorghe, Roxana Vadan
Razvan Cerban, Cristian Gheorghe

Center for Digestive Diseases and
Liver Transplantation, Fundeni Clinical Institute
Bucharest, Romania

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