DYSPEPSIA IN ACUTE FALCIPARUM MALARIA : A CLINICO-PATHOLOGICAL CORRELATION

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Abstract. Gastrointestinal symptoms are common in acute falciparum malaria. Dyspepsia often occurrs in such patients and sometimes it is exceptionally severe. However, the pathogenesis of the dyspeptic symptoms in malaria has not been clearly defined. Upper gastrointestinal endoscopy was performed in 40 patients with acute falciparum malaria in order to correlate the dyspeptic symptoms with the macroscopic (endoscopic) and microscopic (histologic) pathology of stomach and duodenum. The patients were divided into a dyspeptic group (n = 20, male/female ratio = 17/3, age range 18-50 years, mean age = 28.85 + 9.14 years), and a non-dyspeptic group (n = 20, male/female ratio = 16/4, age range 15-47, mean age 26.05 + 9.98 years). The findings revealed that dyspepsia correlated with topographic endoscopic pangastritis (p = 0.0014), the category of endoscopic antral gastritis (p = 0.013), and the histologic severity of antral gastritis (p = 0.0434). The results suggested that gastritis should be considered in acute falciparum malaria patients presenting with dyspepsia.

INTRODUCTION

Patients with acute falciparum malaria commonly present with gastrointestinal symptoms such as abdominal pain, anorexia, nausea, vomiting, and diarrhea (Karney and Tong, 1972). Approximately one-third of the patients had gastrointestinal symptoms during their first attack of malaria (Bartelloni *et al,* 1967). One of the common symptoms in those patients was dyspepsia (abdominal pain, nausea, and vomiting). Upper gastrointestinal endoscopy is a diagnostic technique that offers clinical information in the dyspeptic patients by allowing visual inspection of the mucosal surfaces of the upper gastrointestinal tract.

The objective of this study was to correlate the clinical symptom of dyspepsia and the gastroduodenal pathology in the patients with acute falciparum malaria.

MATERIAL AND METHODS

Definition of dyspepsia : Dyspepsia was defined according to the criteria of the Health and Public Policy Committee (1985).

Patients

Entry criteria: Between August and November 1991, 40 patients with acute uncomplicated falciparum malaria diagnosed by blood smear were admitted to the Hospital for Tropical Diseases (Warrell *et al,* 1989). The patients were divided into two groups, with dyspepsia (n = 20) and without dyspepsia (n = 20). The dyspeptic patients had epigastric pain during the acute phase of the malarial attack prior to admission. All patients received oral quinine and tetracycline as the malarial treatment.

Exclusion criteria: We excluded patients who had taken antibiotics, compounds containing bismuth, anti-ulcer drugs, nonsteroidal anti-inflammatory drugs (NSAIDs) in the previous three months, those who were pregnant or had undergone previous upper gastrointestinal surgery, those who had experienced of epigastric pain in the preceding one month prior to the acute malarial attack.

Methods

All patients, after giving informed consent to the study, underwent upper gastrointestinal endoscopy with mucosal biopsies taken from the antrum

(within 2 cm of the pylorus), the corpus, and the duodenal bulb. All positive endoscopic lesions were also biopsied. The biopsy specimens were fixed in 10% formalin and processed to paraffin. After staining with hematoxylin and eosin, Warthin silver, and also Giemsa, the biopsies were examined for gastritis and duodenitis according to the Sydney system (Misiewicz *et al,* 1990), for *Helicobacter pylori* and for malarial parasites respectively.

This study was approved by the Ethical Committee of the Faculty of Tropical Medicine, Mahidol University.

Statistical analysis

Differences between groups of the patients were assessed using chi-square, Fisher's exact, or Student's *t*-tests as appropriate.

RESULTS

The patients' characteristics are shown in Table 1. There were no statistically significant differences between the two groups.

The macroscopic pathology (endoscopic findings) revealed that the pangastritis (combination of corpus and antral gastritis) was more common in the dyspeptic patients ($p = 0.0014$), while the morphologic findings showed that the two groups had significant differences with respect to the severity of gastritis ($p = 0.0027$) and the category of antral gastritis ($p = 0.013$) (Table 2. Fig 1, 2).

The microscopic pathology (histology) demonstrated that topographic pangastroduodenitis was frequently observed in both groups ($p < 0.75$) while histologically severe antral gastritis was more

Table 1

Clinical and laboratory characteristics of the patients.

	Dyspepsia (n = 20)	Non-dyspepsia (n = 20)
Male/female	17/3	16/4
Age (years) :		
mean + SD	28.85 + 9.14	26.05 + 9.98
range	18-50	15-47
Fever duration before admission (days) :		
mean + SD	4.98 + 0.52	4.74 + 0.43
range	3-5	3-5
Liver size:*		
mean + SD	1.04 + 0.72	1.12 + 0.61
range	0-3	0-4
Splenic size:*		
mean + SD	1.02 + 0.15	1.13 + 0.43
range	0-3	0-5
Geometric mean parasite count (/μl) :		
mean	7,943.28	5,623.41
range	23-132,600	27-223,630

* cm below costal margin.

Table 2

Endoscopic findings.

	Dyspepsia (n = 20)	Non-dyspepsia (n = 20)
Topography		
Gastritis* :	13 (65%)	3 (15%)
corpus*	6 (30%)	0 (0%)
antrum*	13 (65%)	3 (15%)
No gastritis	7 (35%)	17 (85%)
Duodenitis	7 (35%)	1 (5%)
No duodenitis	13 (65%)	19 (95%)
Morphology		
Severity of gastritis* :		
nil	7 (35%)	17 (85%)
mild	3 (15%)	3 (15%)
moderate	7 (35%)	0 (0%)
severe	3 (15%)	0 (0%)
Severity of duodenitis :		
nil	13 (65%)	19 (95%)
mild	1 (5%)	1 (5%)
moderate	4 (20%)	0 (0%)
severe	2 (10%)	0 (0%)
Category of corpus gastritis :		
normal	14 (70%)	20 (100%)
erythematous (E)	2 (10%)	0 (0%)
flat erosive (F)	1 (5%)	0 (0%)
E + F	3 (15%)	0 (0%)
hemorrhagic	0 (0%)	0 (0%)
Category of antral gastritis :		
normal	7 (35%)	17 (85%)
erythematous (E)	5 (25%)	3 (15%)
flat erosive (F)	3 (15%)	0 (0%)
E + F	4 (20%)	0 (0%)
hemorrhagic	1 (5%)	0 (0%)
Category of duodenitis :		
normal	13 (65%)	19 (95%)
erythematous (E)	4 (20%)	1 (5%)
flat erosive (F)	1 (5%)	0 (0%)
E + F	1 (5%)	0 (0%)
hemorrhagic	1 (5%)	0 (0%)

* Significant difference between the dyspeptic and non-dyspeptic patients ($p < 0.05$); all other differences were not significant.

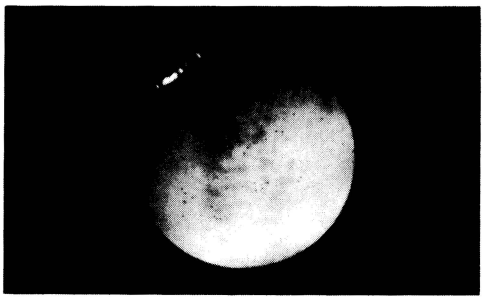

Fig 1—Erythematous antral gastritis, the common endoscopic finding in the dyspeptic patients.

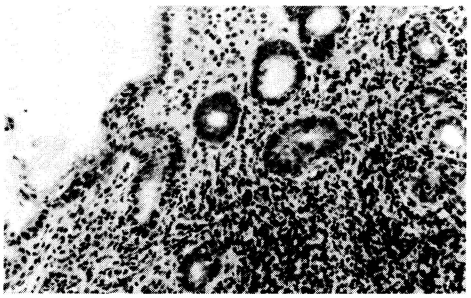

Fig 2—Severe antral gastritis (H&E, × 200).

common in the dyspeptic patients (p = 0.0435) (Tables 3-5, Fig 3, 4).

There were no statistically significant differences between the two groups with respect to sequestered parasitized erythrocytes (p = 0.4845, p = 0.7515, p = 0.4782), capillary congestion (p = 0.2112, p = 0.1163, p = 0.1088), mucosal hemorrhage (p = 0.4288, p = 0.4936, p = 0.1435), mucosal edema (p = 0.5358, p = 0.5368, p = 0.8196) and the presence of *Helicobacter pylori* (p = 0.2633, p = 0.3442, p = 0.1765) in the corpus, antrum, and duodenum, respectively.

Topographic macroscopic and microscopic gastritis revealed no significant correlation (p =

Table 3

Histological findings of corpus.

	Dyspepsia (n = 20)	Non-dyspepsia (n = 20)
Topography		
Gastritis :	17 (85%)	17 (85%)
acute	1 (5%)	0 (0%)
chronic	16 (80%)	17 (85%)
No gastritis	3 (15%)	3 (15%)
Morphology		
Severity of gastritis :		
mild	7 (35%)	6 (30%)
moderate	7 (35%)	9 (45%)
severe	3 (15%)	2 (10%)
Sequestered parasitized erythrocytes	11 (55%)	9 (45%)
Capillary congestion	3 (15%)	6 (30%)
Mucosal hemorrhage	12 (60%)	8 (40)
Mucosal edema	4 (20%)	2 (10%)
Positive *H. pylori*	6 (30%)	2 (10%)

No significant difference (p > 0.05) between the dyspeptic and non-dyspeptic patients.

Table 4

Histological findings of antrum.

	Dyspepsia (n = 20)	Non-dyspepsia (n = 20)
Topography		
Gastritis :	18 (90%)	17 (85%)
acute	2 (10%)	0 (0%)
chronic	16 (80%)	17 (85%)
No gastritis	2 (10%)	3 (15%)
Morphology		
Severity of gastritis :*		
mild	5 (25%)	7 (35%)
moderate	5 (25%)	9 (45%)
severe	8 (40%)	1 (5%)
Sequestered parasitized erythrocytes	9 (45%)	10 (50%)
Capillary congestion	5 (25%)	8 (40%)
Mucosal hemorrhage	10 (50%)	10 (50%)
Mucosal edema	6 (30%)	4 (20%)
Positive *H. pylori*	5 (25%)	3 (15%)

* Significant difference between the dyspeptic and non-dyspeptic patients ($p < 0.05$); all other differences were not significant.

Fig 3—Ring forms of *Plasmodium falciparum* (arrow) (Giemsa, × 400) in corpus gastritis.

0.5). There were 20 out of 40 cases (50%) in which macroscopic and microscopic pathology showed the same topographic findings (16 cases of gastritis and 4 cases of non-gastritis).

DISCUSSION

Acute falciparum malaria is usually associated with a variety of gastrointestinal symptoms (Harinasuta and Bunnag, 1989). Dyspepsia is one of the common gastrointestinal symptoms in the acute phase of malarial infection. Although common, the etiology of dyspepsia in acute malarial attack is unknown. Upper gastrointestinal endoscopy was the first method that could investigate the dyspeptic cause.

In the present study, gastritis and duodenitis were defined according to the recent classification of the Sydney system in order to enable more accurate and extensive correlations between the macroscopic and microscopic pathology. According to this system, the gastritis is acute if neutrophils are the predominant inflammatory cells, while the

Table 5

Histological findings of duodenum.

	Dyspepsia (n = 20)	Non-dyspepsia (n = 20)
Topography		
Duodenitis:	16 (80%)	15 (75%)
acute	0 (0%)	0 (0%)
chronic	16 (80%)	15 (75%)
No gastritis	4 (20%)	5 (25%)
Morphology		
Severity of gastritis :		
mild	3 (15%)	15 (75%)
moderate	3 (15%)	0 (0%)
severe	10 (50%)	0 (0%)
Sequestered parasitized erythrocytes	10 (50%)	6 (30%)
Capillary congestion	1 (5%)	5 (25%)
Mucosal hemorrhage	8 (40%)	7 (35)
Mucosal edema	4 (20%)	1 (5%)
Positive *H. pylori*	4 (20%)	1 (5%)

No significant difference ($p > 0.05$) between the dyspeptic and non-dyspeptic patients.

gastritis is classified as chronic if there is a concomittant increase in chronic inflammatory cells.

The results revealed that topographic endoscopic pangastritis was frequently observed in the dyspeptic patients, while the category of endoscopic antral gastritis correlated with the dyspeptic symptom. However, topographic histological gastroduodenitis was demonstrated in both groups without significant difference. Only the histological severity of antral gastritis correlated with dyspepsia. Histologically severe and moderate forms of antral gastritis were frequently demonstrated in the dyspeptic and non-dyspeptic groups, respectively.

There are no reports on gastric pathology in live malaria patients with dyspepsia. Most reports on gastrointestinal pathology in acute falciparum malaria patients have come from fatal cases (Karney and Tong, 1972; Boonpucknavig *et al,* 1984).

Olsson and Johnston (1969) reported that there was no apparent correlation between abnormal small intestinal biopsies in acute falciparum malaria patients and the presence of gastrointestinal symptoms, however our study showed that the histologic severity of antral gastritis correlated with dyspepsia.

Most of the biopsy specimens (34/40 cases) in both groups showed chronic gastritis associated with predominant mononuclear infiltration according to the Sydney system. Interestingly, malaria infection was in the acute phase of disease while the histology revealed a chronic type of gastritis. Possibly mononuclear cells represented a tissue immune response of the body to malarial infection. The pathogenesis of gastroduodenitis in the patients possibly resulted from cytoadherance of the parasitized erythrocytes to the capillary endothelium

(Macpherson *et al,* 1985) and also the sequestered parasitized erythrocytes within the same vessels, producing muscosal ischemia and injury. If gastritis was severe enough, it might cause dyspepsia. The predominant mononuclear infiltration also confirmed that the patients did not take any NSAIDs prior to admission, because the predominant mucosal inflammatory cells of NSAID users are neutrophils (Whitehead, 1990).

In this study the endoscopically normal mucosa was histologically confirmed in only 50% of the patients. The remaining cases showed various degrees of gastritis. It appeared therefore that the endoscopic diagnosis of normality in the gastroduodenal mucosa was unreliable. Although we used the Sydney system, the correlation between the macroscopic and microscopic pathology was relatively poor.

In summary, our findings showed that dyspepsia in acute falciparum malaria patients correlated with endoscopic pangastritis, especially endoscopic antral gastritis and the histologic severity of the antral gastritis. Thus clinicians should be aware of gastritis in acute malaria, avoiding the use of concomittant treatment with ulcerogenic drugs which may aggravate the severity of the gastritis and possibly lead to upper gastrointestinal hemorrhage. However, many dyspeptic patients benefit from the treatment with antacid or H_2 blockers for relief of this symptom.

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