Chronic gastrointestinal inflammation and cerebrovascular events

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ARTICLES

Ghali WA, Quan H, Feasby TE. *Helicobacter pylori* and cerebrovascular disease. *Stroke* 2001;32:1936.

Keene DL, Matzinger MA, Jacob PJ, Humphreys P. Cerebral vascular events associated with ulcerative colitis in children. *Pediatric Neurology* 2001;24:238-43.

ARTICLE SUMMARIES

Ghali et al, from the University of Calgary, Alberta, reported a cross-Canada study of in-hospital stroke and death complicating carotid endarterectomy. Patients with a diagnosis of peptic ulcer disease (PUD) at the time of admission were found to have a higher likelihood of sustaining a stroke than those without PUD (10.3% versus 4.1%, $P=0.022$). Multivariate analysis adjusting for age, urgency of admission and medical comorbidity resulted in an odds ratio of 2.12 for stroke in patients with PUD.

Keene et al reported three pediatric cases in which a cerebral vascular complication resulted from active ulcerative colitis. The first patient was a five-year-old boy with extensive brain infarction due to intracranial venous stasis or thrombosis. The second patient was a 13-year-old girl with widespread ischemic cerebral injury immediately fol-

lowing a subtotal colectomy. The third patient was a 12-year-old boy with sagittal sinus thrombosis. The case report literature is reviewed and current theories of thrombogenesis in inflammatory bowel disease (IBD) are summarized below.

DISCUSSION

Gastroenterologists are frequently involved in the management of patients with cerebrovascular disease (CVD), usually surrounding issues of feeding difficulties or gastrointestinal bleeding associated with salicylate or anticoagulant therapy. However, patients seldom incur a cerebrovascular event as a consequence of their gastrointestinal disease. Two recent Canadian-authored publications in the neurology literature remind us of the potential pathogenic role of chronic gastrointestinal inflammation in CVD. One pertains to chronic *Helicobacter pylori* infection, the other to IBD.

The article by Ghali et al revealed that patients with a history of PUD are twice as likely to have a stroke complicating carotid endarterectomy than those without. This has been an issue fraught with controversy. Most of the literature in this area addresses the role of *H pylori* as an atherogenic factor in coronary artery disease (CAD), although CVD has also been studied.

There are two proposed mechanisms by which *H pylori* might promote ischemic events: as a direct vascular patho-

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gen, or by upsetting the equilibrium between thrombosis and fibrinolysis by altering levels of inflammatory mediators. Regarding the former mechanism, *H pylori* has been identified in human carotid atherosclerotic plaques by some authors but not others (1,2). However, more attention has been paid to the latter theory, particularly in relation to CAD. Individuals with evidence of CAD have been shown to have a higher prevalence of *H pylori*, even when correcting for other known risk factors. It has been proposed that this higher prevalence is due to elevated fibrinogen levels or peripheral white blood count (3). Similar data were found for atherosclerotic CVD (4). The more virulent CagA-positive *H pylori* strains, which elicit a more vigorous systemic inflammatory response, have been found to be the specific strains associated with CAD (5). However, a more recent review of the literature, including two meta-analyses, has found little evidence to support the hypothesis that *H pylori* plays a major role in atherogenesis (6).

In contrast, the literature on CVD complicating IBD is based largely on case reports. The paper by Keene et al is no exception. In further contrast, cerebrovascular events in patients with IBD are thought to arise from a hypercoagulable state, or rarely from vasculitis, as opposed to atherosclerosis. This is underlined by the relatively high incidence of IBD-related CVD in children compared with adults, and by the large proportion of venous as opposed to arterial events. Results of autopsy studies suggest that 8% of IBD patients have sustained a thromboembolic cerebrovascular injury (7). The majority of these events are thought to occur in relation to the degree of IBD activity (8).

The mechanisms underlying vascular thrombosis in IBD have been recently reviewed (9). Pathogenesis is still poorly understood but likely multifactorial. Factor V Leiden probably plays a significant role in predisposing patients with thrombophilic IBD thrombogenesis. Romagnuolo et al (10) in Edmonton, Alberta, also demonstrated an increased prevalence of hyperhomocysteinemia in patients with IBD – another recognized thrombotic risk factor.

To a gastroenterologist, the possible vascular complications of *H pylori* infection are at least curious, and at best provocative, but currently carry few if any clinical implications. On the other hand, the occurrence and management of thromboembolic disease in IBD patients pose significant challenges. I have been involved in managing two such patients during the past year; both developed deep vein thrombosis while actively bleeding from severe ulcerative colitis. One patient was successfully treated with systemic corticosteroid therapy and placement of an inferior vena cava filter, the other required urgent colectomy. Acute central neurological events in our IBD patients should also alert us to the possibility of a thrombotic vascular complication.

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