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The infamous story of incident stroke and inflamed gall bladder!

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Full Text

The link between gallbladder disease (GD) and stroke has long been recognized, but recently, the relationship has been found to be far more complex.[1] GD, cardiovascular disease (CVD), and stroke are very common public health issues. The current epidemiological transition in low and middle economic countries has pushed the global burden of CVD and stroke higher, accounting for 30% of global deaths, and will continue to lead the global mortality trend in the future.[1],[2]

The association between GD and CVD/stroke assumes three different domains in current understanding and the description available in the published literature. This association is said to be related to the shared features in the pathophysiological mechanisms, i.e., cholesterol accumulation in the gall bladder as well as arteriosclerosis in the arterial wall.[2] The precipitation of excess cholesterol in bile as solid crystals is required for cholesterol gallstone formation. Stroke and CVD have atherosclerotic plaques as the cornerstone of pathology.

First, in the past studies, GD patients showed an increased prevalence of CVD/stroke risk factors, such as hypertension, diabetes, hyperlipidemia, and chronic obstructive pulmonary disease. Another possible explanation for this association may be shared metabolic pathways.[1],[2] It is reported that low plasma levels of insulin-like growth factor-1 [IGF-1] may lead to the development of both GD and CHD. Patients with a low level of IGF-1 have been reported to be susceptible to altered postprandial gall bladder emptying. This results in prolonged nucleation of monohydrate cholesterol crystals from the supersaturated bile to form macroscopic stones.[1],[2]

Inflammation could also play an important role in the association between these two conditions. High circulating levels of total homocysteine, C reactive protein, and other proinflammatory mediators have been incriminated in both the conditions.

Oxidation stress also plays an important role in the development of GD and CVD/stroke.[1],[2]

Many studies indicate that gut microbiota influence the host health.[3],[4] A recent study suggests that altered composition of gut microbiota increase the risk of stroke by derived signaling molecules, and GD is related to microbiota dysbiosis in the gut and biliary tract.[3],[4]

Second, GD is a multifactorial disease with associated risk factors, including gender, age, genetic factors, race, obesity, rapid weight loss, diet, alcohol use, diabetes, hyperlipidemia, drug use, and pregnancy.[1],[2]

Similarly, GD and stroke have certain risk factors in common including gender, age, genetic background, race, obesity, diet, alcohol consumption, diabetes, and hyperlipidemia.[5]

After adjusting for the potential confounding factors, a recent population-based cohort study demonstrated a significant association between GD and increased risk of all strokes, ischemic, and hemorrhagic.[5] GD, therefore, might be a new found risk factor for stroke, including ischemic and hemorrhagic stroke and aneurysmal subarachnoid hemorrhage (SAH).[6],[7] Similarly, Cho et al., reported that in patients presenting with acute cholecystitis, a past history of stroke emerged as a significant independent risk factor. In their study of patients with acute cholecystitis, five independent risk factors, such as age >60 years, male sex, presence of CVD, diabetes, and a past history of stroke (odds ratio [OR] of 8.017; 95% confidence interval [CI] 2.650–24.804), were found. In their report, 84% of patients with a history of stroke presented with acute cholecystitis versus 32.2% without a history of stroke ($P < 0.001$). Hence, patients with a history of stroke had an 98-fold higher risk for the development of acute cholecystitis.[5]

Finally, the third form of association is the occurrence of acute cholecystitis in a patient who presents with acute stroke.[7] This association is certainly rare and not well clarified yet. Acute cholecystitis was reported to follow acute surgical interventions and critical care settings with a variable frequency of 1%–4.6%; occurring within a week-to-one month after the preceding incident. The pathology has been hypothesized as a compromise of the circulation to the gall bladder and biliary obstruction due to the concentration of bile. Not many reports exist linking acute cholecystitis to acute stroke. Koizumi et al., reported that of the 252 patients who presented with acute stroke, which included both ischemic and hemorrhagic stroke and SAH, 2.7% exhibited acute cholecystitis.[8] Ushiyama et al., reported the development of acute cholecystitis in 1.2% of acute stroke patients.[9] Fukuoka et al., reported 1.4% of patients with acute ischemic stroke who developed acute cholecystitis. In the majority of studies, acalculous cholecystitis predominates.[7]

This study reports nearly identical findings emphasizing the importance of being vigilant about the development of acute cholecystitis to optimize outcome.[8]

The mechanisms underlying the development of acute cholecystitis after acute stroke have been hypothesized to be (1) compromised circulation to the gall bladder, and biliary obstruction due to contractile dysfunction as a result of a bed-ridden status; (2) infection caused by gallstones and/or the susceptibility to infection due to the presence of diabetes. Several reports also link the fasting period to the incidence of cholecystitis. This association is likely to be due to the hyposecretion of gastrointestinal hormones such as cholecystokinin, resulting in contractile dysfunction of the gall bladder. Occurrence of autonomic dysfunction in patients with acute ischemic stroke may also cause biliary contractile dysfunction.[7],[9],[10]

It is pertinent to identify the presence of acute cholecystitis and provide suitable treatment in these patients with acute stroke, who otherwise may not be in a position to recognize or complain. Early ambulation and resumption of nutritional intake may also help to prevent the occurrence of acute cholecystitis in patients with acute stroke.

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