Acalculous biliary pain: Motility dysfunction and functional pain

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Most patients with gallstones (up to 80%) experience a satisfactory outcome with relief of symptoms following surgery (1). Such a high response may in part be attributable to high patient expectations that their symptoms will worsen without surgery, their assumption being that surgery will provide a cure. Presumably this biliary-type pain originates either from obstruction of the gallbladder contracting against a fixed (eg, gallstone) or functional (eg, muscle spasm) obstruction at the cystic duct, or at the level of the sphincter of Oddi (SO), or from the inflammation (cholecystitis, cholangitis) that results. The basis of such pain is less clear if gallbladder smooth muscle contractility is defective, as occurs in cholesterol gallstone disease (2). Although biliary pain heralds cholelithiasis and cholecystitis, most (80%) people harbouring gallstones never experience pain (3). Gallstones and abdominal pain are thus not necessarily synonymous. It is, therefore, not surprising that chronic abdominal pain persists in up to 50% following cholecystectomy (4). Many of these complaints are nonspecific, but 14% have true biliary pain attributable to a definable cause, eg, SO dysfunction (5). The figures for surgical failures might be higher with the advent of laparoscopic cholecystectomy, which has dramatically increased the rate of surgeries over the past decade. Predictors of this 'postcholecystectomy syndrome' include psychological vulnerability (6), chronic symptoms before cholecystectomy and pain six weeks after cholecystectomy.

The situation becomes even less clear when no structural abnormality is evident. Such 'functional' biliary type pain (7) (acalculous gallbladder disease) requires careful investigation to eliminate all structural abnormalities, particularly

very small gallstones, as the basis for recurrent biliary-type pain. This includes repeating transabdominal ultrasound, which detects stones larger than 3 to 5 mm in diameter, performing an endoscopic ultrasound for tiny stones smaller than 3 mm in diameter and using accurate microscopy of gallbladder bile to detect microlithiasis (8). The accompanying article by Janowitz et al (pages 363-366) demonstrates that the lipid composition of human gallbladder bile remains stable even when frozen and stored. Although it is best to centrifuge bile immediately and use microscopy to detect cholesterol microcrystals and/or bilirubin granules, if a delay is unavoidable, bile can be frozen for later analysis.

The cholecystokinin (CCK)-provocation test can cause pain in some normal individuals, depending on the rate of CCK infusion. It does not, however, predict a symptomatic benefit from cholecystectomy and should be abandoned when evaluating acalculous biliary pain (9). More accurate is the quantitative measurement of gallbladder emptying under controlled conditions with a slow infusion of CCK – CCK cholescintigraphy (7). In well defined patients with acalculous gallbladder disease and low ejection fractions on CCK ultrasonography, 59% to 75% continue to have symptoms (10,11). Conversely, some 90% experience complete or substantial relief following cholecystectomy (11-13). Here, impaired gallbladder emptying appears to be a marker of acalculous biliary pain. The basis for such impaired gallbladder emptying is a defect in the contractile machinery (14).

Again, the dilemma is, what causes the pain? The biliary tract is a low-pressure conduit in which the gallbladder acts as a reservoir to decompress and regulate its pressure. Bile ducts lack a smooth muscle layer, leaving the SO a prime

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suspect, especially when pain persists after cholecystectomy. The sphincter may be stenotic (from a fixed obstruction due to fibrosis and/or muscle hypertrophy) or exhibit dyskinesia (obstruction from muscular incoordination or hyper-tonicity). The diagnostic criteria outlined by the Rome II consensus conference include the gold standard test, SO manometry (7). This invasive procedure is best reserved for those with objective evidence of intermittent biliary obstruction. Patients suspected of having SO manometry should undergo a preliminary evaluation – a nuclear medicine scan that quantifies the transit time from the hepatic hilus to the duodenum (choledochoscintigraphy). Morphine provocation appears to increase its sensitivity (15). Those with SO stenosis have sufficient criteria for a fixed organic basis and benefit from going directly to sphincterotomy (7).

All functional biliary pain, however, might not relate to motility abnormalities of the gallbladder or the SO. Abnormal manometry of the sphincter may reflect a mere generalized motility disorder of the gut, perhaps involving the duodenum and jejunum (16). Conversely, visceral hypersensitivity, a potential basis for pain in functional gastrointestinal disorders, represents an abnormal sensitivity to a relatively innocuous stimulus. The basis for this could be modified receptor sensitivity at the level of the biliary tract (17) or adjacent viscus (duodenal hyperalgesia) (18), neuronal hyperexcitability in the dorsal horn of the spinal cord and/or altered central modulation of sensory inputs. Such biliary-type pain may even be part of the irritable bowel syndrome.

Thus, acalculous biliary pain means no obvious organic basis (structural or stone disease), but 'functional' is giving way to dysfunction, be it motor or sensory. Further, understanding the basis for the pain implies a potential for medical therapy, drugs acting specifically on the rich neural connections between the gallbladder, SO and the adjacent stomach and duodenum. Functional pain now has meaning.

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