Editorial

Specific radiological findings, if present, can offer high accuracy for the differentiation of Xanthogranulomatous cholecystitis and gallbladder cancer

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Xanthogranulomatous cholecystitis (XGC) is rare form of chronic cholecystitis that is marked by a focal or diffuse destructive inflammatory process. The pathophysiology behind XGC is speculated to be the result of the extravasation of bile into the gallbladder (GB) wall through the vulnerable region such as Rokitansky-Aschoff sinuses or a small ulceration in the mucosa due to an increase of the inner pressure of biliary tract (1). Penetration of bile into the GB wall is generally attributed to the inflammation of intestinal tissue. Prolonged and more intensive infiltration by inflammatory cells turn acute inflammation into chronic inflammation and different amounts of fibrous tissue, inflammatory cells, and lipid-filled macrophages are appeared within the wall of the GB. XGC regions present themselves as yellow masses (2). This inflammatory process is often spreading to adjacent organs and is continuing for a long period. These inflammatory response result in strong adhesions, forming tumor like mass around the GB. Therefore, it is often difficult to differentiate between XGC and malignant GB lesions.

Clinical, laboratory test features

Patients with XGC showed symptoms similar to those of patients with acute or chronic cholecystitis. Signs and symptoms may include: features of acute cholecystitis, chronic cholecystitis, pain, obstructive jaundice, cholangitis, and palpable mass. It is also dilemma to differentiate XGC from other GB problems by laboratory tests. Yu *et al.* found that tumor markers are frequently elevated in XGC, which leads to bother surgeon for differentiating the disease from carcinoma of the GB (3). Therefore, CA19-9 cannot help surgeons determine the difference between XGC and malignant tumors. However, an explanation for the elevated CA19-9 level is that epithelial cells of the GB wall and bile duct have been injured due to inflammatory conditions. Subsequently, the production of CA19-9 in the epithelium increased, becoming very high, especially in obstructive disease. Mann *et al.* showed a relationship between elevated bilirubin and CA19-9 levels (4). If the level of bilirubin decreased, the level of CA19-9 would also decrease.

Radiological findings

Radiological findings are also nonspecific and similar to other forms of cholecystitis and GB carcinoma. However, some recent reports have shown that specific radiological findings, if present, are highly accurate in differentiating between XGC and GB cancer. In my opinion, if contrast-enhanced ultrasound (CEUS) was performed by an experienced sonographer, the combination findings which are characteristic to XGC on CEUS and CT are the better way to distinguish XGC from GBC.

Ultrasonography

Sonogram demonstrates the presence of gallstones or sludge as well as focal or diffuse thickening of the GB wall that is moderate to marked. Kim *et al.* reported observing intramural hypoechoic nodules on sonography in 73% of cases. They also indicated that, when both diffuse wall thickenings and intramural nodules formation are seen ultrasonographically, there is a strong possibility of XGC (5). Yamamoto *et al.* reported that measuring the GB wall blood flow (GWBF) and both resistance index (RI) and pulsatility index (PI), showing vascular resistance by color Doppler US, also helped differentiate between XGC and GBC (6). They speculated that vascular resistance would increase due to hard tissue around the vessels in advanced GB cancer.

Endoscopic ultrasound (EUS)/EUS-guided fine-needle aspiration (FNA)

EUS FNA is a useful modality for sampling various targets and collecting sufficient tissue specimens to facilitate accurate histological evaluation. However, a negative sample does not necessarily imply benign, due to the possibility of sampling from non-representative areas. Japan has accumulated cutting-edge technology in areas of endoscopic ultrasound-guided fine needle. Hijioka *et al.* reported that the accuracy of EUS FNA was 93.3% for detecting malignancy and 80% for final diagnosis (7).

Computed tomography (CT)

CT findings include diffuse or focal wall thickening, intramural hypoattenuating nodules in thickened walls, a continuous mucosal line, intra-mural hypo-attenuated nodules, and the absence of macroscopic hepatic invasion (8). Diffuse GB wall thickening was seen in 91% and 87.8% of patients with XGC by two separate researchers (8,9). Gall bladder wall thickening in XGC is more commonly diffuse than focal and focal thickening is more likely to be related to carcinoma of the GB. Luminal surface enhancement of the GB wall indicated that the luminal epithelial layer would be preserved. Such findings might make it easier for the physician to differentiate XGC from GB cancer. Certain characteristic findings of CT could provide excellent accuracy for making diagnoses between XGC and GBC. Goshima *et al.* reported that meeting the three features out of five CT findings that are characteristic of XGC can present high accuracy for differentiating XGC from GB cancer, and their sensitivity, specificity, and accuracy were 83%, 100%, and 91%, respectively (10). Uchiyama *et al.* retrospectively analyzed 32 patients with XGC. They indicated that, in patients of chronic GB disease with GB stones, CT findings of the enhanced continuous mucosal line in the thickened GB wall are more likely to indicate XGC (11).

Magnetic resonance imaging

Magnetic resonance imaging (MRI) criteria such as nonfocal wall thickening, type I enhancement, THAD (transient hepatic attenuation difference), and the presence of intramural nodules have also been described as helpful for making a differential diagnosis of XGC as opposed to GB carcinoma. Areas of iso- to hyperintense signals in T2-weighted images correspond to areas of significant xanthogranulomas (12). Currently, diffusion-weighted magnetic resonance imaging (DWI) is becoming popular due to its ability to differentiate malignant and benign lesions based on the assumption that malignant lesions generally display higher cellularity. Ogawa *et al.* showed that the positive signal rate with DWI was significantly higher in GB cancer (78%) than in benign GB diseases (22%) (13).

Positron emission tomography

Fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) could discriminate accurately between malignant and benign, and detect malignant change in benign neoplasms. However, FDG can accumulate in inflammatory lesions with the increase rate of glucose uptake, and FDG-PET is not specific for malignant lesions. Therefore, it is important to understand the diagnostic value of FDG-PET combined with other imaging modalities.

Conclusions

When it comes to the treatment of XGC, we should be more than skeptical about diagnosing XGC and suspect the presence of GB cancer. If patients display characteristic findings of XGC during preoperative evaluation, we need to perform fine-needle aspiration cytology of the GC preoperatively (14). Moreover, intraoperative frozen section biopsies may play an important role. In addition to the application of intraoperative frozen section examination, a combination of clinical and radiological factors can aid

in diagnosis and surgery for XGC. We should judge it in a comprehensive manner. However, the interpretation of intraoperative biopsies may not always be straightforward. Since GB carcinoma and XGC may coexist, radical resection is justified when malignancy cannot be completely ruled out.

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Footnote

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