ORIGINAL ARTICLE

Xanthogranulomatous cholecystitis: a European and global perspective

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Abstract

Introduction: Xanthogranulomatous cholecystitis (XGC) is often mistaken for, and may predispose to, gallbladder carcinoma (GB Ca). This study reviews the worldwide variation of the incidence, investigations, management and outcome of patients with XGC.

Methods: Data from 29 studies, cumulatively containing 1599 patients, were reviewed and results summarized by geographical region (Europe, India, Far East and Americas) with 95% confidence intervals (CIs) to present variability within regions. The main study outcomes were incidence, association with GB Ca and treatment of patients with XGC.

Results: Overall, the incidence of XGC was 1.3–1.9%, with the exception of India where it was 8.8%. The incidence of GB Ca associated with XGC was lowest in European studies (3.3%) varying from 5.1–5.9% in the remaining regions. Confusion with or undiagnosed GB Ca led to 10.2% of patients receiving over or under treatment.

Conclusions: XGC is a global disease and is associated with GB Ca. Characteristic pathological, radiological and clinical features are shared with GB Ca and contribute to considerable treatment inaccuracy. Tissue sampling by pre-operative endoscopic ultrasound or intra-operative frozen section is required to accurately diagnose gallbladder pathology and should be performed before any extensive resection is performed.

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Introduction

Xanthogranulomatous cholecystitis (XGC) is an uncommon form of cholecystitis[1,2] which presents with non-specific symptoms and signs, making it indistinguishable from typical acute or chronic cholecystitis.[3–5] XGC is traditionally a histopathological diagnosis of focal or diffuse acute and chronic cholecystitis. Microscopically, lipid containing histiocytes infiltrating into the outer layer of the muscle lining the gall bladder wall may be seen to form xanthogranulomatous foci and fibrosis owing to extravasation of bile into the gallbladder wall.[6,7]

XGC is frequently misdiagnosed as gallbladder carcinoma (GB Ca) on presentation,[8,9] ultrasound,[10,11] computed tomography (CT)[12] and intra-operatively.[8] This is confounded by reports that GB Ca is more frequently associated with XGC than other forms of cholecystitis.[6,8,13–19] Rates of co-existing carcinoma vary from 2–15% of patients with XGC,[8,20,21] suggesting a causal association.[8] An incorrect diagnosis, which may be as high as 25%,[3] results in inappropriate surgery in the form of open exploration or gallbladder bed resection for GB Ca[3,22,23] rather than simple laparoscopic cholecystectomy for XGC or a missed diagnosis of GB Ca in patients undergoing a laparoscopic cholecystectomy[8,9] who require open exploration or gallbladder bed resection. XGC also is associated with an increased rate of conversion from laparoscopic to open operative procedures[5,9,24,25] owing to procedural difficulty related to local inflammation creating dense adhesions[9,26,27] or gallbladder wall thickening.[4]

A pre-operative ultrasound and CT in patients with XGC may display specific features which are suggestive of XGC. These include the presence of intramural echogenic nodules,[1,4,10,28,29] see

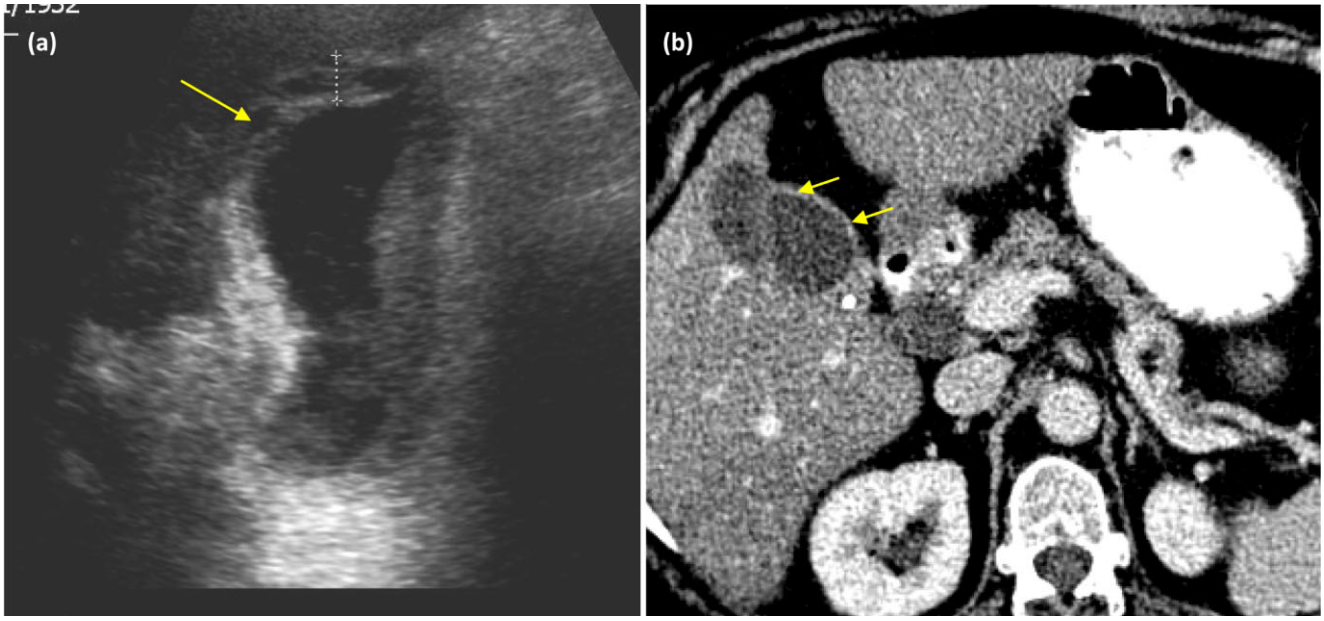

Figure 1 Imaging from patients with xanthogranulomatous cholecystitis (XGC). (a) An ultrasound scan demonstrating diffuse wall thickening (cursor) and intramural echogenic nodules (arrow). (b) Computed tomography (CT) post contrast image demonstrating continuous enhancement of the mucosal wall (small arrows)

Fig. 1, a 'halo sign' (a hypodense curvilinear band),[1,4,10,15,29] intrahepatic duct dilatation[30] and a loss of interface between the gallbladder and the liver.[4,7,11,31–34] Although these features are also seen in GB Ca, visualization of a continuous mucosal line,[4,9,14,34,35] see Figs 1, 2 and 3, and the absence pericholecystic fluid,[34] shown in Fig. 3, which both suggest a diagnosis of XGC rather than GB Ca, may be then used to differentiate between XGC and GB Ca. Although these features have been demonstrated to be effective at detecting XGC and differentiating XGC from GB Ca it is unclear, to date, how frequently these features are reported in routine clinical practice.

The incidence of GB Ca is higher in Indian and Far Eastern populations than in Western populations.[36] As there are a greater number of studies originating from Indian and Far Eastern groups there may also be geographical variation in the incidence, treatment and outcomes of patients with XGC. The aim of this study was to identify the incidence of XGC within a European cohort of patients and to pool these data with published studies to explore geographical variation in rates of XGC and associated GB Ca with the intention of providing the most accurate indication of the true incidence of XGC, its association with GB Ca and outcomes. Secondary outcomes of the study aim to review the proportion of patients who receive correct treatment and the findings and reporting frequency of radiographical investigations for XGC and GB Ca.

Methods

This study was a retrospective study of all patients who underwent a cholecystectomy at St James's University Hospital (SJUH), Leeds, United Kingdom, from June 2005 to December 2010. Patients were identified from the department of pathology database and those with XGC selected for detailed review. Patient notes were reviewed to obtain the presenting signs and symptoms, patient demographic variables, findings at radiological intervention (mucosal line continuity, nodule echogenicity, halo sign, visible loss of interface between the gallbladder and liver, pericholecystic fluid and hepatic duct dilation), the planned and actual operation type, complications, if GB Ca was suspected and histopathological data (gall stones, gallbladder thickening, gallbladder fibrosis and the presence of GB Ca).

Pooling data with other studies

Previously published studies were identified by review of PubMed, Medline, the Cochrane Library and Embase using the search terms 'xanthogranulomatous cholecystitis' and 'fibroxanthogranulomatous fibrosis' (Fig. 4). The reference lists of these studies were searched to identify further studies of relevance. Case reports and case series containing five or less patients with XGC were excluded from review. Of 31 suitable studies, three were excluded as the full paper was not able to be accessed[16,20,37] leaving 29 cohorts, including the present study, for review. Included studies (Table 1) were reviewed for patient demographics, investigative findings, management, operative findings and outcomes, histopathological details of the excised gallbladder, operative complications and the incidence of XGC in the local population. The diagnostic accuracy was also calculated for each study as [1 – (number of missed GB Ca cases + number inappropriate extended resections performed for incorrectly suspected GB Ca)/ total number of XGC patients] × 100. Studies that reported pre-operative radiological findings were recorded.