CASE REPORT

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Xanthogranulomatous Inflammation in Diverse Organ Systems: A Case Report

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Abstract

Background: Xanthogranulomatous inflammation (XGI) is a rare, benign chronic inflammatory condition characterized by the accumulation of lipid-laden foamy macrophages, multinucleated giant cells, fibrosis, and chronic inflammatory infiltrates. Despite its benign nature, XGI often presents with clinical, radiological, and intraoperative features that closely resemble malignant neoplasms, making preoperative diagnosis challenging. Xanthogranulomatous cholecystitis (XGC), the most common form involving the gallbladder, is frequently mistaken for gallbladder carcinoma due to its aggressive appearance.

Case Presentation: We present a hypothetical case of a 56-year-old woman with persistent right upper quadrant abdominal pain, intermittent fever, anorexia, and weight loss. Radiological evaluation demonstrated diffuse gallbladder wall thickening with inflammatory extension into adjacent hepatic tissue, raising a strong suspicion of gallbladder carcinoma. The patient underwent open cholecystectomy, and histopathological examination revealed extensive infiltration by lipid-laden foamy macrophages, multinucleated giant cells, chronic inflammatory cells, fibrosis, and focal necrosis without evidence of malignancy, confirming the diagnosis of xanthogranulomatous cholecystitis. The postoperative recovery was uneventful, and the patient remained symptom-free during follow-up.

Conclusion: This case highlights the significant diagnostic challenge posed by xanthogranulomatous inflammation due to its close resemblance to malignant disease. Histopathological examination remains the gold standard for establishing the diagnosis and differentiating XGI from carcinoma. Greater awareness of this uncommon entity and close multidisciplinary collaboration among clinicians, radiologists, surgeons, and pathologists are essential for accurate diagnosis, appropriate management, and avoidance of unnecessary radical surgical procedures.

Keywords: Xanthogranulomatous inflammation; Xanthogranulomatous cholecystitis; Gallbladder carcinoma; Foamy macrophages; Histopathology; Chronic inflammation; Differential diagnosis; Case report.

Introduction

Xanthogranulomatous inflammation (XGI) is a rare type of chronic destructive inflammation characterized by lipid-laden foamy macrophages, multinucleated giant cells, chronic inflammatory infiltrates, fibrosis, and differing degrees of tissue necrosis [1,2]. Although histologically benign, XGI often mimics a malignant neoplasm on clinical and radiological examination with an infiltrative mass lesion associated with extensive tissue destruction [3,4]. This close similarity presents major problems for clinicians, radiologists and pathologists; resulting in radical surgical interventions that are unnecessary and only providing a definitive diagnosis with histopathological assessment [5,6]. Consequently, knowledge of this rare inflammatory disease is critical to prevent overtreatment and pursue effective management in these patients.

Xanthogranulomatous inflammation was first reported in the kidney and gallbladder but has since been described in other organ systems including the urinary bladder, prostate, testis, epididymis, endometrium, fallopian tube, appendix, colon, pancreas stomach, thyroid gland, salivary glands, and lymph nodes soft tissues [2, 4, 7]. The disease may affect multiple anatomical locations; however, it is a rare disorder [3,8], with the gallbladder and kidney being the most frequent organs involved. Other organ involvement is rare and often leads to diagnostic dilemmas as the clinical and radiological manifestations can closely resemble malignant neoplasms or severe chronic infections [9].

The precise pathogenesis of XGI is not entirely clear, and it is thought to be multifactorial. Chronic bacterial infection, long-standing obstruction, defective lipid transport, impaired macrophage function, immune dysregulation, ischemia and hemorrhage as well as persistent inflammatory stimulation have all been hypothesized to act as potential mechanisms [1,5,10]. For example, these characteristics lead to tissue injury and the deposition of lipid-laden macrophages in which granulomatous inflammation is found with multinucleated giant cells and lymphoplasmacytic infiltrates associated to fibrosis and necrosis [6,11]. Continuous cycles of inflammation and tissue repair finally lead to firm mass-type lesions clinically mimicking infiltrating malignancy [8,12].

The relevant features may be identified on magnetic resonance imaging [9,12], though it is also common for radiological investigations to show abnormal masses with malignancy-mimicking characteristics such as diffuse wall thickening and heterogeneous enhancement with tissue destruction and extension into adjacent structures [4,9,13]. Intraoperatively, the presence of desmoplastic fibrotic tissue, adhesions and inflammatory infiltration increases clinical suspicion for malignancy [5]. Indeed, numerous patients have extensive operations based on a presumed diagnosis of cancer. The gold standard for diagnosis remains histopathological examination, which shows sheets of foamy histiocytes admixed with multinucleated giant cells, lymphocytes, plasma cells and fibrosis with areas of necrosis without cytological evidence of malignancy [2,6,14].

Recognition of the clinicopathological spectrum of XGI holds important therapeutic implications. Despite the commonly needed surgical excision due to diagnostic uncertainty or inevitable irreversible destruction of tissue, timely histopathological diagnosis avoids unnecessary oncological treatment and provides improved reassurance regarding the benignity of the disease occurrence [7,15]. Hence, it is imperative to develop a greater awareness of this rare entity by surgeons, radiologists, and pathologists to enhance diagnostic precision and improve patient management. Moreover, the rare forms define the range of diversity in manifestation and will help to contribute to existing literature [3,10,16].

We now present a rare case of xanthogranulomatous inflammation mimicking malignant neoplasm both clinically and radiologically. We present the clinical presentation, imaging findings, histopathological features, management and outcome with review of current literature to illustrate the diagnostic challenges in this rare inflammatory lesion.

Case Presentation

Patient Information

A 56-year-old female presented to the Department of General Surgery with complaints of intermittent right upper quadrant abdominal pain, low-grade fever, nausea, and loss of appetite for three months. The abdominal pain was dull aching, gradually progressive, and occasionally radiated to the back. She also reported an unintentional weight loss of approximately 4 kg over the previous two months. There was no history of jaundice, vomiting, altered bowel habits, or previous abdominal surgery. Her medical history was

significant for type 2 diabetes mellitus for eight years, controlled with oral hypoglycemic agents. There was no personal or family history of malignancy.

Clinical Examination

On admission, the patient was conscious, oriented, and hemodynamically stable. General physical examination revealed no pallor, icterus, cyanosis, clubbing, lymphadenopathy, or pedal edema. Abdominal examination demonstrated mild tenderness in the right hypochondrium without guarding or rebound tenderness. Murphy's sign was equivocal. No palpable abdominal mass or organomegaly was detected. Examination of other systems was unremarkable.

Laboratory Investigations

Routine laboratory investigations showed a hemoglobin level of 11.2 g/dL, total leukocyte count of 13,800 cells/mm³ with neutrophilic predominance, and an elevated C-reactive protein level of 42 mg/L. Liver function tests demonstrated mildly elevated alkaline phosphatase (186 IU/L), while serum bilirubin, alanine aminotransferase, and aspartate aminotransferase levels were within normal limits. Renal function tests were normal. Tumor markers, including carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9), were within the normal reference range.

Radiological Findings

Ultrasonography of the abdomen revealed a markedly thickened gallbladder wall with multiple gallstones and surrounding inflammatory changes. Contrast-enhanced computed tomography (CECT) demonstrated irregular circumferential thickening of the gallbladder wall with multiple intramural hypodense nodules, dense pericholecystic inflammatory changes, and focal extension into the adjacent hepatic parenchyma. These imaging findings raised a strong suspicion of gallbladder carcinoma.

Surgical Findings

Considering the radiological suspicion of malignancy, the patient underwent an open cholecystectomy. During surgery, the gallbladder was found to be contracted with extensive adhesions to the liver, omentum, and duodenum. The gallbladder wall was markedly thickened and firm, making surgical dissection technically difficult. No enlarged regional lymph nodes or distant metastatic lesions were identified intraoperatively.

Gross Pathological Examination

The resected gallbladder measured 8.5 × 4.0 × 3.0 cm, with diffuse wall thickening measuring up to 1.4 cm. The mucosal surface appeared irregular with multiple yellowish nodular areas and focal ulceration. Multiple mixed cholesterol and pigment gallstones were identified within the lumen. Cut sections demonstrated yellow-white firm nodules extending through the gallbladder wall without evidence of a well-defined tumor mass.

Histopathological Examination

Microscopic examination revealed diffuse infiltration of the gallbladder wall by numerous lipid-laden foamy macrophages intermixed with multinucleated giant cells, lymphocytes, plasma cells, and occasional neutrophils. Extensive fibrosis, cholesterol clefts, and focal areas of necrosis were also observed. The inflammatory infiltrate extended into the perimuscular connective tissue, resulting in marked architectural distortion. Multiple tissue sections failed to demonstrate epithelial dysplasia, cytological atypia, or invasive carcinoma.

Final Diagnosis

Based on the clinicopathological correlation and histopathological findings, a final diagnosis of Xanthogranulomatous Cholecystitis was established.

Treatment and Follow-up

The postoperative period was uneventful. The patient received intravenous antibiotics for five days followed by oral antibiotic therapy and supportive treatment. She was discharged on the seventh postoperative day in stable condition. During the three-month follow-up, she remained asymptomatic, with complete resolution of symptoms and no evidence of postoperative complications or disease recurrence.

Discussion

Xanthogranulomatous inflammation (XGI) is an uncommon type of chronic inflammatory process that is characterized by the accumulation of lipid-laden foamy macrophages, multinucleated giant cells, chronic inflammatory cells, fibrosis and a variable degree of tissue necrosis [1,2]. Histologically benign, XGI shows aggressive clinical, radiological and intraoperative characteristics overlapping with malignant neoplasms. Due to this similarity, it often presents a challenge in diagnosis and can lead to unnecessary extensive surgeries before the histopathological examination [3,4].

The gallbladder and kidney are the most common organs affected, with xanthogranulomatous cholecystitis (XGC) and xanthogranulomatous pyelonephritis (XGP), respectively [5]. However, reports have also shown the isolated involvement of other organs such as the endometrium, fallopian tube, testis, prostate, urinary bladder, pancreas, appendix, thyroid gland, colon and salivary glands which are included in uncommon presentations alongside [6,7]. The infrequency with which these lesions occur often leads to a delayed diagnosis as clinicians will typically prefer malignant or severe infective conditions at the top of their differential.

The precise etiology of XGI is still largely unknown. Various hypotheses have been proposed: chronic bacterial infection, sustained obstruction, ischemic tissue injury, defective lipid metabolism, defective macrophage function and immune dysregulation as well as repeated inflammatory attacks [2-8]. Gallstones and long-standing biliary obstruction are thought to play an important role in the pathogenesis of xanthogranulomatous cholecystitis. When the intraluminal pressure is elevated, Rokitansky-Aschoff sinuses may rupture leading to bile leakage into the gallbladder wall, which in turn can trigger a robust inflammatory response that is marked by an infiltration of lipid-laden macrophages and granulomatous inflammation [9]. Such mechanisms, including chronic infection and obstruction, have been reported in xanthogranulomatous lesions involving other organ systems.

The hypothetical case presented here had both classical clinical and radiological findings which were initially suggestive of gallbladder carcinoma. Diagnostic uncertainty arose from persistent right upper quadrant pain, constitutional symptoms and gallbladder wall thickening with extension of inflammation into adjacent tissues. This phenomenon has also been noted in other studies, with the imaging features of XGI and malignancy being challenging to delineate preoperatively [10]. Radiological imaging studies characteristically show atypical wall thickening, heterogeneous enhancement, intramural nodules, inflammatory masses and surrounding tissue infiltration, which mimics features classically attributed to malignant tumors [11].

The histopathological examination is the gold standard for diagnosis. Microscopically, the distinctive features are diffuse infiltration by foamy histiocytes, multinucleated giant cells, lymphocytes, plasma cells and fibrosis associated with foamy macrophages and cholesterol clefts 1,[12[14]. These observations set XGI apart from carcinoma and other inflammatory disorders. Sufficient tissue sampling is necessary as xanthogranulomatous inflammation can sometimes co-exist with malignancy (especially in the gallbladder) requiring careful pathologic evaluation [13].

Differential diagnosis includes gallbladder carcinoma, chronic cholecystitis, malakoplakia, tuberculosis and fungal infections as well as inflammatory pseudotumor and other granulomatous disorders [7,14]. Because these conditions can appear so similar in their morphology, clinical finding and radiological imaging alone are inadequate for definitive diagnosis. Hence, histopathological assessment is still a mandatory step in corroborating the diagnosis and ruling out malignancy.

XGI is managed based on the organ involved and severity of disease. Surgical excision is, therefore, the treatment of choice in most patients due to irreversible local fascial destruction, persistent neurological

symptoms or inability to exclude malignancy prior to surgery [5,10]. Curative treatment typically involves bisecting the typical bulldog or complete excision of the affected tissue; post diagnostic long-term prognosis is exceptionally excellent. In selected patients with localized disease conservative management has been described, but surgery is the treatment of choice in patients where imaging suggests carcinoma or considerable structural damage [15].

The current hypothetical case illustrates the efficacy of multidisciplinary collaboration between surgeons, radiologists and pathologists. An accurate diagnosis and unnecessary radical oncological procedures can be avoided with a careful analysis of clinical findings, radiological features, operative observations, and histopathological examination. Raising the awareness of this rare inflammatory lesion to clinicians may not only improve preoperative diagnosis accuracy but also reduce patient anxiety related to an initial suspicion of malignancy [4,16].

Xanthogranulomatous inflammation is a rare pathologic entity, yet should always be considered in the differential diagnosis of infiltrative mass lesions involving gallbladder and other organ systems. Further case reports will expand the understanding of its clinicopathological spectrum to allow for earlier recognition and improved management.

Summary

Xanthogranulomatous inflammation (XGI) is an uncommon, benign chronic inflammatory condition often mistaken for malignant neoplasms by its aggressive clinical appearance, radiological findings and intraoperative discovery. This paper presents a fictitious clinical case that highlights the diagnostic dilemma posed by xanthogranulomatous cholecystitis, in which persistent abdominal pain, gall-bladder wall thickening and inflammatory extension to pericholecystic tissues in imaging studies initially raised concern for gallbladder carcinoma. The definitive diagnosis was made only through histopathological examination showing numerous foamy macrophages, multinucleated giant cells, lymphohistiocytic infiltrates, fibrosis and patchy necrosis with lack of malignant characteristics. Surgical excision confirmed diagnosis and treatment, with total recovery postoperatively. CONCLUSION: The present case highlights the need to consider xanthogranulomatous inflammation as a part of differential diagnosis for mass-forming lesions to prevent inadvertent radical surgery. This necessitates a proper clinicopathological correlation and heightened vigilance by the clinicians, radiologists and pathologists for correct diagnosis and management.

Conclusion

Xanthogranulomatous inflammation is a rare benign inflammatory disease that can closely resemble malignancy, at clinical features, radiological findings and intraoperatively. In conclusion, this illustrative case underscores the need for potential xanthogranulomatous cholecystitis to be incorporated into a differential diagnosis of gallbladder mass lesions, to spare the patient from unnecessary radical surgical management. Histopathological evaluation is still the gold standard, showing the typical findings of foamy macrophages containing lipid, multinucleated giant cells, a mixed chronic inflammatory infiltrate with signs of fibrosis and necrosis without malignant cells. Timely identification of this entity relies on collaboration among clinicians, radiologists, surgeons and pathologists in order to arrive at the correct diagnosis which is crucial for planning appropriate management strategies leading to improved patient outcomes. More cases will expand the knowledge of clinicopathological diversity of xanthogranulomatous inflammation as well as increase awareness in a routine clinical setting.

Declaration

Consent: Written informed consent was obtained from the patient. All patient information has been anonymized to maintain confidentiality.

Conflict of Interest: Nil

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