Section: Pathology

Original Research Article

MULTISYSTEM XANTHOGRANULOMATOUS LESIONS: A DIAGNOSTIC MASQUERADER OF MALIGNANCY

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ABSTRACT

Background: Xanthogranulomatous inflammation (XGI) is an uncommon chronic inflammatory condition that frequently presents as a mass-forming lesion, closely simulating malignant tumors on clinical and radiological evaluation. This misleading presentation often results in aggressive surgical management despite its benign nature. This study analyzes a series of Xanthogranulomatous lesions involving multiple organ systems and emphasizes the diagnostic challenges encountered in differentiating these lesions from malignancy.

Materials and Methods: Nine histopathologically confirmed cases of Xanthogranulomatous inflammation from different organ systems were reviewed for the clinical features, radiological impressions, operative findings and histopathological characteristics were analyzed.

Results: The study included nine patients (five-females and four-males; age range 29–63 years). Organs involved were gallbladder, kidney, endometrium, fallopian tube, testis, and prostate. All cases were clinically suspected as severe infective pathology or malignancy. Histopathology consistently demonstrated foamy macrophages, multinucleated giant cells, lymphoplasmacytic infiltrate, fibrosis with or without necrosis and no evidence of malignancy.

Conclusion: Xanthogranulomatous inflammation represents a significant diagnostic pitfall due to its close resemblance to malignancy. Awareness of its clinicopathological spectrum is essential to prevent unnecessary radical surgical interventions.

Keywords: Xanthogranulomatous inflammation; chronic inflammation, diagnostic mimic, histopathology, foamy macrophages, case series.

INTRODUCTION

Xanthogranulomatous inflammation is a distinctive form of chronic inflammatory response characterized by accumulation of lipid-laden macrophages, multinucleated giant cells, lymphoplasmacytic infiltration, fibrosis, and variable necrosis. Although most commonly described in the kidney and gallbladder, xanthogranulomatous lesions have been reported in several organs including the endometrium, ovary, prostate, testis, and gastrointestinal tract.[1-4]

The principal diagnostic challenge of xanthogranulomatous inflammation lies in its striking resemblance to malignant neoplasms. Clinically, these lesions often present as mass-forming and infiltrative processes. Radiologically, they demonstrate irregular thickening, tissue destruction and apparent invasion into surrounding structures. Even frozen section analysis may fail to conclusively differentiate xanthogranulomatous inflammation from malignancy, particularly when necrosis and fibrosis predominate the histological architecture.[5-7] Intraoperatively, dense adhesions and firm consistency further strengthen the suspicion of carcinoma. Consequently, many patients undergo radical surgery before the benign nature of the lesion is established.

The etiopathogenesis is multifactorial and remains incompletely understood. Chronic infection,

obstruction, impaired lipid metabolism, defective macrophage function and immune dysregulation have all been proposed as contributory factors. Despite advances in imaging, histopathological examination remains the definitive diagnostic modality. This case series aims to emphasise the multisystem involvement of xanthogranulomatous inflammation and reinforce its importance as a major diagnostic mimic of malignancy.

MATERIALS AND METHODS

Study Design: This descriptive observational study included surgical specimens received in the Department of Pathology, Shri Atal Bihari Vajpayee Medical College and Research Institute, Bengaluru, from January 2025 to December 2025.

Inclusion Criteria: All specimens showing histopathological features diagnostic of xanthogranulomatous inflammation.

Exclusion Criteria: Autolyzed or inadequately fixed specimens were excluded.

Processing of specimens: Specimens were fixed in 10% neutral buffered formalin and grossed using standard protocols. Representative sections were processed routinely. Hematoxylin and eosin–stained sections of 3–5 µm thickness were examined. Two independent pathologists confirmed each diagnosis. [Table 1]

Diagnostic Criteria: Diagnosis was based on the presence of:

- Abundant foamy macrophages
- Multinucleated giant cells
- Lymphoplasmacytic infiltrate
- Fibrosis
- Destruction of normal tissue architecture

RESULTS

Table 1: Clinicopathologic features of the study group

	Age (years)	Gender	Clinical presentation	Clinical Diagnosis	Treatment	Histopathology diagnosis
Case 1	63	F	Pain in the right hypochondriac region	Chronic calculous cholecystitis	Laparoscopic Cholecystectomy	Xanthogranulomatous cholecystitis
Case 2	29	F	Pain in the right hypochondriac region	Chronic calculous cholecystitis	Laparoscopic Cholecystectomy	Xanthogranulomatous cholecystitis
Case 3	46	M	Pain in the right hypochondriac region	Chronic calculous cholecystitis	Laparoscopic Cholecystectomy	Xanthogranulomatous cholecystitis
Case 4	50	M	Pain abdomen	Gall stones	Laparoscopic Cholecystectomy	Chronic calculus cholecystitis with xanthogranulomatous inflammation
Case 5	52	F	Abnormal uterine bleeding and pain abdomen	Pyometra with intrauterine contraceptive device.	Total abdominal hysterectomy with bilateral salpingectomy	Xanthogranulomatous Endometritis with Salpingitis
Case 6	35	F	Abnormal uterine bleeding and pain abdomen	Abnormal uterine bleeding	Total abdominal hysterectomy with bilateral salpingo oopherectomy	Xanthogranulomatous salphingitis
Case 7	57	M	Pain and swelling in the left scrotum	Left testicular and scrotal abscess	Left orchidectomy and lavage	Xanthogranulomatous orchitis
Case 8	58	F	Left flank pain and fever. Previous history of recurrent urinary tract infections.	Suspicious of Renal Cell Carcinoma	Nephrectomy	Xanthogranulomatous pyelonephritis
Case 9	62	M	Urinary hesitancy and weak stream.	? Prostate Carcinoma. PSA 120 ng/ml.	Transurethral Resection of Prostate (TURP).	Xanthogranulomatous prostatitis

Case Presentations

Xanthogranulomatous Cholecystitis: Four patients presented with right hypochondrial pain and were clinically diagnosed as chronic calculous cholecystitis. Grossly, gallbladders showed thickened walls, yellowish brown granular mucosa, and multiple calculi. Microscopy revealed transmural infiltration by foamy macrophages, lymphoplasmacytic infiltrate, multinucleated giant cells, and necrosis. [Figure 1]

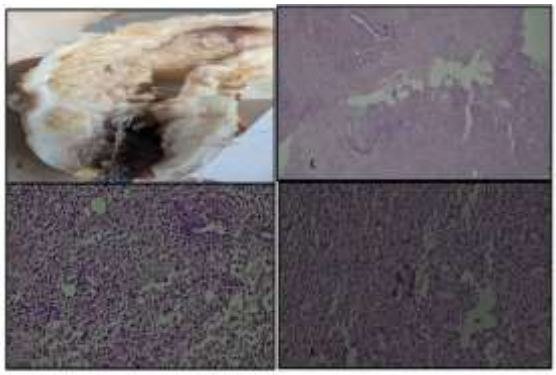

Figure 1: Xanthogranulomatous cholecystitis. (A) Gross- yellowish granular, ulcerated mucosa with thickened wall. (B and C, D) Thickened gallbladder wall with xanthogranulomatous inflammation extending through the wall (4X, &10X).

Xanthogranulomatous Endometritis with Salpingitis: A 52-year-old woman with retained intrauterine device presented with pyometra. Gross examination showed purulent material within an atrophic uterus and dilated fallopian tubes. Histopathology demonstrated extensive xanthogranulomatous inflammation replacing normal endometrial and tubal architecture. [Figure 2]

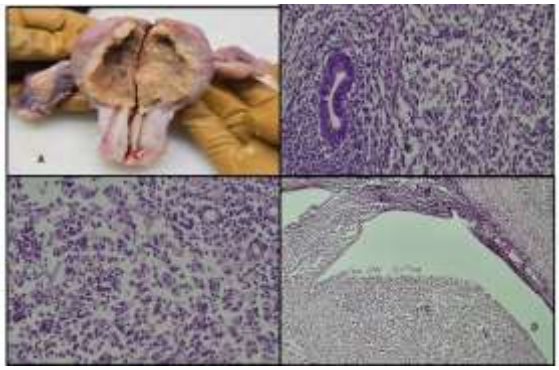

Figure 2: Xanthogranulomatous endometritis. (A) Gross picture showing thickened endometrium with yellowish granular, purulent exudate and dilated fallopian tubes (B, C) Extensive mixed inflammatory infiltrate replacing normal endometrial glands (10X). (D) Fallopian tube with dilated lumen filled with foamy histiocytes along with giant cells (4X).

Xanthogranulomatous Salpingitis: A 35year-old woman with abnormal uterine bleeding and pain abdomen. Gross examination showed dilated fallopian tubes with grey brown material in the lumen. Histopathology demonstrated extensive xanthogranulomatous inflammation replacing the tubal architecture. [Figure 3]

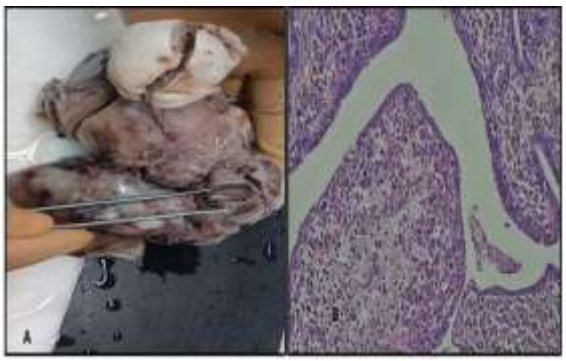

Figure 3: Xanthogranulomatous salpingitis. (A) Gross picture of dilated and occluded fallopian tube with greybrown granular material. (B) Short and thick tubal plicae with mucosal expansion by foamy histiocytes, pigment laden macrophages and chronic inflammation (10X).

Xanthogranulomatous Orchitis: A 57-year-old man with scrotal swelling underwent orchidectomy. The testis was replaced by yellowish granular tissue with hemorrhage and necrosis. Microscopically, sheets of foamy macrophages and chronic inflammatory cells replaced seminiferous tubules. [Figure 4]

Figure 4: Xanthogranulomatous orchitis. (A) Gross-Enlarged testicle; Yellowish-tan, granular with hemorrhage, necrosis and tunica vaginalis thickening (B) Extensive replacement of testicular parenchyma with mixed inflammatory infiltrate (4X). (C, D) Sheets of foamy macrophages, multinucleated giant cells, and lymphoplasmacytic infiltration (10X).

Xanthogranulomatous Pyelonephritis: A 58-year-old woman with recurrent urinary infections had a nonfunctioning enlarged kidney radiologically suspicious for carcinoma. Histology showed complete architectural destruction by xanthogranulomatous inflammation with fibrosis and necrosis (Figure 5 A, B).

Xanthogranulomatous Prostatitis: A 62-year-old man with markedly elevated PSA and nodular prostate clinically suspected carcinoma. TURP specimens revealed dense xanthogranulomatous inflammation without malignancy. [Figure 5 C, D]

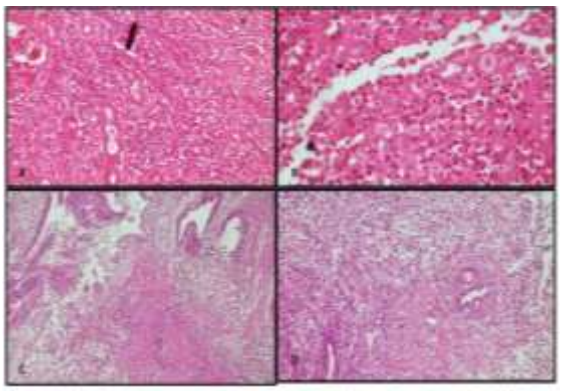

Figure 5: (A, B) Xanthogranulomatous pyelonephritis showing extensive replacement of renal parenchyma with foamy histiocytes and chronic inflammatory infiltrate (4X, &10X). (C, D) Xanthogranulomatous prostatitis revealing dense xanthogranulomatous inflammation replacing prostatic stroma by sheets of lipid-laden foamy macrophages (4X, &10X).

DISCUSSION

Xanthogranulomatous inflammation is a benign chronic inflammatory condition that frequently mimics malignant disease in both clinical and radiological settings due to its mass-forming appearance and extensive tissue involvement. The present case series demonstrates its ability to affect diverse organ systems, it exhibits uniform and reproducible histopathological characteristics, including prominent collections of lipid-laden foamy macrophages, lymphocytes, plasma cells, multinucleated giant cells and variable fibrosis.[1,2]

The exact etiopathogenesis of xanthogranulomatous inflammation remains incompletely understood, though multiple contributing factors have been identified. Chronic infection and obstruction appear to play prominent roles, particularly evident in the gallbladder cases where calculi create chronic irritation and obstruction. Disordered lipid metabolism and defective lipid transport have been proposed as contributory factors to the characteristic foamy macrophage accumulation, while immune dysregulation and altered macrophage activity may further sustain the inflammatory milieu, though the exact immunopathological mechanisms remain incompletely understood. The fibrosis represents the outcome of prolonged tissue remodeling contributing significantly to the mass-forming appearance,[1,2,8]

Radiologically, xanthogranulomatous inflammation commonly manifests as irregular wall thickening or mass-forming lesions that closely simulate carcinoma, while intraoperative findings of tissue destruction and apparent invasion further reinforce this impression.[8]

In the testicular xanthogranulomatous inflammation, USG and MRI findings of an abscess-like lesion with mass effect created sufficient diagnostic uncertainty to warrant surgical intervention.[9] The radiological investigations in the testicular and gallbladder cases raised concern for the complex infection. The patient with endometrial involvement presented with a history of contraceptive device associated pyometra, highlighting the fundamental diagnostic challenge posed by these lesions.

Histologically, xanthogranulomatous lesions are distinguished from malignancy by preserved vascular architecture and a gradual transition to adjacent normal tissue, in contrast to the infiltrative margins typical of carcinomas. The absence of neoplastic cells, increased mitotic activity, and cytological atypia further supports a benign inflammatory process.

Xanthogranulomatous cholecystitis (XGC) and xanthogranulomatous pyelonephritis (XGP) represent the most extensively characterized subtypes of xanthogranulomatous inflammation. Xanthogranulomatous cholecystitis presents with a thickened gallbladder wall and dense pericholecystic adhesions appear indistinguishable from gallbladder carcinoma on imaging and operative inspection.[10] This diagnostic uncertainty is well supported in the literature. Bourm et al. described five computed tomography features favoring xanthogranulomatous cholecystitis over gallbladder carcinoma: (1) diffuse gallbladder wall thickening, (2) preservation of a continuous mucosal line, (3) presence of intramural hypoattenuated nodules, (4) absence of intrahepatic bile duct dilatation, and (5) lack of hepatic invasion. When three or more of these findings were identified, sensitivity, specificity, and accuracy reached 83%, 100%, and 91%, respectively, indicating that careful radiological assessment can significantly improve preoperative diagnostic precision.[11]

The literature documents that adenocarcinoma can coexist with xanthogranulomatous cholecystitis in 0.2–35.4% of cases.[12] adding additional complexity to diagnosis and management. Cholecystectomy remains the appropriate definitive management in symptomatic cases, but preoperative recognition of the possibility of xanthogranulomatous inflammation can help prevent unnecessary staging procedures for suspected malignancy and the associated patient anxiety. Krishna et al. documented 93 cases of xanthogranulomatous inflammation, with the gallbladder being the most frequently affected organ (75.27%) similar to our study, followed by the kidney (5.37%) and gastrointestinal tract.[8]

In our case of Xanthogranulomatous endometritis with salpingitis in a 52- year female, hysterectomy was performed due to the concern of malignancy. The association with retained intrauterine devices provides insight into the role of chronic irritation in pathogenesis.[13]

Xanthogranulomatous orchitis illustrated a significant diagnostic challenge given the overlap with testicular malignancy in clinical presentation and imaging findings. The critical distinction lies in the histopathological demonstration of benign xanthogranulomatous inflammation rather than seminoma, non-seminomatous germ cell tumors, or lymphoma. However, once xanthogranulomatous orchitis is suspected clinically, orchidectomy may

remain appropriate given the risk of ongoing infection and possible sepsis. This case illustrates the emphasis on preoperative awareness and appropriate patient counselling regarding the benign nature of the final diagnosis.[9,14]

Vijayvergiya et al. reported a case series of four male patients with xanthogranulomatous epididymitis/orchitis presenting with scrotal swelling, tenderness, or pain with histological findings showing both diffuse and focal subtypes characterized by extensive parenchymal destruction and widespread ischemic necrosis.[15]

Similarly, xanthogranulomatous pyelonephritis typically affects middle-aged women, presenting with a non-functioning enlarged kidney frequently associated with chronic obstruction and recurrent infections. Radiological appearance of enlarged nonfunctioning kidney and yellow nodular kidney on gross appearance mimics renal cell carcinoma.[16,17] Histologically, XGPN demonstrates sheets of foamy macrophages, multinucleated giant cells, lymphoplasmacytic infiltration, necrosis, and fibrosis. The critical distinction from renal cell carcinoma lies in the absence of neoplastic cells and cellular atypia. Immunohistochemistry showing CD68 positivity in macrophages and absence of cytokeratin expression definitively resolves diagnostic uncertainty.[18]

While xanthogranulomatous inflammation predominantly affects urological organs, rare cases have been documented in the prostate. Xanthogranulomatous prostatitis (XGP) is an unusual benign inflammatory lesion that clinically, biochemically, and radiologically mimics prostatic carcinoma representing a significant diagnostic challenge. Patients typically present with obstructive urinary symptoms, with digital rectal examination revealing a hard, nodular prostate indistinguishable from malignancy. Serum prostate-specific antigen (PSA) elevation (ranging from 6 to 150 ng/ml) further compounds diagnostic confusion, leading to unnecessary therapeutic interventions.[19,20]

Hence, xanthogranulomatous inflammation should be considered a mandatory differential diagnosis in all mass-forming inflammatory lesions, particularly in organs commonly affected by carcinoma.

Clinical Implications

Failure to recognize xanthogranulomatous inflammation can result in unnecessary radical surgeries and increased patient morbidity. Radiologists should include this entity in differential diagnoses when suggestive features are present. Pathologists must ensure adequate sampling. Multidisciplinary communication is essential for accurate interpretation and optimal patient care.

CONCLUSION

Xanthogranulomatous inflammation is a benign but aggressive-appearing inflammatory process capable of involving multiple organ systems and convincingly simulating malignancy. This series of cases highlights the rare involvement of endometrium, testis and prostate where the prevalence of xanthogranulomatous lesions are less documented. Histopathological examination remains the cornerstone of diagnosis.

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Conflict of Interest

The authors declare no conflicts of interest.

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