

Incidental Eosinophilic Cholecystitis in a Young Female with Gallstones: A Case-Report and Literature Review

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ABSTRACT

Background: Eosinophilic cholecystitis (EC) is a rare inflammatory condition of the gallbladder characterized by dense eosinophilic infiltration, with an incidence ranging from 0.25% to 6.4% of all cholecystitis cases. Its pathogenesis remains poorly understood, potentially involving allergic, autoimmune, or idiopathic mechanisms, with gallstones present in a minority of cases.

Case Presentation: This case report describes a 25-year-old female presenting with postprandial right upper quadrant pain and gallstones, diagnosed with EC following laparoscopic cholecystectomy. Histo-pathological examination revealed over 90% eosinophilic infiltration and a strawberry-like mucosal appearance, with no systemic eosinophilic disorders identified.

Discussion: A comprehensive literature review of 20 studies (1979–2024) synthesizes EC's clinical and pathological spectrum, highlighting its association with systemic conditions such as hyper-eosinophilic syndrome, eosinophilic granulomatosis with polyangiitis, parasitic infections, and drug-induced reactions. Approximately 30% of cases involved gallstones, suggesting a multifactorial etiology. Laparoscopic cholecystectomy was the primary treatment, with systemic therapies like corticosteroids or antiparasitic agents used for underlying conditions. This case and review underscore EC's diagnostic challenges, emphasizing the need for histo-pathological confirmation and multidisciplinary management to address its heterogeneous presentations. Further research is essential to elucidate EC's mechanistic pathways and optimize therapeutic approaches.

1. INTRODUCTION

Eosinophilic cholecystitis (EC) is a rare and poorly understood inflammatory disorder of the gallbladder, characterized by a dense eosinophilic infiltration of the gallbladder wall, often exceeding 90% of the inflammatory cell population on histo-pathological examination (1). Unlike conventional acute or chronic cholecystitis, which is typically driven by gallstone-related mechanical obstruction or bacterial infection, EC presents a distinct clinic-pathological profile that may implicate allergic, autoimmune, or idiopathic mechanisms (2). The condition is exceptionally uncommon, with an estimated incidence of 0.25% to 6.4% of all cholecystitis, and its association with gallstones is even less frequently reported, suggesting a potentially unique interplay between mechanical and immunological factors (3). The pathogenesis of EC remains elusive, with hypotheses ranging from hypersensitivity reactions to parasitic infections or drug-related triggers, though definitive

causative pathways are yet to be established (4). The presence of gallstones in EC cases introduces additional complexity, as



gallstones may exacerbate local inflammation or serve as a coincidental finding rather than a primary driver of eosinophilic infiltration (1). Clinically, EC may mimic typical cholecystitis, presenting with right upper quadrant pain, nausea, or systemic symptoms, but its diagnosis is often delayed due to its rarity and reliance on postoperative histopathology for confirmation (5). This case report describes a rare instance of eosinophilic cholecystitis in a young female patient with symptomatic gallstones and no known systemic eosinophilic disorder, detailing the clinical presentation, diagnostic workup, histopathological findings, and management, with the aim of contributing to the limited literature on this enigmatic condition and elucidating potential mechanistic associations.

2. CASE PRESENTATION

Clinical Presentation

A 25-year-old female presented with a 3-month history of right upper quadrant abdominal pain radiating to the back, primarily postprandial, without jaundice or prior hospitalization. The patient denied fever, jaundice, food allergies, asthma, or recent travel. Physical examination revealed a soft, non-distended abdomen with a negative Murphy's sign. Laboratory investigations, including peripheral eosinophil count, were within normal limits. Vital signs remained stable pre- and postoperatively.

Abdominal ultrasonography identified multiple small gallbladder calculi without evidence of acute cholecystitis. The common bile duct was unremarkable, and the gallbladder wall was mildly thickened.

The patient underwent an elective laparoscopic cholecystectomy. Gallstones were removed intra-operatively, and the gallbladder was submitted for histo-pathological examination.

Pathology Findings

The gallbladder measured 7×2 cm with a wall thickness of 0.2 cm. No calculi were present in the submitted specimen, as they were removed intra-operatively. The mucosa displayed a strawberry-like appearance.

Histological sections demonstrated an intact mucosal layer with fibrosis of the lamina propria and scattered lymphoid cells. Focal clusters of eosinophils, constituting over 90% of the cellular infiltrate, were noted, confirming the diagnosis of eosinophilic cholecystitis as seen in Figure1 and Figure 2. No dysplasia or malignancy was identified.

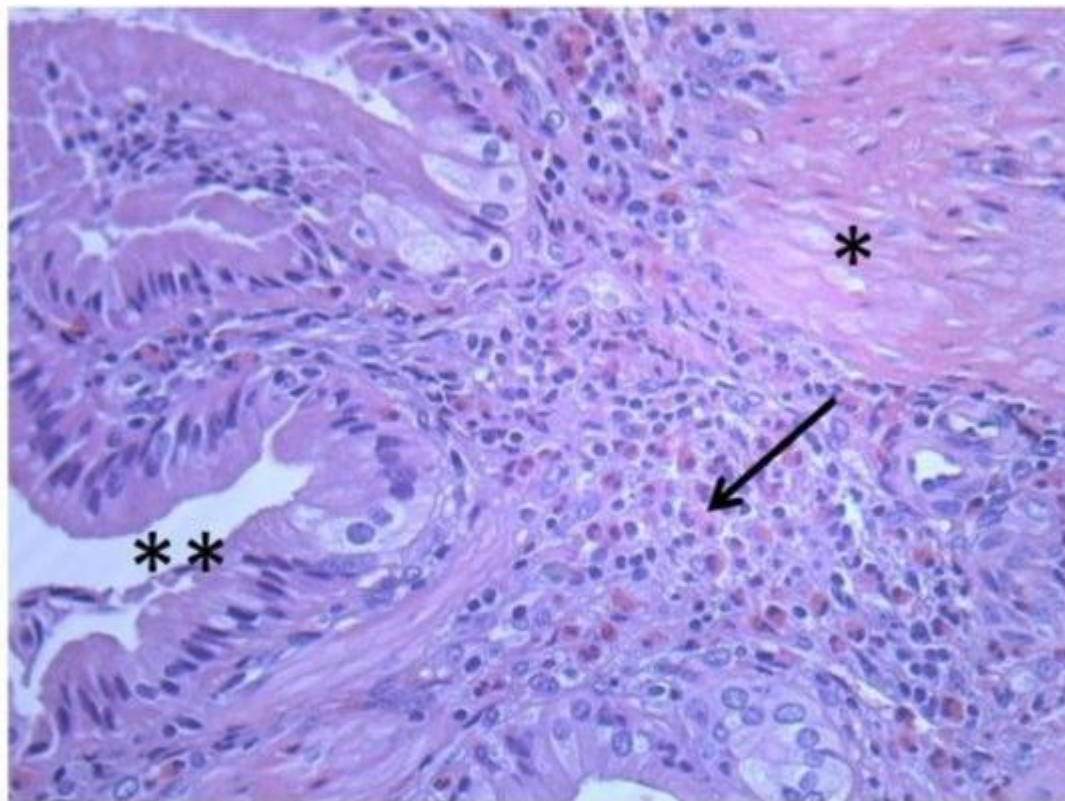


Figure 1 : The gallbladder mucosa exhibits a marked infiltrate of eosinophils. Arrow points to eosinophilic cells, “*”: points to the inner layer of the mucosa, “**”: points to the outer layer of the mucosa.

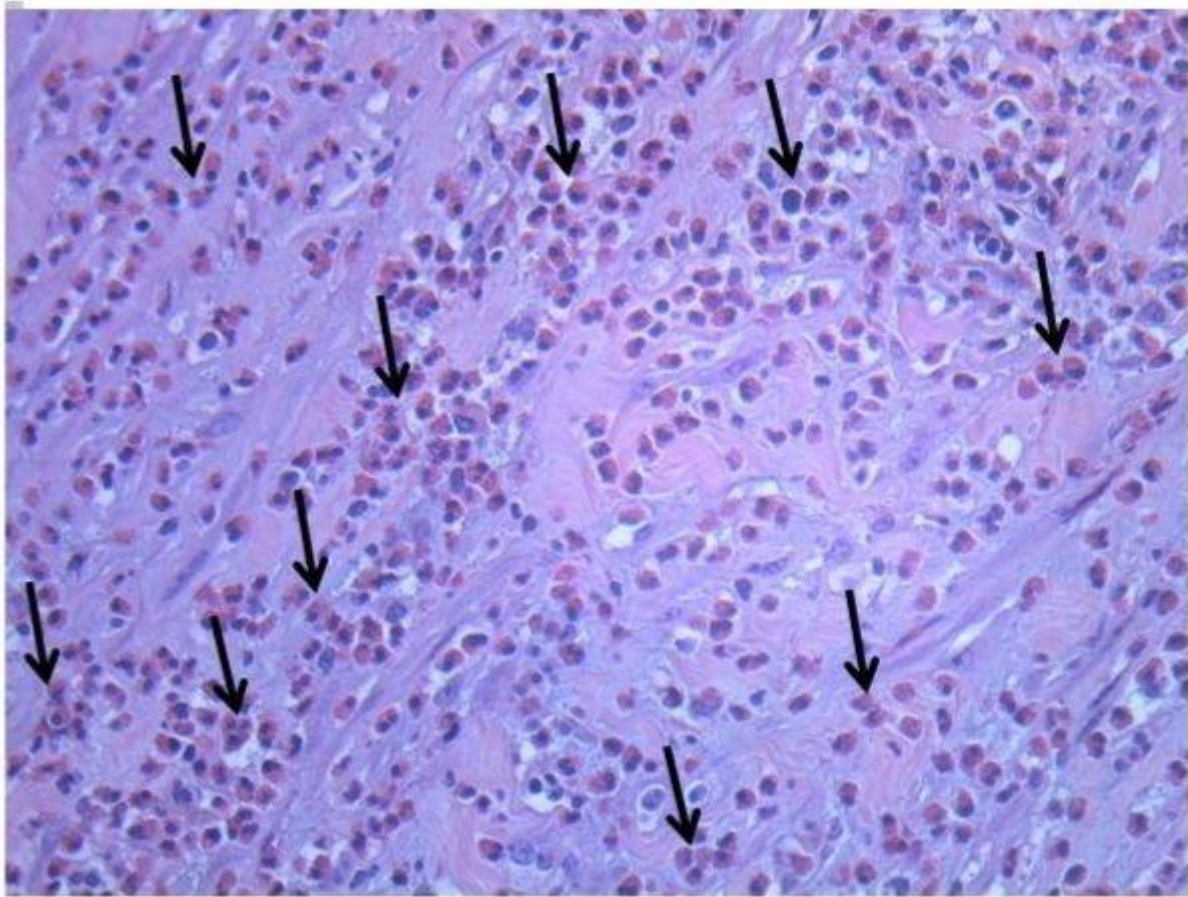


Figure 2: gallbladder lamina propria with marked eosinophilic cells infiltrate.
Arrows point to eosinophilic cells.

3. DISCUSSION

In the present case, mild eosinophilic infiltration was observed incidentally, without clinical manifestations suggestive of eosinophilic syndromes. The clinical presentation of EC typically mirrors that of conventional cholecystitis, and its management aligns with standard therapeutic protocols for cholecystitis. Nonetheless, accurate identification of EC is critical due to its potential association with systemic conditions, particularly in cases exhibiting pronounced eosinophilic infiltration (5, 6).

This case contributes to the sparse body of literature on idiopathic EC with mild presentation in young adults, particularly in the context of gallstone disease. The observed "strawberry mucosa" appearance may be indicative of cholesterosis (7, 8), which has been noted to occasionally coexist with eosinophilic inflammation.

After searching the English literature on Scopus and PubMed using the term "Eosinophilic cholecystitis", we have reviewed 20 articles (1979–2024) on eosinophilic cholecystitis (EC) and their summary is in table 1, This review synthesizes key findings regarding patient demographics, associated disorders, gallstone presence, potential etiologies, and treatment approaches, offering insights into the clinical and pathological spectrum of EC.

Table 1. Summary of 20 eosinophilic cholecystitis case reports in the literature.

Study ID	Publication year	Age (years)	Sex (M/F)	Associated disorders	Chronic medication	Associated gallstones	Possible cause	Treatment
• Yama moto, Kiyohi	2024	35	F	NA	NA	No	NA	Laparoscopic cholecystectomy

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	2023	14	F	Severe IHES	NA	Yes	Immune dysfunction, supported by the positive results of APS-related antibodies.	glucocorticoids (2 mg/ kg/d) were prescribed for IHES. 3 wk later, pleural effusion and re-elevated AEC prompted administration of imatinib for 3 months. After 3 months, mepolizumab can be a novel option for the treatment of refractory IHES cases in children.
• Jin, Jing et.al. (9)	2023	64	M	Polymyalgi a rheumatic (in remission), pemphigus vulgaris (in remission for 2 years after receiving 2 cycles of rituximab), and rosacea. Allergies topiroxicam and topical ivermectin.	Topical Metronida zole for rosacea	NA	DRESS with skin, gallbladder, and liver involvement triggered By his recent exposure to topical diclofenac	The patient received intravenous fluids and piperacillin– tazobactam. On hospital day 2, he underwent laparoscopic cholecystectomy.
Tsevat, Rebecca et.al. (18)	2023	27	F	The patient had no remarkable personal or family history	No chronic medicatio ns	Yes	Idiopathic	laparoscopic cholecystectomy
		30	M	The patient had no remarkable personal or family history	No chronic medicatio ns	Yes	Idiopathic	laparoscopic cholecystectomy
	2020	60	M	3-year history of bronchial asthma and sinusitis then	NA	No	EGPA	Corticosteroid therapy was initiated at a dose of 40 mg, which was subsequently reduced to 30 mg

					diagnosed with EGPA				after 4 weeks. Cyclophosphamide was administered as an immunosuppressant at a dose of 700 mg on the 7th and 35th days after prednisolone administration. Endoscopic transnasal gallbladder drainage for cholecystitis.
•	Al-janabi, Moatasem Hussein et.al. (21)	2020	27	F	Occasional itching and a skin rash	NA	No	Hypereosinophilic syndrome which was missed	She was immediately resuscitated with fluid and noradrenaline and Piperacillin-Tazobactam and Levofloxacin. Open cholecystectomy, CBD exploration, and T-Tube.
•		2019	19	M	Thalassemia intermedia, favism.	Folic acid tablets, periodic pneumococcal vaccinations, and at rare times a blood transfusion.	Yes	EC was associated with favism and thalassemia Intermediate.	The patient was prescribed cephalosporin and penicillin during his hospital stay and underwent an open splenectomy due to his splenic crisis and a cholecystectomy due to his chronic cholecystitis.
•		2017	74	M	Chronic obstructive pulmonary disease, eosinophilic enteritis, ampullary stenosis.	NA	No	Associated eosinophilic enteritis, ampullary stenosis.	Laparoscopic cholecystectomy.
Ito, Hiroyuki et.al. (12)		2016	52	F	Chronic Obstructive Pulmonary Disease.	Salbutamol and Spiriva inhalers.	No	Talc pleurodesis.	Laparoscopic cholecystectomy.

	2016	20	F	Spirometra mansoni infection, EGPA.	NA	No	EGPA that was caused by parasite infection.	For Spirometra mansoni infection, praziquantel (60~70 mg/kg) was used for three days, combined with use of dexamethasone (10 mg/day). For cholecystitis, Laparoscopic cholecystectomy. For tonic-clonic seizures, phenobarbital sodium. 6- methylprednisolon e 1 g daily was used to treat vasculitis, mannitol 50 g twice a day was used to control cerebral edema, and gamma globulin 1 g daily was used for endogenous allergic pathogenic factors for 3 consecutive days. Then oral prednisolone (from 1 mg/kg/day).
• Keyal, Niraj Kumar et.al. (10)	2016	36	F	Toxocara canis infestation, common bile duct stricture.	NA	Yes	Idiopathic HES.	The patient was treated with mebendazole with the presumption of dog hookworm infestation, then treated with thiabendazole on the presumption of toxocara infection. laparoscopic cholecystectomy for cholecystitis then oral dose of 50 mg of prednisone.
	2013	15	M	NA	No chronic medications.	No	Idiopathic	exploratory laparotomy and cholecystectomy.
• Ranae e, Mohammad et.al.	2012	39	F	Goiter for ten years and associated with Autoimmun	NA	NA	Associated with Autoimmune Pancreatitis.	With minimal sphincterotomy, a stent was inserted into the proximal portion of the narrowed area.

(23)			e Pancreatitis				Then, the patient underwent pancreaticoduodenectomy (Whipple operation) with Cholecystectomy.	
	2007	28	F	No specific past medical history including allergic reactions.	No chronic medications.	No	Ascaris lumbricoides.	Treatment with albendazole (600 mg/d).
Saks, Karen et.al. (28)		65	M	NA	NA	Yes	Clonorchis Sinensis	NA
		50	M	NA	NA	No	Infestation in the Common Bile Duct.	Cholecystectomy
• Caesar J et.al. (25)	1979	27	F	There was no significant antecedent or other history.	No chronic medications.	No	Hepatic Echinococcosis with leakage of cyst contents into gallbladder.	A decision was made to treat the patient conservatively. Then, exploratory laparotomy and Cholecystectomy.
•	2001	35	M	Asthma and an episode of pancreatitis 9 months earlier.	NA	No	Acalculous EC and eosinophilic pancreatitis in the absence of gallstones is attributed to the herbal medicine.	A laparoscopic cholecystectomy. Discontinuation of this herbal medicine and treatment with weaning doses of steroids.
Zeng, Mingbing et.al. (13)	2000	43	F	Eosinophilia myalgia syndrome, Hypertension.	Amlodipine	No	Possible late manifestation of Eosinophilia myalgia syndrome.	Intravenous ciprofloxacin and metronidazole, and 12 days later he underwent a laparoscopic cholecystectomy.
•	1995	44	M	Mononeuritis multiplex, Eosinophilic Colitis Associated with HES.	NA	No	HES	Laparotomy and cholecystectomy.
Mehanna, Daniel et.al. (27)	1993	44	M	Hypersensitivity rash after exposure to	No chronic medications.	No	The possible etiologic role of cephalospori	Intravenous cefoxitin and underwent a cholecystectomy.

penicillin and a depressive disorder, possible HES.	n hypersensitiv ity leading to HES.
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HES: Hyper-eosinophilic Syndrome, NA: not available in the article, M: male, F: female, EGPA: Eosinophilic granulomatosis with polyangiitis, DRESS: Drug Reaction With Eosinophilia and Systemic Symptoms, IHES: Idiopathic Hyper-eosinophilic Syndrome, EC: eosinophilic cholecystitis, APS: anti-phospholipid syndrome.

The studies encompass a diverse patient cohort, with ages ranging from 14 to 74 years (mean age approximately 37 years) and a balanced sex distribution (10 males, 10 females). EC presentations varied, with some cases identified incidentally during cholecystectomy and others linked to systemic conditions. The heterogeneity in age and sex suggests EC is not confined to a specific demographic, warranting broad clinical consideration.

EC was frequently associated with systemic eosinophilic or hypersensitivity disorders, including hypereosinophilic syndrome (HES) (9-11), eosinophilic granulomatosis with polyangiitis (EGPA) (12, 13), and parasitic infections (e.g., *Spirometra mansoni*, *Toxocara canis*, *Clonorchis sinensis*, *Ascaris lumbricoides*, *Echinococcus*) (14-16). Other associations included autoimmune conditions like autoimmune pancreatitis (17) and drug-induced reactions like DRESS syndrome and herbal medicine (18, 19). Idiopathic EC was noted in several cases (22-20), highlighting diagnostic challenges in the absence of clear etiologic triggers. The presence of gallstones was reported in approximately 30% of cases, suggesting a potential but non-universal association with cholelithiasis.

Chronic medications were infrequently reported, with notable instances including folic acid for thalassemia (23), amlodipine for hypertension (24), and inhalers for chronic obstructive pulmonary disease (25). Potential triggers included drug hypersensitivity (e.g., diclofenac, cephalosporin) and parasitic infections, emphasizing the role of environmental and iatrogenic factors in EC pathogenesis (18, 26).

Laparoscopic cholecystectomy was the predominant treatment, performed in 14 of 20 cases, reflecting its role as the standard management for symptomatic EC, as known in conventional cholecystitis. Open cholecystectomy was less common but utilized in complex cases (10, 23). Systemic therapies, including corticosteroids (12, 13, 27), immunosuppressants (e.g., cyclophosphamide, imatinib), and antiparasitic agents (e.g., albendazole, mebendazole, thiabendazole) (15, 27), were employed in cases with systemic eosinophilic or parasitic etiologies. Novel therapies, such as mepolizumab for refractory HES (9), highlight emerging treatment options for pediatric and complex cases. The presence of eosinophilic enteritis, biliary obstruction, and immune-mediated disorders further supports the notion that EC may be part of a systemic eosinophilic process in certain patients (28).

The presence of gallstones in 6 of 20 cases suggests a potential link between cholelithiasis and EC, though the majority of cases were acalculous, underscoring the multifactorial nature of EC.

Luz Nérida Garzón G et.al (29) studied EC in pediatric population and reviewed 134 consecutive laparoscopic cholecystectomies performed at HOMI, confirming histological cholecystitis in 95.5% of cases. The cohort was predominantly female (73%) with a mean age of 12.9 years. Notably, 6% meeting criteria for eosinophilic cholecystitis (EC). These eosinophil-predominant cases presented acutely with confirmed cholecystitis and cholelithiasis; No associations with allergies, parasites, or hypereosinophilic syndromes were identified. One case involved hereditary spherocytosis.

4. CONCLUSION

This compilation of EC cases underscores its clinical heterogeneity, ranging from idiopathic presentations to those linked with systemic eosinophilic, autoimmune, or parasitic conditions. Laparoscopic cholecystectomy remains the cornerstone of treatment, supplemented by targeted therapies for underlying disorders. These findings highlight the importance of recognizing EC in differential diagnoses of gallbladder pathology and the need for multidisciplinary management in cases with systemic involvement. Further studies are warranted to clarify the mechanisms driving EC and to optimize therapeutic strategies.

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