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Hepatobiliary Conditions

Eosinophilic cholecystitis in children: Case series

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ABSTRACT

Introduction: Eosinophilic cholecystitis (EC) is rarely seen in the pediatric population. Most of the available literature comes from adult patients, while only anecdotal cases have been reported in children.
Objective: To describe the clinical course, management, and outcomes of all EC cases treated at a children's hospital.
Material and methods: All cholecystectomy specimens obtained between 2011 and 2017 were retrospectively reviewed. EC was diagnosed when more than 90% of the inflammatory cells in the gallbladder wall were eosinophils, whereas lymphoeosinophilic cholecystitis (LEC) was diagnosed when the percentage of eosinophils was between 50 and 90. We analyzed all clinical aspects of patients with EC and LEC.
Results: We identified and reviewed 134 cholecystectomy specimens. Of them, 8 (6.0%) were classified as EC, and 3 (2.2%) as LEC. The mean age at presentation was 12.6 (2–17) years. The female-to-male ratio was 1.5/1. One patient had a history of hereditary spherocytosis, and 3 patients had systemic eosinophilia. All patients presented with clinical and radiological signs of acute cholecystitis and underwent cholecystectomy. Acute cholecystitis was confirmed by histopathology in all cases. All cases of EC and LEC had cholelithiasis. None of the patients required additional treatment. All patients recovered uneventfully.
Conclusions: EC is rarely seen in children, it does not have a specific clinical presentation, and it is always associated with cholelithiasis. The diagnosis is made postoperatively by histopathology. All patients in our study presented with acute cholecystitis.
Type of study: Retrospective review.
Level of evidence: Level IV.

Gallbladder disease is seen in children with increasing incidence. The spectrum of this disease includes eosinophilic cholecystitis (EC), which is an uncommon entity with a clinical course indistinguishable from calculous cholecystitis, and is occasionally associated with systemic eosinophilia [1,2].

EC was first described in 1949 and was subsequently characterized in 1993 [3,4]. The diagnosis is made by histopathology when 90% or more of the inflammatory infiltrate in the gallbladder is made up of eosinophils [4]. It has an unknown etiology, although it has been associated with hypersensitivity to bile, parasite infections, and drug abuse [5]. EC may be associated with systemic hypereosinophilic syndromes or affect exclusively the gallbladder. It usually has a favorable prognosis [2].

Most studies on EC come from adult patients, and there are scant data in the literature on its clinical features in children. Our review, conducted at a referral hospital Fundación Hospital Pediátrico la Misericordia (HOMI) in Bogotá, Colombia, provides relevant data of this unusual condition in the pediatric population.

1. Materials and methods

We conducted a retrospective clinicopathological review. The HOMI Pathology Service database was reviewed to collect data on all cholecystectomy specimens from patients less than 18 years of age obtained between January 1, 2011 and December 31, 2017. Cases with significant eosinophilic infiltration were selected. Pathology slides stained with hematoxylin and eosin were rereviewed by two independent pathologists. Cases were divided in two groups: the first group included cases of EC, in which the eosinophilic infiltrate in the gallbladder wall was greater than 90%, and the second group included patients with mixed inflammatory infiltrate in which 50% to 90% corresponded to eosinophils ("lymphoeosinophilic cholecystitis", LEC). Patients who did not meet any of these criteria were excluded from the study. The evaluation of the histological sections allowed identifying the layer of the gallbladder wall where eosinophil infiltration was predominant: mucosal, muscle,

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Table 1
Clinical and pathological data of patients with eosinophilic cholecystitis.

	Age	Sex	BMI	MRCP	BI	Percentage of eosinophils	Blood disorder	S	% and location of eosinophils	
1	16	F	22.5	Y	N	[a]	N	Y	>90%	Mucosa
2	13	F	[a]	N	N	6.40%	N	Y	>90%	Serosa
3	15	F	[a]	N	N	0.60%	N	Y	>90%	Mucosa
4	15	M	18.6	N	N	0.60%	N	Y	>90%	Muscle
5	13	M	21.2	Y	Y	10%	N	Y	>90%	Transmural
6	10	M	18.1	Y	N	0.70%	Y	Y	>90%	Mucosa
7	7	F	[a]	N	N	1.50%	N	Y	>90%	Submucosa
8	13	M	18.4	N	N	0.90%	N	Y	>90%	Serosa
9	11	F	17.9	N	N	[a]	N	Y	50%–90%	Serosa
10	15	F	[a]	N	N	6.70%	N	Y	50%–90%	Mucosa
11	11	F	13.9	Y	N	1.80%	N	Y	50%–90%	Muscle

BMI: body mass index; MRCP: magnetic resonance cholangiopancreatography; BI: biliary instrumentation; S: stones; Y: yes; N: no.
[a] No information found in the medical records.

serosa, or a combination of them (transmural). Subsequently, the medical records of EC and LEC patients were retrospectively reviewed to collect demographic, laboratory and clinical data, to determine the potential association with other diseases, allergies, or parasitic infections, and to determine the potential history of drug abuse. This study was approved by the HOMI Ethics Committee (Acta 001 CEI 34-17).

2. Results

During the study period we performed 134 cholecystectomies at HOMI, all by laparoscopy. Cholecystitis was confirmed histologically in 128 (95.5%) cases. The mean age at presentation was 12.9 (2–17) years. Most cases (73%) occurred in females. In 11 (8.2%) of these cases, eosinophils were predominant in the inflammatory infiltrate of the gallbladder wall. Eight of them (6%) fulfilled criteria for EC, while the remaining 3 (2.2%) were diagnosed with LEC. The mean age of these 11 patients was 12.6 (7–16) years, most cases being females (7/11). All patients presented to the emergency department with symptoms of acute cholecystitis, which was confirmed by blood work and ultrasound. Blood eosinophilia was detected in 3 patients (27.2%), without findings of an association with hypereosinophilic syndromes [6]. One patient had hereditary spherocytosis with hepatosplenomegaly and nonconjugated hyperbilirubinemia. No patients had a history of allergies, parasitic infections, or recent drug abuse (Table 1).

Abdominal ultrasound confirmed cholecystitis, and showed cholelithiasis in all patients. In four cases we had a clinical suspicion of choledocholithiasis [7]. Those four patients underwent magnetic resonance cholangiopancreatography (MRCP). Choledocholithiasis was documented in one patient, who had pancreatitis. Once the pancreatitis improved with medical management, endoscopic retrograde cholangiopancreatography (ERCP) with stent and cholecystectomy were performed during the same hospitalization. Pancreatobiliary maljunction was found in 1 patient (Table 1). All patients underwent laparoscopic cholecystectomy without complications. The histopathology study revealed that the eosinophils were predominantly located in the mucosal layer in one-third of the cases, and was transmural in one case (Table 1) (Fig. 1).

3. Discussion

EC is a rare entity. To the best of our knowledge this is the first case series reported in the pediatric population. The prevalence of EC and LEC in adults varies from 1.6% to 6.5% [4,5]. Our study found that 8.2% of all cases of pediatric cholecystectomy had this pathology (6% for EC and 2.2% for LEC). In adults, the most common age at presentation is between 30 and 40 years. In the pediatric population most cases occur during teenage years, but cases have been reported in patients as young as 7 years of age [1,8]. In our series, 63% of the patients were females, which is similar to what has been reported in the literature [4,5].

In this experience all patients were admitted to the emergency department with signs and symptoms of acute cholecystitis. This differs from the adult literature, which reports that most patients with EC have symptoms of chronic cholecystitis [2,5,8]. There are also differences between adults and children regarding the percentage of cases with cholelithiasis: 100% in our series versus 40%–90% in adults [2,5,8].

The etiology of eosinophilic cholecystitis is unclear. The literature associates EC with eosinophilic gastrointestinal infiltration (eosinophilic gastroenteritis, eosinophilic granulomatous hepatitis or eosinophilic ascites, eosinophilic cholangitis), eosinophilia–myalgia syndrome, idiopathic hypereosinophilia syndrome, infestation by parasites in the gallbladder such as *Echinococcus*, *Clonorchis sinensis* or *Ascaris lumbricoides*, antibiotics such as erythromycin or cephalosporins, and even secondary to talc pleurodesis in one case [2,9–15]. If a parasitic infection is identified on histopathology, further treatment would obviously be warranted. If all of these potential causes are ruled out, EC is classified as idiopathic [5,14,16]. No association with these diseases was found in our series, and all were classified as idiopathic.

The diagnosis of EC is purely histological, since its clinical features are not different from non-EC cholecystitis. A preoperative finding of systemic eosinophilia, however, would allow to suspect EC. This study

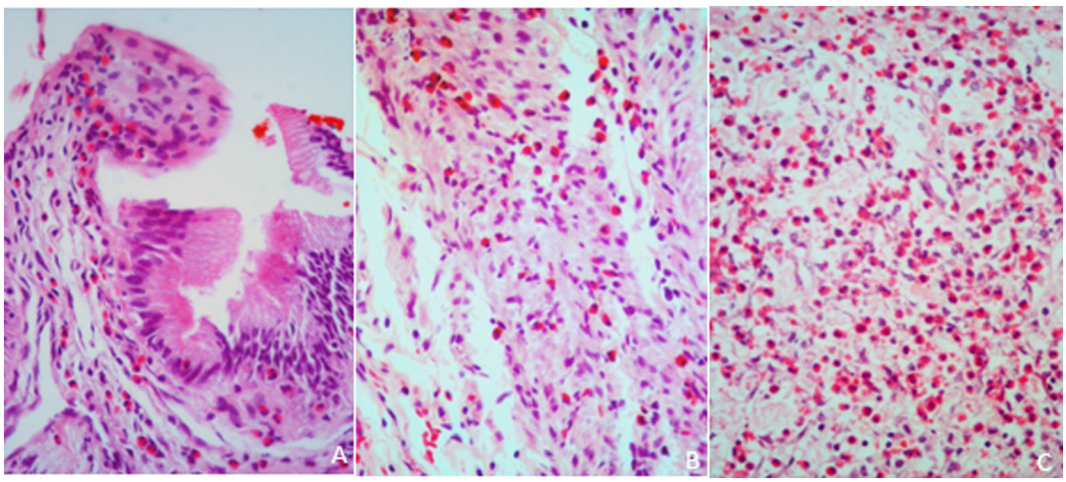

Fig. 1. Microphotograph of 3 patients with eosinophilic cholecystitis. (A) Gallbladder mucosa with inflammatory infiltrate composed exclusively of eosinophils. (B) Eosinophil infiltration permeating the muscle layer of the gallbladder. (C) Eosinophil infiltration predominates in the subserosal layer of the gallbladder. H&E 400×.

found eosinophilia in 27.3% of the cases, a figure similar to that reported by Yeom et al., who found that 20% of the cases were associated with systemic eosinophilia compared to 3.3% of other causes of cholecystitis. For this reason, systemic eosinophilia could be considered an independent predictive factor [13]. The only treatment needed in idiopathic EC is cholecystectomy [2,14].

4. Conclusion

EC is rarely seen in children. Its clinical features are similar to those of patients with non-EC acute cholecystitis. All cases in our series had associated cholelithiasis. The majority of cases appear to be idiopathic and the only required treatment is the cholecystectomy. The diagnosis can only be made postoperatively by histology.

Conflicts of interest

The authors declare that there is no conflict of interest.

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