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Adenomyomatosis of the Gallbladder as a Cause of Abdominal Pain in Pediatrics: A Case Report of an Adolescent and a Literature Review

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Objectives: Adenomyomatosis (ADM) of the gallbladder is a benign condition, which is characterized by mucosal hyperplasia of the gallbladder and formation of intramucosal invagination through the thickened mucosal layer. The pathogenesis is unclear. This condition is rare in children. The aim of this publication is to present the case of a teenager with ADM of the gallbladder and review the pediatric literature on this topic.

Methods: A 17-year-old female presented with severe postprandial right upper quadrant abdominal pains. The abdominal ultrasound revealed ADM of the gallbladder.

Results: A curative laparoscopic cholecystectomy was performed. Since 1998, eleven of the 13 pediatrics cases reported with ADM of the gallbladder were symptomatic and a cholecystectomy was curative in all of them.

Conclusion: ADM of the gallbladder should be considered in the differential diagnosis of recurrent right abdominal upper quadrant pains in pediatrics. Abdominal ultrasound is the best diagnostic procedure. In symptomatic patients, a cholecystectomy is curative.

Keywords: Rokitansky Aschoff sinuses, cholecystectomy, abdominal ultrasound, hyperplastic cholecystoses

INTRODUCTION

Gallbladder adenomyomatosis (GA) is a benign condition, which is characterized by mucosal hyperplasia of gallbladder and formation of intramucosal invagination through the thickened mucosal layer which is known as the Rokitansky Aschoff sinuses (RAS) (1). Adenomyomatosis, also known as adenomyoma or adenomyomatous hyperplasia of the gallbladder, is one of the two hyperplastic cholecystoses. The other hyperplasic cholecystosis is cholesterolosis or "strawberry gallbladder" in which triglycerides and cholesterol are deposited in the lamina propria of the gallbladder wall (2).

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GA is more common in adults and is rare in children. It is discovered incidentally in 1% to 9 % of adult cholecystectomy specimens and its prevalence is increased after 50 years of age (3). Since 1998, 14 pediatric cases including ours have been described in the literature. This condition is generally classified anatomically into 3 types; diffuse, segmental, and localized (fundal). The imaging modality of choice for diagnosis is abdominal ultrasound (4).

In this article, we present a case of an adolescent with adenomyomatosis of the gallbladder and review the literature on this disease.

CASE PRESENTATION

A 17-year-old girl, known to suffer from gastroesophageal reflux disease (GERD) and migraines, presented with a 7-month history of severe and constant right upper quadrant abdominal pains with episodic exacerbations. The pain worsened after fatty or spicy meals. She had undergone an upper endoscopy in an outside hospital, which had shown mild gastritis on macroscopic exam and moderate chronic antral gastritis on biopsy with no *Helicobacter pylori*. She was unresponsive to proton pump inhibitors. She had experienced a 30-lb (13.6 kg) weight loss since the beginning of her symptoms.

Investigations revealed increased ALT initially at 109 U/L with a maximum value of 215 U/L (N: 8–24 U/L), increased GGT to a maximum value of 50 U/L (N: 6–22 U/L) normal bilirubin, CBC, C-reactive protein, and lipase. The serology screening for Hepatitis A, B, C, EBV, and CMV were all negative. Abdominal ultrasound showed a gallbladder with "comet tail" artifacts without dilatation of the common bile duct or presence of gallbladder stones; the liver appeared normal (Fig. 1) (5). (The comet-tail V-shaped artifact is one of the commonly seen features of GA on ultrasound. This finding is highly informative and represents the acoustic signature of highly abundant cholesterol deposits in the RAS lumina).

An abdominal magnetic resonance imaging showed the "Phrygian cap sign" (see Fig. 2) (Phrygian caps are the most common congenital anatomic variants of the gallbladder and denote folding of the fundus back upon the gallbladder body). A repeat upper endoscopy in our center revealed nodularity in the antrum and the biopsies showed a chronic gastritis with *Helicobacter pylori* positivity, sensitive to metronidazole and amoxicillin. A colonoscopy to the terminal ileum was normal as were the biopsies. A liver biopsy was performed as the ALT remained elevated. A full negative work-up included normal serum IgG, normal serum ceruloplasmin, normal serum copper, negative anti-LKM antibody, positive anti-ANA 1:40, negative, anti-ds DNA antibody, negative antismooth muscle, and antimitchondrial antibodies. The liver biopsy was normal except for a discrete focal sinusoidal dilatation. A scintigraphy of the bile ducts showed normal emptying of the gallbladder after a fatty meal not in favor of gallbladder dyskenisia.

At first, the patient's abdominal pains were wrongly believed to be functional in origin and not secondary to the GA. The description she gave of constant right upper quadrant pains throughout the day were not typical of GA. As time passed by, her pains became

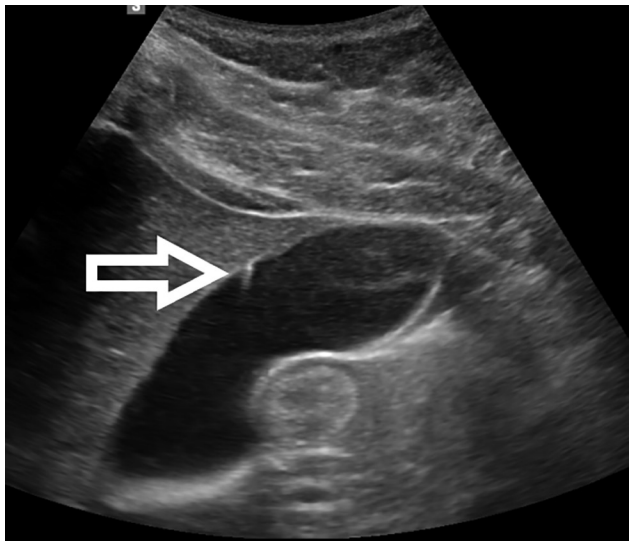

FIGURE 1. Comet tails on abdominal ultrasound.

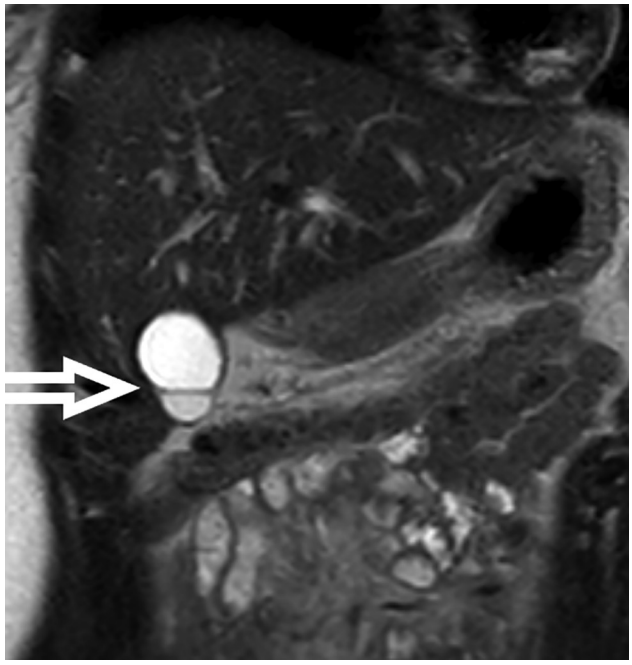

FIGURE 2. A Phrygian cap on MRI. MRI indicates magnetic resonance imaging.

excruating with exacerbation after fatty meals. After 28 months of persistent pain, she underwent a laparoscopic cholecystectomy, which allowed complete relief of her symptoms thereafter. During the cholecystectomy, a small breech was made in the gallbladder through which bile sludge and microlithiasis were expelled. The macroscopic specimen of the gallbladder showed a diffuse thick and rigid wall. The pathologist did not describe any gallstones. The microscopic examination revealed a thick mucosal layer with invagination of RAS (Fig. 3).

DISCUSSION

Adenomyomatosis of the gallbladder is a benign-acquired alteration of the gallbladder wall mucosa characterized by excessive

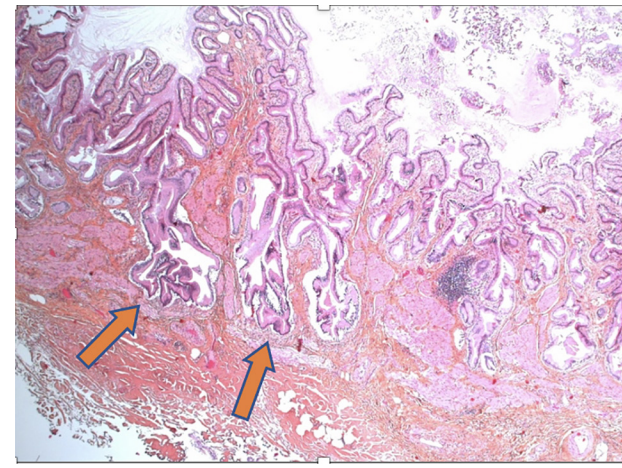

FIGURE 3. Invagination of the Rokitansky Aschoff sinuses on H & E stain.

epithelial proliferation with hyperplasia of the muscularis propria, resulting in gallbladder wall thickening. This excessive epithelial proliferation leads to epithelial infoldings within the underlying muscular layer with subsequent formation of epithelium-lined diverticular pouches, the so-called Rokitansky–Aschoff sinuses (4). The pathogenesis is unclear. The increase in gallbladder pressure seems to be an important factor in the pathogenesis. Stagnation of bile in the gallbladder, neurogenic dysfunction, hormonal influence by estrogen, and the insufficiency of gallbladder buds during embryonic period in infants, are all potential factors implicated in the development of adenomyomatosis (6). The inflammation can lead to intramural dystrophic calcification. Most patients are asymptomatic: if they do have symptoms, right upper quadrant pain is the most common.

Abdominal ultrasound is the best diagnostic examination. The ultrasound findings of the gallbladder wall can include as follows: anechoic cystic spaces, echogenic spots, comet-tail artifact, and twinkling artifacts on color Doppler ultrasound (4,5,7). Ultrasound is the most commonly used tool to investigate GA. If not diagnostic, CT or MRI are effective in attempting to differentiate a benign or malignant cholecystic mass (5,7).

Magnetic resonance cholangiopancreatography may play a role in the diagnosis of unclear cases, but it is not the goal standard. On our patient's abdominal MRI, a phrygian cap was described (Fig. 2). The Phrygian cap is an abnormality of the fundus of the gallbladder where the gallbladder fundus has a fold on itself. The Phrygian cap per se is not associated with abdominal pains but because of its structural abnormality may be associated with gallstones.

To our knowledge, only 14 cases (including ours) of adenomymatosis of the gallbladder have been described in the pediatric age group since 1998 (Table 1) (1,8–19). The age at presentation varied between few weeks of age to 17 years, and there was no gender discrimination. Eleven of the 14 cases were symptomatic. All the symptomatic cases presented with right upper quadrant pain; 10/11 were diagnosed by abdominal ultrasound. All of the symptomatic cases were treated by cholecystectomy, either open or laparoscopic, with relief of their symptoms. The asymptomatic infants were less than 4 months of age, and the radiological findings were incidental. There was spontaneous resolution of the adenomyomatosis on the follow-up abdominal ultrasound in these 3 cases.

The clinical presentation of these pediatric cases was different from the one described in adults where GA is most of the time an incidental finding. But when GA is symptomatic the presentation is very similar in children and in adults.

TABLE 1. Cases of Adenomyomatosis of the Gallbladder Reported in Children

Case	Publication	Age/Gender	Type	Main Symptom	Imaging	Treatment
1	Alberti et al (5)	5 yr/M	Localized	Abdominal pain	US, technetium 99 m HIDA, PTC	Laparoscopic cholecystectomy
2	Cetinkursun et al (6)	6 yr/M	Diffuse	Abdominal pain, fever, nausea	US, CT, MRCP	Open cholecystectomy
3	Zani et al(7)	5 yr/M	Segmental	Abdominal pain	US, MRI	Open cholecystectomy
4	Akcam et al(8)	9 yr/ F	Diffuse	Abdominal pain	US, MRCP	Open cholecystectomy
5	Alpati et al (9)	Neonat/F	No data	Incidental finding	US	Spontaneous resolution 8 months later
6	Zarat et al (10)	4 m/F	Localized	Incidental finding	US	No data
7	Parolini et al (11)	11 yr/ M	Diffuse	Abdominal pain, vomiting, nausea	US, MRI	Laparoscopic cholecystectomy
8	Eroglu et al (12)	8 yr/ F	Diffuse	Abdominal pain, vomiting, nausea	US	Open cholecystectomy
9	Eda et al (13)	8 yr/ F	Localized	Abdominal pain	MRCP, ERCP	Open cholecystectomy
10	Agrusti et al (14)	14 yr/ F	segmental	Abdominal pain	US	Laparoscopic cholecystectomy
11	Kinosshita et al (1)	12 yr/ M	Fundal and segmental	Abdominal pain	CT, US, MRI/MRCP	Laparoscopic cholecystectomy
12	Pasierbek et al (15)	17 yr/ F	Segmental	Syncope, weight loss, lumbar pain	US, CT, MRI	Laparoscopic cholecystectomy
13	Chen and Kabbany (16)	6 w/ M	No data	Incidental finding	US	Spontaneous resolution 15 weeks later
14	Our case	17 yr/ F	Diffuse	Recurrent abdominal pain, weight loss	US, MRI	Laparoscopic cholecystectomy

The most common symptom is nonspecific abdominal pain localized at the right upper quadrant and epigastrium. The pain is similar to that of gallstone and is typically intermittent and self-limiting. Nausea, vomiting, fatty food intolerance can also occur.

Three types of GA are recognized: fundal, segmental, and diffuse type. In fundal GA, there is focal thickening involving the GB fundus. In segmental GA, there is circumferential overgrowth of the GB wall that leads to formation of compartments. In diffuse GA, there is disseminated thickening and irregularity of the mucosa and musculari. Coexisting gallstone (GS) occur in more than 50% of patients with GA and in up to 90% of segmental GA (20). In adults the most common type is localized GA also called fundal GA. In our case series, the diffuse pattern seemed more frequent but data were missing in two cases. In our patient, bile sludge and fine microlithiasis were expelled during cholecystectomy but were never described on previous imaging.

GA is generally not considered to be a precancerous lesion of gallbladder cancer, but this remains controversial. Gallbladder cancer was reported concomitantly in 6.4% with segmental GA, whereas no clear association was found between fundal and diffuse type GA with GC (21)

In our patient, her constant right upper quadrant pains throughout the day were not typical of GA but were also not typical of functional abdominal pains, as they were lateralized. She also presented with other functional complaints as migraines and intractable GERD.

The corresponding author was asked to evaluate the patient when she presented at the emergency room for exacerbation of her pains but because of her unusual presentation, a cholycestectomy was not considered by the surgical team initially. As time passed by, her pains became excruating and debilitating with exacerbation after fatty meals and a laparoscopic cholecystectomy appeared to be the best option. She has remained symptom free for more than 35 months.

CONCLUSION

Adenomyomatosis of the gallbladder is rarely diagnosed in the pediatric age group. Although uncommon, it should be considered in the differential diagnosis of recurrent right upper quadrant abdominal pain when the characteristic radiologic findings are present on ultrasound. In symptomatic patients, a cholecystectomy should be offered. There is no universally accepted guideline for the management of GA at present. We postulate that asymptomatic children could be followed by yearly abdominal ultrasounds.

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Informed consent of the patient was obtained for publication of this case. When the writing of this case begun the patient was more than 18 years old.

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