

Decision for surgery in the management of a rare condition, childhood gallbladder polyps, and the role of ultrasonography

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Gallbladder polyps are tumors or tumor-like protrusions of the gallbladder. They are rarely seen in the pediatric age. Most important issue about these mostly incidental lesions is the risk of malignant transformation. Size more than 10 mm is the classical cut-off for determining this risk, but it is rarely valid in children. Ultrasonography is the method of choice for follow-up, but it rarely demonstrates change of size or malignant transformation. Hereby, we report 6 cases of childhood gallbladder polyps, none of which had a genetic risk factor. Follow-up was uneventful in 4 of them. Two patients had undergone surgery, but none of the lesions were neoplastic. In the follow-up, a single experienced radiologist should handle the patient, in order to prevent inter-observer variation. The cut-off size for deciding surgery should be 10 mm for those cases with genetic background creating malignancy risk (metachromatic leukodystrophy, pancreaticobiliary duct abnormalities, achondroplasia, Peutz-Jeghers syndrome) or with accompanying cholelithiasis, and 15 mm for those without any risk factors to prevent any unnecessary operations.

Key words: Gallbladder polyp, pediatrics, children, management, inter-observer variation, ultrasonography

Nadir bir durum olan; çocukluk çağı safra kesesi poliplerinin tedavisinde cerrahi kararı ve ultrasonografinin rolü

Safra kesesi polipleri, safra kesesinin tümör veya tümör benzeri çıkıntılardır. Çocukluk çağında nadir görülürler. Klasik olarak bilinen risk sınırı olan 10 mm, çocuklarda nadiren geçerlidir. Takipte tercih edilmesi gereken yöntem ultrasonografidir ve nadiren büyüme veya malign değişim gösterir. Burada hiçbirinde genetik risk faktörü bulunmayan 6 çocukluk çağı safra kesesi polibi vakasını sunuyoruz. Takipte, 4'ünde sıkıntı olmazken, 2'sine cerrahi uygulanmış, hiçbirinde de neoplazi bulunmamıştır. Takipte bakıcılar arasında oluşabilecek farkların önlenmesi için hastaları hep aynı tecrübeli radyolog izlemelidir. Cerrahi kararı verirkenki sınır, genetik risk faktörü (metakromatik lökodistrofi, pankreatiko - bilier kanal anormallikleri, akondroplazi, Peutz - Jeghers sendromu) veya eşlik eden safra taşı olgularda 10 mm ve diğer olgularda 15 mm olarak alınırsa, gereksiz cerrahi girişimler önlenmiş olur.

Anahtar kelimeler: Safra kesesi polibi, çocuk, tedavi, bakıcılararası varyasyon, ultrasonografi

INTRODUCTION

Gallbladder polyps (GPs) are tumors or tumor-like protrusions of the mucosal surface of the gallbladder. In the general population, prevalence is reported to be 4-7 % (1-5). In contrast to adults, polypoid lesions of the gallbladder are extremely rare in the pediatric age group (6). They are mostly incidentally found. There are numerous studies describing the prevalence, clinical significance, and

management of polypoid gallbladder lesions in adult population, but only a few in children (2).

Most important issue about the clinical significance is the risk of malignant transformation. This risk is reported to be quite small in these lesions, which are detected mostly incidentally. Most important issue determining the risk of malignant transformation has been shown to be the size of

the polyp in some elegant studies performed in the adult age group. The cut-off size is suggested to be 10 mm in most studies and 15 mm according to some other studies (7, 8). Some co-factors such as older age (>65), presence of gallstones, male gender, and presence of diabetes mellitus further increase the risk.

Principal problem arises in the gold standard method of diagnosis and follow-up, which is ultrasound (US) (9). After the rapid developments in the US technology and wide availability, many asymptomatic lesions like GPs are incidentally detected in daily routine. It is advantageous over the other diagnostic modalities (i.e. magnetic resonance imaging and computed tomography) because it is easy to perform, with no radiation exposure, and less need for patient compliance. On the other hand, there is a well-known, significant risk of intra-observer as well as inter-observer variations (10, 11). This can be particularly important in the pediatric age group. In this age group, the second problem is taking decision about the management of an asymptomatic child with an incidental GP and concerned parents.

This is the report of the prospective follow-up of 6 children with asymptomatic GPs, diagnosed by abdominal US examination, and the review of the literature about this clinical entity rarely reported in pediatric population. The purpose of this review was to describe the shortcomings of US and the role of surgery in the management of such cases.

CASE REPORTS

Case 1

A 17-year-old female patient presented with a 3-day history of right lower quadrant abdominal pain. Physical examination only revealed mild right lower quadrant tenderness. Her growth and development was normal, without any signs of a genetic syndrome. Presumptive diagnoses were appendicitis, mesenteric lymphadenitis, and ovarian cyst. All laboratory results were normal. Abdominal US showed minimal amount of free fluid in the right paraovarian region, but no ovarian cyst, inflamed appendix, or lymphadenitis. US also revealed a 7 mm non-mobile mass that was adherent to the gallbladder wall. There was neither evidence of wall thickening nor dilatation of the common bile duct or intrahepatic biliary vessels. The condition was resolved with supportive care. The abdominal US at 8, 24, and 48 weeks after the initial pre-

sentation, again revealed the polyp with no changes in the diameter, shape, location, and echogenicity. Two years after the follow-up, surgeons decided to operate the patient. Results revealed cholesterol polyp.

Case 2

A 10-year-old boy was admitted to the hospital with recurrent abdominal pain. This patient was followed up for two years due to GPs. In physical examination, there were no localizing signs of inflammation. His growth and development were normal. Laboratory tests were normal, except for the serum alkaline phosphatase (ALP) level of 639 IU/L (Normal=0-400 IU/L). ALP level was initially detected to be high 2 years ago (640-642 IU/L in 1-year intervals). US scan revealed multiple, small (maximum diameter, 5 mm), non-mobile, echogenic polyps that were adherent to the gallbladder wall, without acoustic shadow. 6 months later, gallbladder was reported to be normal on US scan of abdomen. Further US scans performed, by the same radiologist 1, 4, 6, 12, 18, 24, and 30 months later showed no changes in the appearance and size of the polyps. During the follow-up, 3 different experienced pediatric radiologists measured 3 different sizes of the biggest polyp as 3 mm, 3.5 mm, 4 mm each 3 months apart from each other.

Case 3

A 15-year-old girl was admitted to the hospital with slight epigastric pain and discomfort. Physical examination and blood tests were all normal except for a single 3.7 mm polyp in the gallbladder visualized on US. The patient was followed for 14 months, and no increase in the size or character of the polyp has been detected.

Case 4

A 17-year-old boy was admitted to the hospital with postprandial dyspeptic complaints. Physical examination and laboratory investigation revealed nothing but a 9 mm solitary polyp with irregular surface in the gallbladder detected by US. There were neither signs of thickening in the adjacent wall nor any stone in the lumen. The patient did not have any signs of a genetic syndrome. 3 months later, the US done by another radiologist revealed the size to be 10 mm, which is the cut-off value to recommend surgery for the adults. In the control performed by the initial radiologist did not show a change in size, so the boy has been followed for 15 months with stable GP dimensions.

Case 5

A 16-year-old girl was admitted to the hospital with right upper quadrant pain. US examination revealed a GP with a diameter of 6 mm (Figure 1). The patient was completely asymptomatic, without any co-morbidity. Although the indication was not so clear, she was performed laparoscopic cholecystectomy (Figure 2). Pathological examination showed cholesterol polyp, without any signs of pre-malignant condition (Figure 3).

Case 6

A 15-year-old girl attended the hospital with mild epigastric discomfort. Routine blood tests were normal. US examination showed a polyp of 5 mm in diameter, which did not change in size at 1-year follow-up

DISCUSSION

Polypoid lesions of the gallbladder are classified into two groups as, neoplastic and non-neoplastic. Among all GPs, 95% are non-neoplastic. Most common non-neoplastic polyps are cholesterol polyps comprising 60% of all GPs, which are mostly less than 10 mm in diameter. Adenomyomatosis, inflammatory polyps, adenomas, leiomyomas, lipomas, neurofibromas, carcinoids, adenomatous or adenomyomatous hyperplasias, and heterotopias are the known types of polyps (12).

Known risk factors for polyp development and malignant transformation are obesity, glucose intolerance, male gender, cholelithiasis, and hereditary polyposis syndromes (13). All the information regarding the GPs is coming from adult studies. Moreover, there is a lack of consensus among the authors, even in the adult patients. Most of the authors recommend to perform cholecystectomy when the polyp(s) reach to a size more than 10 mm, whereas some recent evidence revealed that in cases without co-existing risk factors (e.g. old age (≥ 65 y) and diabetes mellitus), surgery can be delayed until the polyp size is more than 15 mm (7). Nearly none of the patients in the pediatric age group have these risk factors. In the 17 cases reported up till now, the lesion diameter ranged between 2 and 20 mm, most of them being below 10 mm and only 2 of which were larger than 15 mm.

US is the method of choice in diagnosis and follow-up of GPs, having remarkable sensitivity (93%) and specificity (95.8%) (8). On the other hand, it has several short-comings. First of all, benign-malignant discrimination is quite difficult. Several

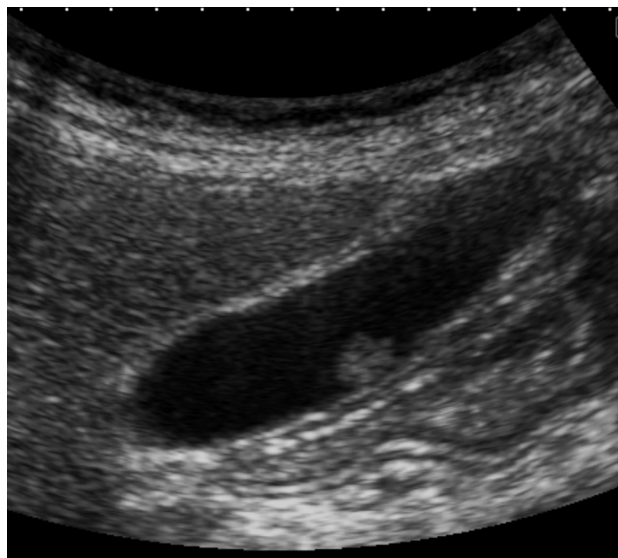


Figure 1. A single 6 mm polyp seen at the gallbladder corpus.

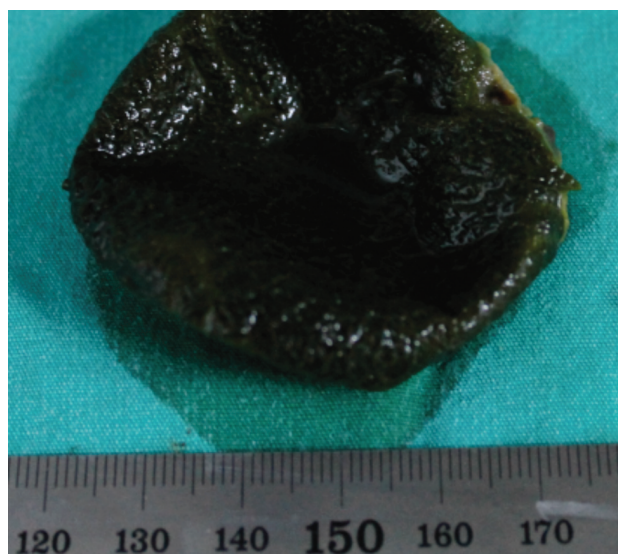


Figure 2. Gross macroscopic view of the same polyp at the surgical specimen.

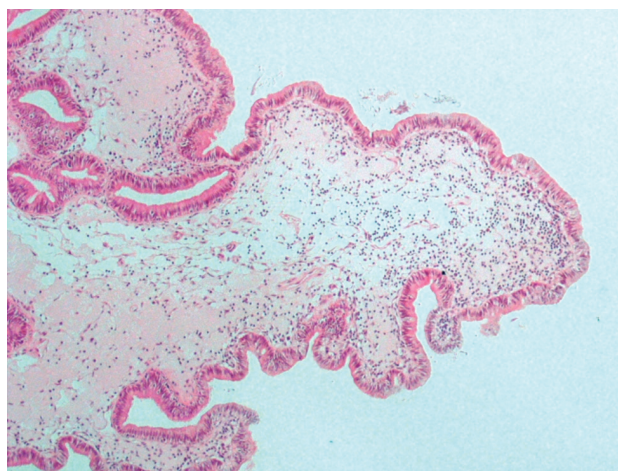


Figure 3. Microscopic view of the cholesterol polyp with H&E stain (x100).

findings are related to neoplastic change. Cholesterol polyps usually but not always have stalks, on the contrary to sessile adenomas. Large number of polyps is a property of cholesterol polyps, and size more than 10 mm, concurrent gallbladder wall thickness, and presence of stone increase the risk of malignancy, thus the lesions should be operated (14).

Further problem due to the technical difficulty of US is high rates of false positivity, creating the issue of unnecessary operations. Among 213 cases with GPs, 83% of those below 5 mm, 70% of those between 6-10 mm, and even 23% of those larger than 21 mm, no polyp was seen in the pathology specimen (15). According to the same study, polyp size >9 mm, age >52 years, invasion at the liver interface in US, and wall thickening >5 mm, especially in the presence of gallstones, are determined to be the factors raising the suspicion of malignancy. This phenomenon is most probably due to the dissolution of cholesterol polyps impacted to the gallbladder wall during tissue processing at the pathology department (16). Endoscopic US can be the method of choice in large polyps (>6 mm) to evaluate thoroughly for the malignancy risk (12).

Furthermore, in children, US by itself can be a scary movie with a dark room and a white shirt doctor that is the symbol of pain and suffering, using a strange television to see his inside! They tend not to cooperate, and their anxious parents do not ease the situation. This of course creates the problem of non-cooperation, making hard to see the polyp thus being a big challenge for the radiologist. This is why, we suggest that an experienced pediatric radiologist should perform the examination and continue the follow-up, introducing himself to the patient, which increases the cooperation.

In the follow-up of such polyps, Roland and colleagues found that there was no change in 100 cases, decrease in 5, disappear in 15, and increase in size in only 8 cases out of 203 (9). In the 13 cases that had been operated, none showed malignant transformation. Frequency of gallbladder cancer, which is the main reason of fear, is very low (1-2.5 per 100.000 in the USA), and almost none of the cases arose from an underlying GP (16). US follow-up of GPs creates an anxiety to the patient and a seemingly unnecessary high economic burden over the health care system. That is why most of the authors do not recommend following of the GPs less than 6-10 mm (9, 17, 18). Up till now, only ne-

arly 30 cases of gallbladder adenoma in a polyp less than 10 mm of diameter have been reported in the literature (19, 20). This is another evidence supporting the necessity for follow-up in these cases. In our group of patients, neither of them had change in polyp size during up to 30 months of follow-up.

In the Evaluation of the Childhood Cases

There are only 17 child age cases between 4-16 years of age reported in the English literature (M/F=8/9) in case reports (6, 13, 21-29). Four of them were with Peutz-Jeghers syndrome, 6 had metachromatic leukodystrophy, 2 were papilloma, 2 were hyperplastic polyps (with pancreaticobiliary maljunction), 2 were gastric heterotrophy, and 2 had cholesterol polyps (13). Most of the cases were admitted to the hospital with complaints of abdominal pain, nausea, and vomiting. They were either followed conservatively or operated, taking into account the cut-off size in the adult age group, i.e. 10 mm (6, 13, 22, 26, 30). However, there are only 10 cases of gallbladder malignancy in the pediatric literature.

Beck et al. claimed that the risk factors shown for the adult age group can be used for children as well, plus in the presence of accompanying metachromatic leukodystrophy, pancreaticobiliary duct abnormalities (maljunction), achondroplasia, Peutz-Jeghers syndrome, operation should be the method of choice (13). Likewise, Stringer recommended follow-up if asymptomatic, no co-morbidities as mentioned above, and less than 10 mm in size (6). Many authors do recommend the follow-up in appropriate circumstances (22, 26, 29, 30). At least 2 separate examinations are required for confirmation of the diagnosis, according to Stringer. Because US is an operator-dependent procedure, different radiologist yielded different results in his study. When the initial operator did the control, there was no significant change in the size of the polyp. He suggests that the follow-up should be performed by the same operator when possible. In the second case presented here also, size erroneously would have been detected to be progressively getting bigger due to this inter-observer variation. This is also in line with the knowledge that there is a significant inter-observer variation in the nature of US (6, 10, 11). Follow-up by the same experienced radiologist would prevent unnecessary operations that could create many problems, in the long expected life of the child patients.

The main risk factors of the gallbladder malignancy are demonstrated as polyp size >10-15 mm, age >50-65 years, presence of diabetes, and gallstones. None of these are typical or possible for the pediatric age group. So, we suggest that GP without the specific congenital, or genetic co-morbidities like metachromatic leukodystrophy, pancreaticobiliary maljunction, achondroplasia, and Peutz-Jeghers syndrome should be followed using US performed by the same experienced radiologist.

More evidence should be available in order to arrange a proper management algorithm. The cut-off size for deciding surgery should be 10 mm for those cases with genetic background creating malignancy risk (metachromatic leukodystrophy, pancreaticobiliary duct abnormalities, achondroplasia, Peutz-Jeghers syndrome) or with accompanying cholelithiasis, and 15 mm for those without any risk factors to prevent any unnecessary operations.

REFERENCES

1. Myers RP, Shaffer EA, Beck PL. Gallbladder polyps: epidemiology, natural history and management. *Can J Gastroenterol* 2002; 16:187-94.
2. Jørgensen T, Jensen KH. Polyps in the gallbladder. A prevalence study. *Scand J Gastroenterol* 1990; 25:281-6.
3. Segawa K, Arisawa T, Niwa Y, et al. Prevalence of gallbladder polyps among apparently healthy Japanese: ultrasonographic study. *Am J Gastroenterol* 1992; 87:630-3.
4. Kratzer W, Haenle MM, Voegtle A, et al. Ultrasonographically detected gallbladder polyps: a reason for concern? A seven-year follow-up study. *BMC Gastroenterol* 2008; 8:41.
5. Inui K, Yoshino J, Miyoshi H. Diagnosis of gallbladder tumors. *Intern Med* 2011; 50:1133-6.
6. Stringer MD, Ceylan H, Ward K, Wyatt JI. Gallbladder polyps in children--classification and management. *J Pediatr Surg* 2003; 38:1680-4.
7. Cha BH, Hwang JH, et al. Pre-operative factors that can predict neoplastic polypoid lesions of the gallbladder. *World J Gastroenterol* 2011; 17:2216-22.
8. Matos AS, Baptista HN, Pinheiro C, Martinho F. Gallbladder polyps: how should they be treated and when? *Rev Assoc Med Bras* 2010; 56:318-21.
9. Pedersen MR, Dam C, Rafaelsen SR. Ultrasound follow-up for gallbladder polyps less than 6 mm may not be necessary. *Dan Med J* 2012; 59:A4503.
10. Festi D, Lalloni L, Taroni F, et al. Inter and intra-observer variation in ultrasonographic detection of gallstones: the Multicenter Italian study on epidemiology of cholelithiasis (M.I.COL.). *Eur J Epidemiol* 1989; 5:51-7.
11. Grantcharov TP, Rasti Z, Rossen B, et al. Interobserver agreement in ultrasound examination of the biliary tract. *Acta Radiol* 2002; 43:77-9.
12. Gallahan WC, Conway JD. Diagnosis and management of gallbladder polyps. *Gastroenterol Clin North Am* 2010; 39:359-67.
13. Beck PL, Shaffer EA, Gall DG, Sherman PM. The natural history and significance of ultrasonographically defined polypoid lesions of the gallbladder in children. *J Pediatr Surg* 2007; 42:1907-12.
14. Tomić DV, Marković AR, Alempijević TM, et al. Ultrasound diagnosis of gallbladder polyps. *Acta Chir Jugosl* 2011; 58:31-5.
15. Konstantinidis IT, Bajpai S, Kambadakone AR, et al. Gallbladder lesions identified on ultrasound. Lessons from the last 10 years. *J Gastrointest Surg* 2012; 16:549-53.
16. Randi G, Franceschi S, La Vecchia C. Gallbladder cancer worldwide: geographical distribution and risk factors. *Int J Cancer* 2006; 118:1591-602.
17. Andrén-Sandberg A. Diagnosis and management of gallbladder polyps. *N Am J Med Sci* 2012; 4:203-11.
18. Corwin MT, Siewert B, Sheiman RG, Kane RA. Incidentally detected gallbladder polyps: is follow-up necessary?--Long-term clinical and US analysis of 346 patients. *Radiology* 2011; 258:277-82.
19. Csendes A, Burgos AM, Csendes P, et al. Late follow-up of polypoid lesions of the gallbladder smaller than 10 mm. *Ann Surg* 2001; 234:657-60.
20. Park KW, Kim SH, Choi SH, Lee WJ. Differentiation of nonneoplastic and neoplastic gallbladder polyps 1 cm or bigger with multi-detector row computed tomography. *J Comput Assist Tomogr* 2010; 34:135-9.
21. Barzilai M, Lerner A. Gallbladder polyps in children: a rare condition. *Pediatr Radiol* 1997; 27:54-6.
22. Kikiros C, Arunachalam P, Lam MH. Adenomatous hyperplastic polyp of the gall bladder associated with cholelithiasis in a child. *Pediatr Surg Int* 2003; 19:118-9.
23. Leyman P, Saint-Marc O, Hannoun L, Parc R. Heterotopic gastric mucosa presenting as gallbladder polyps. *Acta Chir Belg* 1996; 96:128-9.
24. Mogilner JG, Dharan M, Siplovich L. Adenoma of the gallbladder in childhood. *J Pediatr Surg* 1991; 26:223-4.
25. Mullick S, Gothi R, Mukerjee A. Case report: papillary adenoma of the gall-bladder in a child of 9 years. *Clin Radiol* 1993; 47:432-3.
26. Ochiai M, Funabiki T, Marugami Y, et al. Hyperplastic polyp of the gallbladder in a child. *J Hepatobiliary Pancreat Surg* 2000; 7:448-51.
27. Schimpl G, Schaffler G, Sorantin E, et al. Polypoid gastric heterotopia in the gallbladder: clinicopathological findings and review of the literature. *J Pediatr Gastroenterol Nutr* 1994; 19:129-31.
28. Sirinelli D, Vanthournout I, Robert M, et al. Ultrasound diagnosis of gallbladder papilloma in childhood. *Pediatr Radiol* 1989; 19:203.
29. Stringel G, Beneck D, Bostwick HE. Polypoid lesions of the gallbladder in children. *JSL* 1997; 1:247-9.
30. Okada T, Sasaki F, Honda S, et al. Hyperplastic polyp of the gallbladder associated with pancreaticobiliary maljunction in a 9-year-old girl. *Pediatr Surg Int* 2009; 25:999-1002.