Case Report

Pyloric gland adenoma of gallbladder with squamoid morules in pediatric age

Ashutosh Gupta¹, Amit Choraria¹*, Shantanu Tiwari¹, Vishakha Tikeykar², Vivek Chaudhary³

¹Dept. of Surgical Oncology, Regional Cancer Center, Pt. JNM Medical College, Raipur, Chhattisgarh, India
²Dept. of Pathology, SRL Diagnostics, Mumbai, Maharashtra, India
³Dept. of Radiotherapy, Regional Cancer Center, Pt JNM Medical College, Raipur, Chhattisgarh, India

ABSTRACT

Case Report: 7 year old symptomatic girl was diagnosed with gall bladder polyp on ultrasonography and MRCP (magnetic resonance cholangiopancreatography). Laparoscopic cholecystectomy was performed and patient was discharged on 2nd post operative day without any complications. Histopathology and Immunohistochemistry revealed pyloric gland adenoma with squamoid morules.

Discussion: Gall bladder polyps are seen in 5% of the adult population around the world but rarely seen in children. Polyps have the potential to convert into malignancy and hence early diagnosis and differentiation is necessary.

Most of the patients with gall bladder adenomas are adult females. Majority of the adenomas (91%) are single. Squamoid morules was found in 28% and columnar oxyphil cells in 2% of these adenomas. High-grade dysplasia/carcinoma in situ was seen in 27% of them and low-grade dysplasia in 15%. However, only 1% invasive adenocarcinomas were diagnosed in pyloric gland adenomas, both of which were intestinal type. For symptomatic patients who have pain and dyspepsia, cholecystectomy is the recommended treatment. For asymptomatic or incidentally detected patients, the indications for cholecystectomy should be age more than 50 years, solitary polyp greater than 10mm in largest dimension, accompanying gall stones and increase in size on serial sonographies.

Conclusion: As per our knowledge the case we report is the first case of gallbladder pyloric adenoma with squamoid morules in pediatric age group. Treatment with simple cholecystectomy is recommended in view of literature suggesting pre malignant lesion.

© 2020 Published by Innovative Publication. This is an open access article under the CC BY-NC-ND license (https://creativecommons.org/licenses/by/4.0/)

1. Case Report

A 7 year old girl presented at our center with complaints of pain in upper abdomen on and off since 2 months. She was being treated with pain killers, but with no relief. An ultrasonography of the abdomen was performed which revealed a 2 x 1.3 x 0.83 cm echogenic polypoidal mass which had a vascular pedicle [Figure 1]. A low impedance flow was observed in the mass. An MRCP was performed which revealed an endophytic polypoidal T2 hypotense lesion measuring approximately 1.8 x 1.3 x 1.2 cm in size. It was found to be arising from the anterior fundal wall showing mild homogenous post contrast enhancement [Figure 2]. The pericholecystic fat planes were maintained. There was no evidence of biliary obstruction. A likely diagnosis of gall bladder adenoma was made.

A standard four port Laparoscopic Cholecystectomy was performed and the specimen was retrieved in plastic bag through the umbilical port. It was sent for histopathological examination and immunohistochemistry. No peritoneal drain was used. The patient was discharged on 2nd post operative day. No post operative complications were observed.
On gross examination the gall bladder measured 4.5 cm x 1.5 cm x 1 cm with a wall thickness of 0.3 to 0.4 cm. A polypoidal superficial growth was identified 2 cm away from the cystic duct margin measuring 1.5 x 1 x 1 cm with a tiny 0.2 to 0.3 cm stump (attachment to wall).

Microscopic examination of the specimen showed a benign appearing papillary-cystic glandular growth with minimal atypia situated superficial to the wall of gall bladder. No wall invasion or high grade dysplasia could be identified. Also present were several “squamoid morules” which consisted of vague spindle cell whorls without keratinization [Figure 3]. As per these features it was labeled as adenoma.

Immunohistochemical studies showed positive CK 7, CK 19, CEA, Beta- Catenin. CDX2 was positive in few cells and Ki-67 was also positive (8-10%). CK20 and p53 were negative [Figure 4]. As per these features it was labeled as Pyloric Gland Adenoma with squamoid morules with no evidence of malignancy.

2. Discussion

Gall bladder polyps are seen in 5% adult population of the world but rarely seen in children. Incidence has greatly increased by widespread use of ultrasonography. Investigators have observed malignant change on follow up of some of these adenomas and consider them as precancerous lesions. Kurt Elster first described Pyloric gland adenoma, but since 1990 pyloric gland adenoma has been categorized in WHO classification of gastric tumors as a distinct neoplastic entity.

Previous literature reports pyloric gland adenomas are mostly seen in the stomach (69%), followed by gallbladder (14%), duodenum (12%), oesophagus, gastroesophageal junction, bile duct, pancreatic duct and rectum (together <5%).

Most of the patients with gall bladder adenomas are adult females. The mean age group is approximately 70 years. More than half (58%) of them present with gall stones. Majority adenomas (91%) are single. The reported mean tumour size is 0.6-3.5 cm.

A large study of 165 cases of pyloric gland adenomas showed 28% contained squamoid morules and 2% contained columnar oxyphil cells. 27% of them carried high-grade dysplasia/carcinoma in situ and low-grade dysplasia was found in 15% of the cases. However, only 1% invasive adenocarcinomas, both of intestinal type were
Fig. 3: A–D): H&E sections show morphology of a gall bladder pyloric gland like tubular adenoma with squamoid morules. The poypoidal lesion displays tallcolumnar epithelium with very low grade adenomatous features and incospicuous mitotic activity. There are few prominent squamoid morules and no evidence of necrosis; E): KI67 displays proliferation index of 8- 10%; F): P53 is negative excluding malignancy

Fig. 4: A): Beta Catenin –nuclear positive; B): CDX2 –few cells positive; C): CEA- negative; D): CK7 – positive; E): CK19- negative; F): CK20- negative
diagnosed in pyloric gland adenomas. Their results indicate a minor role in pathway of gallbladder carcinogenesis. Literature suggests the risk of malignant transformation into adenocarcinoma in up to 47% of cases of all locations. The pyloric gland adenoma may lead to the sequence of metaplasia-dysplasia-carcinoma in gallbladder and bile duct carcinogenesis. Literature suggests gastric metaplasia in gallbladder, pancreas, rectum and duodenum are associated with pyloric gland adenomas. Comparative genomic hybridization analyses suggest pyloric gland adenoma has a precancerous nature explained by adenoma-adenocarcinoma sequence with a great potential for invasive malignancy. Pathologically PGA of GB is low grade in 70.8% and high grade/carcinomas in 29.2% of cases. Immunohistochemically, MUC6 is diffusely positive whereas MUC2, MUC5AC, and CDX2 are only focally positive. A study suggested unique histology, phenotype and molecular status of PGA of GB when compared with other sites like stomach, duodenum and pancreas. The mutation of CTNNB1 was seen in 100% and KRAS in 4.2% cases. Ki67 expression and p53 mutations also suggest malignant transformation.

For symptomatic patients who have pain and dyspepsia, cholecystectomy is the recommended treatment. For asymptomatic or incidentally detected patients, the indications for cholecystectomy should be age more than 50 years, solitary polyp greater than 10mm in largest dimension, accompanying gall stones and increase in size on serial sonographies. If the polyp shows no increase in size, no signs of malignancy and is 6-9mm in size, it should be followed up 6 monthly for at least a year.

3. Conclusion
As per our knowledge the case we report is the first case of gallbladder pyloric adenoma with squamoid morules in pediatric age group. Treatment with simple cholecystectomy is recommended in view of literature suggesting pre malignant lesion.

4. Compliance with ethical standards
This work is in compliance with ethical standards with following below mentioned details

5. Source of Funding
The authors declare no funding was obtained.

6. Conflict of Interest
The authors declare that they have no conflict of interest.

7. Informed Consent
Written informed consent was taken from participant of the study for publication of details and photographs regarding her case.

References
1. Myers RP, Shaffer EA, Beck PL. Gallbladder Polyps: Epidemiology, Natural History and Management.  Con J Gastroenterol. 2002;16(3):187–94.
2. Ito H, Hann LE, Angelica D, M. Polypoid lesions of the gallbladder: diagnosis and followup.  J Am Coll Surg. 2009;208:570–575.
3. Kozuka S, Tsubone M, Yasui A, Hachisuka K. Relation of adenoma to carcinoma in the gallbladder. Cancer. 1982;50(10):2226–34.
4. Gupta A, Choraria A, Tiwari S. Laparoscopic radical cholecystectomy for carcinoma gallbladder: A case series. Int J Hepatobiliary Pancreat Dis. 2017;7:18–22.
5. Bosman FT, Carneiro F, Hubran RH. WHO classification of tumours of the digestive system. Lyon: International Agency for Research on Cancer; 2010.
6. Chen ZM, Scudiere JR, Abraham SC. Pyloric gland adenoma: an entity distinct from gastric foveolar type adenoma.  Am J Surg Pathol. 2009;33:186–93.
7. Vieth M, Kushima R, ichi Mukaisho K, Sakai R, Kasami T, Hattori T. Immunohistochemical analysis of pyloric gland adenomas using a series of Mucin 2, Mucin 5AC, Mucin 6, CD10, Ki67 and p53. Virechows Archiv. 2010;457(5):529–36.
8. Bakotic BW, Robinson MJ, Sturm PDI, Hubran RH, Johan G, Offerhaus A, et al. Pyloric Gland Adenoma of the Main Pancreatic Duct.  Am J Surg Pathol. 1999;23(2):227–31.
9. Kato N, Akiyama S, Motoyama T. Pyloric gland-type tubular adenoma superimposed on intraductal papillary mucinous tumor of the pancreas. Virechows Archiv. 2002;440(2):205–8.
10. Kushima R, Vieth M, ichi Mukaisho K, Sakai R, Okabe H, Hattori T, et al. Pyloric gland adenoma arising in Barrett’s esophagus with mucin immunohistochemical and molecular cytogenetic evaluation. Virechows Archiv. 2005;446(5):537–41.
11. Wani Y, Notohara K, Fujisawa M. Aberrant expression of an “intestinal marker” Cdx2 in pyloric gland adenoma of the gallbladder. Virechows Archiv. 2008;453(5):521–7.
12. Oh MG, Cho SJ, Lee JH. A spongiform mass in the stomach: pyloric gland adenoma with a transition to adenocarcinoma. Korean J Gastroenterol. 2010;56:1–5.
13. Gutierrez-Grobe Y, Gavilanes-Espinar J, Uribe M. Pyloric Gland Adenoma: Case Report. Rev Gastroenterol Mex. 2010;75:360–2.
14. Amarasi J. Intraductal mucinous papillary tumor and pyloric gland adenoma of the pancreas. Gastrointest Endosc. 2002;56:441–4.
15. Kushima R, Remmele W, Stolte M, Borchard F. Pyloric gland type adenoma of the gallbladder with squamoid spindle cell metastasis. Pathol Res Pract. 1996;192(9):963–9.
16. Kushima R, Rüthlein JJ, Stolte M, Bamba M, Hattori T, Borchard F. ‘Pyloric gland-type adenoma’ arising in heterotopic gastric mucosa of the duodenum, with dysplastic progression of the gastric type. Virechows Archiv. 1999;435(4):452–7.
17. Vieth M, Kushima R, de Jonge JPA, Borchard F, Oellig F, Stolte M. Adenoma with gastric differentiation (so-called pyloric gland adenoma) in a heterotopic gastric corpus mucosa in the rectum. Virechows Archiv. 2005;446(5):542–5.
18. Vieth M, Kushima R, Borchard F, Stolte M. Pyloric gland adenoma: a clinico-pathological analysis of 90 cases. Virechows Archiv. 2003;442(4):317–21.
19. Albores-Saavedra J, Chablé-Montero F, González-Romo MA, Jaramillo MR, Henson DE. Adenomas of the gallbladder. Morphologic features, expression of gastric and intestinal mucins, and incidence of high-grade dysplasia/carcinoma in situ and invasive carcinoma. Human Pathol. 2012;43(9):1506–13.
20. Goljer D, Probst A, Wagner T, Messmann H. Pyloric-gland adenoma of the stomach: case report of a rare tumor successfully treated with
endoscopic submucosal dissection. *Endosc.* 2008;40(S 02):E110–E1.

21. Albores-Saavedra J, Chablé-Montero F, Méndez-Sánchez N, Ángel Mercado M, Villotoba-Chapa M, Henson DE. Adenocarcinoma with pyloric gland phenotype of the extrahepatic bile ducts: a previously unrecognized and distinctive morphologic variant of extrahepatic bile duct carcinoma. *Human Pathol.* 2012;43(12):2292–8.

22. Kushima R, Vieth M, Borchard F, Stolte M, ichi Mukaisho K, Hattori T. Gastric-type well-differentiated adenocarcinoma and pyloric gland adenoma of the stomach. *Gastric Cancer.* 2006;9(3):177–84.

23. Schaefer IM, Cameron S, Middel P, Homayounfar K, Schwörer H, Vieth M. Pyloric gland adenoma of the cystic duct with malignant transformation: report of a case with a review of the literature. *BMC Cancer.* 2012;12(1):570.

24. He C, Fukumura Y, Toriyama A. Pyloric Gland Adenoma (PGA) of the Gallbladder: A Unique and Distinct Tumor from PGAs of the Stomach, Duodenum, and Pancreas. *Am J Surg Pathol.* 2018;42(9):1237–45.

25. Andrén-Sandberg Å. Diagnosis and management of gallbladder polyps. *N Am J Med Sci.* 2012;4(5):203–11.

Author biography

Ashutosh Gupta Associate Professor
Amit Choraria Assistant Professor
Shantanu Tiwari Senior Resident
Vishakha Tikeykar Consultant
Vivek Chaudhary Professor & Head

Cite this article: Gupta A, Choraria A, Tiwari S, Tikeykar V, Chaudhary V. Pyloric gland adenoma of gallbladder with squamoid morules in pediatric age. *Indian J Pathol Oncol.* 2020;7(2):338-342.