

Squamous Cell Carcinoma of Gallb—Bladder – An Uncommon Presentation.

Abstract

A 51-year-old male patient presented with pain in the right hypochondriumupper right quadrant of the abdomen since 2 months, associated with weight loss and fever. **Contrast enhanced computed tomography** abdomen revealed gall bladder with wall thickening which was asymmetric and heterogeneous at junction of body. A provisional diagnosis of cholecystitis with element of cholangitis and **abnormal wall thickening with multiple tiny calculi** was considered. Open radical cholecystectomy was done. Microscopic and immunohistochemical findings established the diagnosis of moderately differentiated squamous cell carcinoma of the gallbladder. Adjuvant chemotherapy regimen consisting of paclitaxel 175mg/m² and carboplatin AUC 6 was given three times3 weekly for six6 cycles in the present case. Six months after treatment completion, patient is on regular follow up and disease free on clinical and radiological examination.

Keywords

Cholecystitis, gallbladder, squamous cell carcinoma

Introduction

Gallbladder carcinomas are uncommon and constitute only 2 to 4% of all gastrointestinal malignancies. Most common histology encountered in gallbladder malignancies are adenocarcinoma. Incidence of Squamous cell carcinoma (SCC) **may reach 12.7%** of tumours of the gallbladder ^[1].

We report a single case of SCC of gallbladder that was clinically diagnosed as cholecystitis with element of cholangitis and **abnormal wall thickening with multiple tiny calculi**.

Case Report

A 51-year-old male presented with complaints of intermittent pain in the upper right quadrant of the abdomen ~~right~~ and weight loss for two~~2~~ months with associated fever. Patient was known a case of diabetic and on regular medication.

On per abdominal examination, there was tenderness in right hypochondrium and there was no clinically palpable organomegaly. Vital signs were normal. Complete haemogram and renal function tests were within normal limits. Liver ~~f~~Function ~~t~~Tests showed elevated Aspartate transaminase (184 U/L), aAlanine ~~t~~ransaminase (208 U/L), ~~and~~& aAlkaline ~~p~~hosphatase levels (243 U/L) with normal serum bilirubin levels s.

Magnetic ~~r~~esonance ~~i~~maging (MRI) of the upper abdomen with ~~m~~Magnetic ~~r~~esonance ~~c~~holangiopancreatography (MRCP) revealed gallbladder wall thickening, sludge, ~~and~~ calculus, and no obvious biliary ductal dilatation or filling defects (~~F~~igure 1). Contrast enhanced ~~c~~omputed ~~t~~omography (CECT) of the aAbdomen revealed pathological gall-bladder with wall thickening which was asymmetric and heterogeneous at the junction of the body region (~~F~~igure 2) and there were mild thickening and enhancement of the proximal extrahepatic bile duct walls. On this basis, a clinical diagnosis of cholecystitis with ~~element of~~ cholangitis and abnormal wall thickening with multiple tiny calculi was considered, and the patient underwent open radical cholecystectomy which include resection of gallbladder, ~~segment-IV B~~ and~~&~~ V, segments of liver, pericholedochal lymph nodes, hepatoduodenal tissue, and hepatic artery ~~lymph nodes~~, celiac ~~lymph nodes~~ and gastric lymph nodes. Operative findings included a hard mass in *fundus* and body of gallbladder invading into liver. There were no obvious metastasis~~deposits~~ in liver, peritoneum, and omentum. ~~There were enlarged~~ The pericholedochal, periportal and hepatic artery nodes were enlarged.

The ~~m~~Macroscopic findings were: polypoidal growth measuring 2x2 cm inside the gallbladder, infiltrating the muscle layer, but underlying liver was grossly free of tumor ~~grossly~~. Multiple samples were obtained~~given~~ from representative areas and routinely processed. Histopathological examevaluation revealed moderately differentiated squamous cell carcinoma of gallbladder with area of poor differentiation infiltrating the entire thickness of the wall (Figures 3 and& 4). Nineteen lymph nodes were identified and all were free of tumors. Immunohistochemical study showed that tumor cells were negative for cytokeratin 7, cytokeratin 20 and& p63 antibodies, but showed equivocal result with hHigh mMolecular wWeight cCytokeratin. Postoperative period was uneventful.

~~Then-t~~The patient was planned for adjuvant chemotherapy with paclitaxel 175mg/m²-and carboplatin AUC 6, both intravenously, three times weekly, into a total of six cycles. Six months after the operation, the pPatient is on regular follow up every month for six month and-is disease free on clinical and radiological examinations.



Figure (1)- MRI sScan of the aAbdomen (tTransverse view) showing the gall bladder with asymmetric and heterogenous wall thickening (arrow), and multiple tiny gallstones.



Figure (2)- CT sScan of the aAbdomen (transverse view) showing gall-bladder with asymmetric wall thickening (arrow).

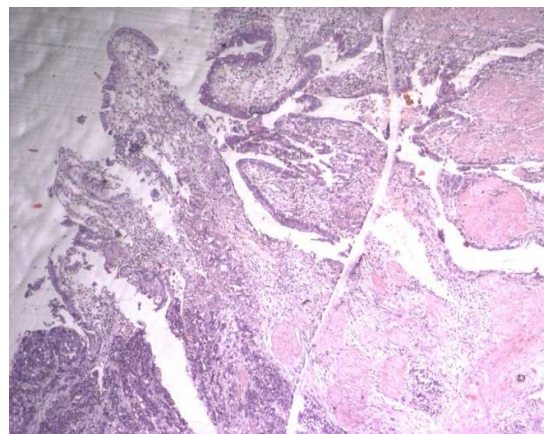


Figure (3-) Photomicrograph showing the gall-bladder wall with infiltration by carcinoma (H&E, 100X).

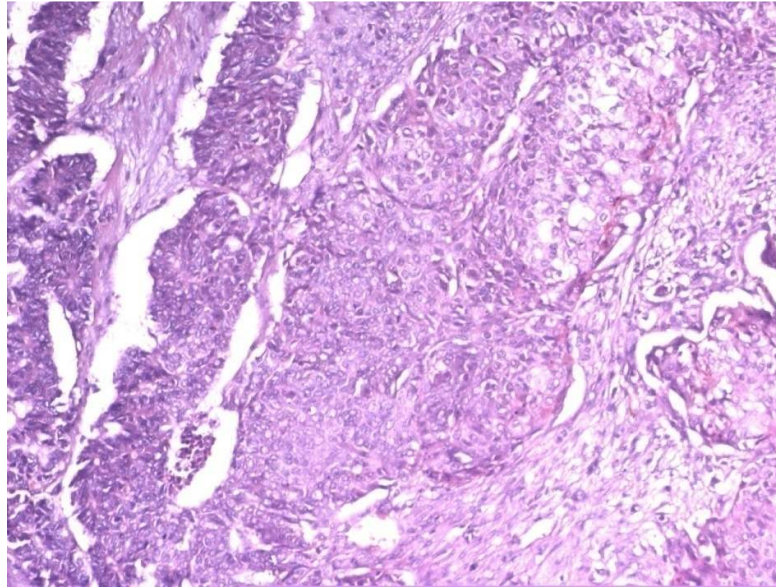


Figure - (4-) Photomicrography ~~(high power view)~~ showing the tumor cells with squamoid differentiation. (H&E, 100X).

Discussion

Squamous cell carcinoma (SCC) of the gallbladder is a rare and aggressive form of gallbladder cancer. Long term prognosis for patients who have SCC of gallbladder is poorer than patients who have adenocarcinoma of gallbladder ^[2-3]. The most common type of gallbladder cancer is adenocarcinoma ~~of the gallbladder and it predominates in female~~ with female/~~to~~ male ratio ~~is~~ 3:1. The cCommonly presenting age group for gallbladder cancer is 40 to 60 years ^[3].

Early stages of gallbladder cancers do not produce any symptoms. When symptoms are present, ~~then,~~ the presentation is similar to biliary colic or chronic cholecystitis ^[6]. SCC of gallbladder is characterized by rapid growth, diffusely local and regional infiltration, and early metastatic dissemination. Despite of these characteristics, peritoneal seeding is rare while hepatic metastases are more frequent ^[3]. The time for duplication for adenocarcinoma is two times lower~~twice~~ as that for SCC of gallbladder; thus, the ~~that is~~ SCC growth is faster

than that of adenocarcinoma. ~~and is~~ Therefore, SCC is more aggressive with poor prognosis as compared to adenocarcinoma ^[2-3].

Roppongi *et al.* ^[5] mentioned that due to inclusion of heterogenous neoplasm such as adenosquamous carcinomas and some misdiagnoses, SCC of gallbladder comprise up to 12.7% of gallbladder cancers ^[6]. According to the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute, out of 3038 patients with gallbladder cancer only 45 (1.7%) were SCC ^[3,6].

Due to foregut origin of gallbladder, most gallbladder carcinomas are heterogeneous during neoplastic transformation ^[7]. As a result, pure SCC of the gallbladder is a rare entity. SCC of the gallbladder is thought to arise from the basal cell layer of the epithelium either due to squamous metaplasia or squamous differentiation of a pre-existing adenocarcinoma. Others believe SCC originates from squamous differentiation of the adenocarcinoma via expression of mixed phenotypes within a single tumor ^[3].

Radical resection is the mainstay of treatment with curative intent for patients with locally invasive SCC. The most important parameter in determining survival is the extent of tumor invasion at the time of diagnosis. Death occurs within six months of diagnosis without radical surgery ^[2-3]. Laparoscopy should not be done if gallbladder cancer is suspected ^[8]. Postoperative radiotherapy and chemotherapy may be used; however, results are inconsistent ^[4].

Oohashi *et al.* ^[9] compared radical resection and primary tumor resection alone in terms of survival in adenosquamous carcinoma of gallbladder. These authors ~~and~~ found that 5- year survival of 48.6% with radical resection compared to a 3-year survival of 7.7% with primary tumor resection alone. Residual tumor *status* was the only significant independent prognostic factor. Patients with no residual tumor had a 5-year survival of 62.9% compared to patients ~~who~~ with residual tumor whose the 5-year survival was nil ^[9].

Conclusion

SCC of gallbladder is a rare malignancy. Main treatment modality is surgery. Even though chemotherapy and radiation therapy has been used in the adjuvant setting, it does not provide additional benefits. Careful radiological examination may help to decrease the mortality associated with this disease enabling early detection at an earlier stage.

Reference

1. Karasawa T, Itoh K, Komukai M et al. Squamous cell carcinoma of gallbladder - Report of two cases and review of literature. *Acta Pathol Jpn* 1981;31:299-308.
2. Roa JC, Tapia O, Cakir A, et al. Squamous Cell and Adenosquamous Carcinomas of the Gallbladder: Clinicopathological Analysis of 34 Cases Identified in 606 Carcinomas. *Mod Pathol*. 2011;24(8):1069-78.
3. Waisberg J, Bromberg SH, Franco MI, et al. Squamous Cell Carcinoma of the Gallbladder. *Sao Paulo Med J*. 2001;119(1):43.
4. D'Angelica M, Jarnagin W, "Tumors of the Gall-bladder," In B. L. Saunders, Ed., *Surgery of the Liver, Biliary Tract, and Pancreas*, 4th Edition, Elsevier, Amsterdam, 2006, pp. 764-781.
5. Roppongi T, Takeyoshi I, Ohwada S, et al. Minute Squamous Cell Carcinoma of the Gallbladder: A Case Report. *Jpn J Clin Oncol*. 2000;30(1):43-5.
6. Henson DE, Albores-Saavedra J, Corle D. Carcinoma of the Gallbladder. Histologic Types, Stage of Disease, Grade, and Survival Rates. *Cancer*. 1992;70(6):1493-97.
7. K. Moore, "The Developing Human," W.B. Saunders Company, Philadelphia, 1982.

8. Memon MA, Anwar S, Shiwani MH, et al. Gallbladder Carcinoma: A Retrospective Analysis of Twenty-Two Years Experience of a Single Teaching Hospital. *Int Semin Surg Oncol*. 2005;2(1):6.
9. Oohashi Y, Shirai Y, Wakai T, *et al*. Adenosquamous Carcinoma of the Gallbladder Warrants Resection Only If Curative Resection Is Feasible. *Cancer*. 2002;94(11):3000-05.