

Gallbladder Squamous Cell Carcinoma Presented as chronic cholecystitis

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Abstract

One of the common malignancies of the gallbladder called Squamous cell carcinoma (SCC). Primary SCC of the gallbladder accounts for about 3.3% of the gallbladder cancers. Pure SCC is a very rare condition with an unknown histogenesis. Herein, we presented a 45-year-old female with a history of vague abdominal pains diagnosed with pure SCC. In the results of histopathological examination a well-differentiated keratinized SCC has been revealed. The patient was subjected to surgery based on the presumptive diagnosis of acute cholecystitis. Considering the poor prognosis of this lesion, the achievement of knowledge on the clinical presentations of this lesion is of paramount importance. The choice of therapeutic strategy for the management of this carcinoma depends on its locoregional extension; however, surgical resection is usually the choice.

Keywords: chronic Cholecystitis, squamous Cell Carcinoma (SCC), adenocarcinoma, cancer.

Introduction

The most common malignancy of the biliary tract is gallbladder cancer, which ranks fifth among the digestive tract cancers (adenocarcinoma). About 90-95% of the patients with the histological subtype of gallbladder cancer are diagnosed with adenocarcinoma. In addition, only 3% of malignant tumors are

gallbladder cancers (Rekik et al., 2011).

The main risk factors for this disease include female gender, age older than 50 years, and white skin complexion (Roa et al., 2011). Adenosquamous carcinoma and squamous cell carcinoma (SCC) are the next common malignancies, which are known to be less aggressive than adenocarcinoma (Rai et al., 2009). About 0.5-12.7% of gallbladder cancers are primary SCCs of the gallbladder (Khaira, Awad and Thompson, 1995).

Studying the characteristics of primary pure SCC of the gallbladder has shown that the most significant characteristic is prominent keratinization, which is in the form of keratin pearls. The malignant glandular transformation is not observed in the primary stage of this tumor (Alpuerto et al., 2017). Clinical signs and symptoms of SCC appear very late and are non-specific. This carcinoma is diagnosed in the advanced stages due to the similarity of its clinical symptoms with those of other gallbladder carcinomas (Rekik et al., 2011; Meena et al., 2015).

The association between the gallstone and gallbladder carcinoma is a challenging issue. Despite the high prevalence of adenocarcinoma as a malignancy in the gallbladder, pure SCC is a very rare condition. However, the areas of squamous differentiation are seen in adenocarcinoma (Roa et al., 2011). This lesion has an unknown histogenesis.

While some pieces of evidence suggest the pre-existing squamous metaplasia of the gallbladder epithelium as the source of SCC, others propose the squamous differentiation of the neoplastic cells of adenocarcinoma as the origin of this carcinoma. The rarity of SCC has made the diagnosis and management of this tumor challenge. Herein, we reported a pure case of SCC to highlight the importance of obtaining knowledge regarding the clinical presentation of this tumor.

Case Presentation

A 45-year-old female with a history of vague abdominal pains, deteriorated by the consumption of fatty foods, referred to Rasool Akram Hospital, Tehran, Iran, in August 2017. The pains were occasionally accompanied by nausea. The pregnancy test was negative. She had undergone three cesarean sections and

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tubectomy. The patient had a hearing loss of 2%. Her family history included cancer in grandmother and cardiac diseases. Moreover, she had a history of hypertension managed with pantoprazole, cefotaxime, and acetaminophen.

The urinary and stool test results were normal. The patient had a heart rate of 80 bpm, respiratory rate of 12 breaths per minute, and body temperature of 37°C. Furthermore, she had ischemic heart disease. The abdominal pain had been exacerbated for two months. Therefore, she was subjected to an abdominal ultrasound, which revealed a 50-mm mass in the gallbladder. The gallbladder was dilated and contained sludge, and the diameter of the common bile duct (CBD) was 10 mm.

The magnetic resonance cholangiopancreatography (MRCP) have been performed in the patients and based on its findings, the gallbladder was completely enlarged with an irregular border and liver parenchyma. The mass lesion resulted in the displacement of the CBD. A suspicious stone was detected in the gallbladder fundus. Accordingly, the presumptive diagnosis was gallbladder cancer with or without underlying cholecystitis. There was no evidence suggesting obvious distal CBD stone or mass.

In addition, According to the findings of Computed tomography (CT), the gallbladder was multi-folded, large, and distended and had an enhanced thick wall. Mild dilatation of intrahepatic and the extrahepatic biliary tree was also reported. Therefore, it was essential to rule out severe cholecystitis or infiltrative tumoral lesion.

In order to perform open cholecystectomy, the patient was subjected to the right subcostal incision under general anesthesia. Subsequently, segments 4 and 5 of the liver were resected with a margin of 2 cm, followed by the removal of the anterior wall involving the first part of the duodenum (D1). The anterior wall of the gallbladder was repaired using acrylic thread (number 3.0) and a jejunal patch. The metastasis of SCC to the duodenum and liver was diagnosed by means of cryosection. In the next step, the mass was resected with a 2-cm margin from the fourth and fifth segments of the liver using an Argon cutter. An adhesion was detected between the mass and the anterior wall of D1.

Discussion

Pure SCC of the gallbladder is a very rare condition (Roa et al., 2011; Hosseinzadeh, Shokripur and Salahi, 2012). Accordingly, this disease was reported to have an incidence rate of 1% among 606 carcinomas of the gallbladder, and 5.6% of the cases had squamous differentiation. The mean age of the patients with SCC is reported 65 years. This condition affects the males and females in an equal proportion (3.8%) (Roa et al., 2011). However, in the present study, we reported a 45-year-old female, who was younger in comparison with other reported cases.

The pure SCC of the gallbladder with large size without metastasis is suspected of carcinoma (Kendre et al., 2017). This condition can occur without any symptoms in some cases. Hosseinzadeh et al. studied about a 70-year-old man with acute

right upper quadrant abdominal pain, diagnosed with acute cholecystitis, which was completely asymptomatic (Hosseinzadeh, Shokripur and Salahi, 2012). Likewise, our case complained of abdominal pain, which was worsened by the consumption of fatty foods.

Why and how the pure SCC emerges is not exactly clear yet. Three pathogenetic possibilities have been proposed for this carcinoma, which includes gallstones, parasitic infestation, and metaplasia-dysplasia-carcinoma sequence (Roppongi et al., 2010; Karasawa et al., 1981). Moreover, some patients with this carcinoma show different degrees of atypical epithelial modifications in the vicinity of the invasive tumor (Roppongi et al., 2010; Karasawa et al., 1981; Mingoli et al., 2005).

Primary SCC has been presented as acute cholecystitis in some studies (Hosseinzadeh, Shokripur and Salahi, 2012; Gupta, Gupta and Aryya, 2004). In this regard, Gupta et al. reported wall thickening with multiple gallstones during cholecystectomy in a patient with SCC of the gallbladder (Verlicchi et al., 2015). Additionally, another study presented a primary SCC case of the gallbladder penetrating to the adjacent hepatic parenchyma in an old woman (Rekik et al., 2011).

Despite the rarity of lymphatic spread in pure SCC, local invasion commonly occurs in this condition. Rapid growth, primary locoregional extension, and lack of a muscularis mucosae layer in the gallbladder wall are among the features usually observed near the hepatic tissue, D1, and different parts of the colon are suggestive of the invasion of this lesion (Rekik et al., 2011).

Histopathologically, large cells, including big nuclei and eosinophilic cytoplasm, with obscure histogenesis have been found in squamous cell tumors (Verlicchi et al., 2015). In a number of studies, researchers reported that the pre-existing metaplastic squamous epithelium can be an etiology of SCC. There is also evidence suggesting the squamous differentiation of the adenocarcinoma cells, through the expression of mixed phenotypes in a single tumor as the source of this lesion. In this regard, the pure SCC cells may outpace the epithelial component of adenosquamous carcinoma in duplication and replacement with them. However, the association between squamous cell metaplasia and adenocarcinoma is a challenging issue (Rekik et al., 2011). Rekik et al. observed squamous cell metaplasia, along with a continuum of squamous epithelial cells; however, they detected no adenocarcinoma element (Rekik et al., 2011).

Treatment of gallbladder SCC depends on the degree of locoregional infiltration. Surgical resection is usually the treatment of choice for this condition, followed by extended cholecystectomy and hepato-pancreatic-duodenectomy (Rekik et al., 2011). Furthermore, radiation therapy and chemotherapy can be used as complementary treatments in this domain.

The early diagnosis of pure SCC is a matter of paramount importance given the poor prognosis of adenosquamous and SCC. Furthermore, since pure SCC has a better prognosis, compared to adenocarcinoma with squamous differentiation, the distinction

between these conditions is of great significance. In this regard, the former condition is aggressive and widely metastatic, whereas the latter is localized, slow growing, and rarely metastatic (Roa et al., 2011; Roppongi et al., 2000). The mean survival time of this condition depending on the size of the tumor and degree of locoregional extension is 6 months after diagnosis. Herein, we presented a case with pure SCC of the gallbladder, which can be used for differentiation with adenocarcinoma or adenosquamous variants.

Conclusion

It is investigated that the pure SCC of the gallbladder is a rare condition. Although pure primary SCC is more aggressive than gallbladder adenocarcinoma, its symptoms are similar to those of gallbladder adenocarcinoma. Considering the poor prognosis of this lesion, obtaining knowledge on the clinical presentations of this lesion is of crucial importance. The adoption of a proper therapeutic strategy for the management of this carcinoma depends on its locoregional extension. In most of the conditions, the choice is surgical resection.

References

- Alpuerto AC, Mora ME, Robitsek RJ, Schubl SD. Primary pure squamous cell carcinoma of the gallbladder locally invading the liver, duodenum, and stomach: a case report and literature review. *Case reports in surgery*. 2017;2017, 5 pages.
- Gupta S, Gupta S, Aryya N. Primary squamous cell carcinoma of gallbladder presenting as acute cholecystitis. *Indian journal of pathology & microbiology*. 2004;47(2):231-3.
- Hosseinzadeh M, Shokripur M, Salahi H. Primary pure squamous cell carcinoma of gallbladder presenting as acute cholecystitis. *Iranian journal of medical sciences*. 2012 Dec;37(4):271-273.
- Karasawa T, Itoh K, Komukai M, Ozawa U, Sakurai I, Shikata T. Squamous Cell Carcinoma of Gallbladder: —Report of Two Cases and Review of Literatures—. *Pathology International*. 1981 Mar;31(2):299-308.
- Kendre P, Kataria P, Patel A, Mittal L, Mule T. Metastasis as initial presentation of squamous cell carcinoma of gallbladder: A rare clinical entity. *Indian Journal of Pathology and Microbiology*. 2017 Jul 1;60(3):440.
- Khaira HS, Awad RW, Thompson AK. Squamous cell carcinoma of the gallbladder presenting with a biliary-colic fistula. *European Journal of Surgical Oncology*. 1995 Oct 1;21(5):581-2.
- Meena RN, Tiwary SK, Khanna R, Khanna AK. Primary Pure Squamous Cell Carcinoma of Gallbladder: A Rare Entity. *World Journal of Surgical Research*. 2015 Jul 18;4(3).
- Mingoli A, Brachini G, Petroni R, Antoniozzi A, Cavaliere F, Simonelli L, Chirletti P, Modini C. Squamous and adenosquamous cell carcinomas of the gallbladder. *Journal of experimental & clinical cancer research: CR*. 2005 Mar;24(1):143-50.
- Rai A, Ramakant KS, Pahwa H, Kumar S. Squamous cell carcinoma of the gallbladder: an unusual presentation. *The Internet Journal of Surgery*. 2009; 22:1. 4 pages.
- Rekik W, Fadhel CB, Boufaroua A, Mestiri H, Khalfallah M, Bouraoui S, et al. Case report: Primary pure squamous cell carcinoma of the gallbladder. *Journal of visceral surgery*. 2011; 148(2), 169-172.
- Roa JC, Tapia O, Cakir A, Basturk O, Dursun N, Akdemir D, Saka B, Losada H, Bagci P, Adsay NV. Squamous cell and adenosquamous carcinomas of the gallbladder: clinicopathological analysis of 34 cases identified in 606 carcinomas. *Modern Pathology*. 2011 Aug; 24(8), 1069–1078.
- Roppongi T, Takeyoshi I, Ohwada S, Sato Y, Fujii T, Honma M, Morishita Y. Minute squamous cell carcinoma of the gallbladder: a case report. *Japanese journal of clinical oncology*. 2000 Jan 1;30(1):43-5.
- Verlicchi L, Blons H, Hannoun L, Bachet JB. Squamous-cell gallbladder carcinoma: how to treat. *J Cell Sci Ther*. 2015 Jan 1;6(212):2.