

Sarcomatoid carcinoma of the gallbladder: a case report

Journal of International Medical Research

48(6) 1–6

© The Author(s) 2020

Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/0300060520935283

journals.sagepub.com/home/imr

Yunfu Shi^{1,2,*}, Jiabin Chen^{1,*}, Hua Chen¹ and
Xiufang Hong³ 

Abstract

Sarcomatoid carcinoma is a rare type of gallbladder cancer with no specific clinical manifestation. The final diagnosis depends on pathological and immunohistochemical examination. Sarcomatoid carcinoma is characterized by early lymphatic metastasis, rapid progression, a high short-term recurrence rate, and a worse prognosis than adenocarcinoma. This report describes a 60-year-old woman with poorly differentiated adenocarcinoma of the gallbladder. She underwent treatment with chemotherapy and surgery. Palliative surgery was performed for treatment of tumor recurrence in April 2018. Postoperative pathology showed infiltration of poorly differentiated carcinomas, most of which were sarcomatoid. After four cycles of chemotherapy, the disease continued to progress. Anlotinib tablets were given from August 2018 to November 2018 but were then stopped because of gastrointestinal bleeding. The patient died in April 2019. This paper reports the whole process of diagnosis and treatment in this case of gallbladder sarcomatoid carcinoma, thus providing a reference for treatment.

Keywords

Sarcomatoid carcinoma, gallbladder, surgical treatment, chemotherapy, targeted therapy, case report

Date received: 19 January 2020; accepted: 27 May 2020

Introduction

Sarcomatoid carcinoma is a malignant tumor that originates from omnipotent mesenchymal stem cells. Morphologically and immunohistochemically, sarcomatoid carcinoma shows epithelioid and mesenchymal components. Sarcomatoid tumors are rare and can occur in all parts of the body, but they mainly develop in the

¹Department of Oncology, Tongde Hospital of Zhejiang Province, Hangzhou, China

²The First School of Medicine, Zhejiang Chinese Medical University, Hangzhou, China

³Department of Geriatrics, Zhejiang Hospital, Hangzhou, China

*These authors contributed equally to this work.

Corresponding author:

Xiufang Hong, Department of Geriatrics, Zhejiang Hospital, 12 Lingyin Road, Hangzhou, Zhejiang 310013, China.

Email: 952420845@qq.com



Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative

Commons Attribution-NonCommercial 4.0 License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).

kidneys, lungs, prostate, and upper respiratory tract. Sarcomatoid carcinoma of the gallbladder is rarely observed.¹ Surgical treatment is the preferred approach for patients with early-stage sarcomatoid carcinoma, while radiotherapy, chemotherapy, and other treatments such as targeted therapy and immunotherapy may help to prolong the survival time in patients with advanced disease. Only a few reports of gallbladder sarcomatoid carcinoma have been published to date, and the clinical characteristics and treatment methods of gallbladder sarcomatoid carcinoma are still in the exploratory stage. In this report, the whole diagnostic and treatment process of a case of gallbladder sarcomatoid carcinoma is described to provide a reference for the diagnosis and treatment of gallbladder sarcomatoid carcinoma.

Case report

A 60-year-old woman with a 1-month history of mid-upper abdominal pain and abdominal distension was admitted to the Second Affiliated Hospital of the Medical College of Zhejiang University in May 2017. Physical examination revealed mid-upper abdominal tenderness. Abdominal enhanced computed tomography (CT) showed that the gallbladder wall was

significantly thickened, and further examination was recommended to exclude the possibility of a malignant tumor (Figure 1).

Laparoscopic exploration and omental biopsy were then performed. The volume of ascites in the abdominal cavity was about 1500 mL. Miliary gray-white nodules were found in the liver, omentum, abdominal wall, and pelvis. The nodules in the greater omentum were obtained for analysis, and the frozen sections were sent for pathological examination. The pathological findings revealed poorly differentiated adenocarcinoma. The diagnosis was established based on the presence of gallbladder cancer with abdominal metastasis combined with the patient's medical history and auxiliary examination results. After the operation, the patient was treated with gemcitabine + oxaliplatin + tiggitto capsules for two cycles and albumin-bound paclitaxel combined with oxaliplatin for four cycles with an unknown dosage, and the curative effect was judged as a partial response (PR). Radical cholecystectomy + intestinal adhesiolysis + laparoscopic exploration + omental excision were performed in November 2017. During the operation, gallbladder consolidation, invasion of the serosa, dense adhesion between the serosa and transverse colon, and hepatic surface adhesion were observed; no other obvious metastases were observed in

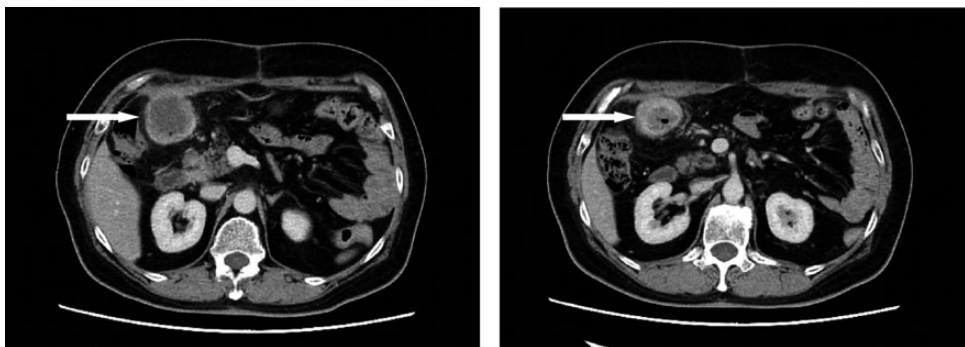


Figure 1. Abdominal computed tomography scan on 29 May 2017 showed that the gallbladder wall was significantly thickened.

the abdominal cavity. Postoperative pathologic examination revealed poorly differentiated adenocarcinoma with infiltration of cancer tissue at the incision margin.

In April 2018, whole-body positron emission tomography–CT showed postoperative changes of gallbladder cancer, low-density mass lesions with an abnormal increase in fluorodeoxyglucose metabolism in the operative area, and tumor recurrence involving the left lateral lobe of the liver and hepatic flexure of the colon. The slightly low-density shadow in the gallbladder fossa accompanied by increased fluorodeoxyglucose metabolism was considered to be possible tumor infiltration. The patient then underwent right hemicolectomy + special hepatectomy + complex intestinal adhesiolysis + jejunal nutritional fistula formation + duodenal bulb repair. Intraoperative examination revealed gallbladder cancer recurrence, invasion of the colonic flexure, and colonic obstruction. The postoperative pathology results showed infiltration of poorly differentiated cancer tissues, most of which were metastatic sarcomatoid carcinoma of the right colon (Figure 2). None of the nine intestinal wall lymph nodes were metastatic, and the hepatic margin, ileum, and colon margins appeared negative. Albumin-bound paclitaxel combined with oxaliplatin chemotherapy

was given for four cycles from May 2018 with an unknown dose. CT examination after chemotherapy indicated tumor progression.

The patient then visited our hospital for treatment. Anlotinib tablets (12 mg orally every 24 hours, days 1–14, every 3 weeks) were given from August 2018. In September 2018, abdominal CT showed obvious lesion necrosis with cavity formation, and the curative effect was evaluated as PR. A comparison of the PR before and after treatment is shown in Figure 3. After two cycles, the anlotinib was reduced to 10 mg orally every 24 hours, days 1 to 14, every 3 weeks because of intolerable adverse effects including fatigue and hypertension. In November 2018, the patient stopped taking anlotinib because of gastrointestinal bleeding, and she died in April 2019.

Discussion

Sarcomatoid carcinoma was first reported by Landsteiner in 1907.² It can occur in all parts of the body but mainly develops in the kidneys, lungs, prostate, and upper respiratory tract.³ Sarcomatoid carcinoma of the gallbladder is rare.¹ The etiology of gallbladder sarcomatoid carcinoma is still unclear; studies have shown that it might be related to gallstones,⁴ gallbladder polyps, and estrogen.⁵ The age at onset of

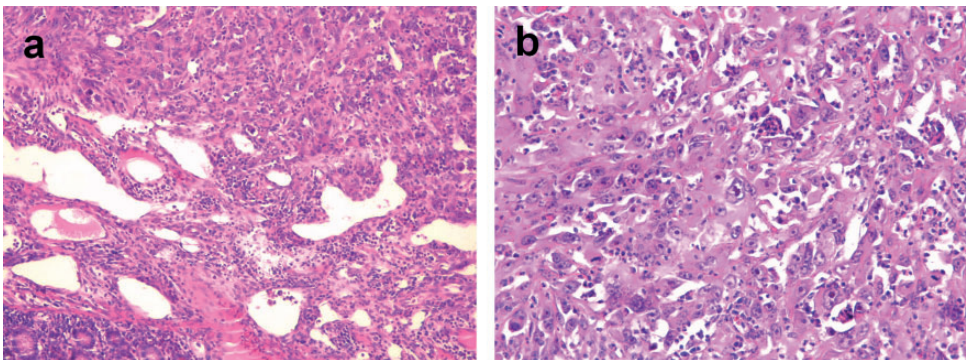


Figure 2. Representative hematoxylin and eosin staining of tumor tissue. (a) $\times 200$. (b) $\times 400$.

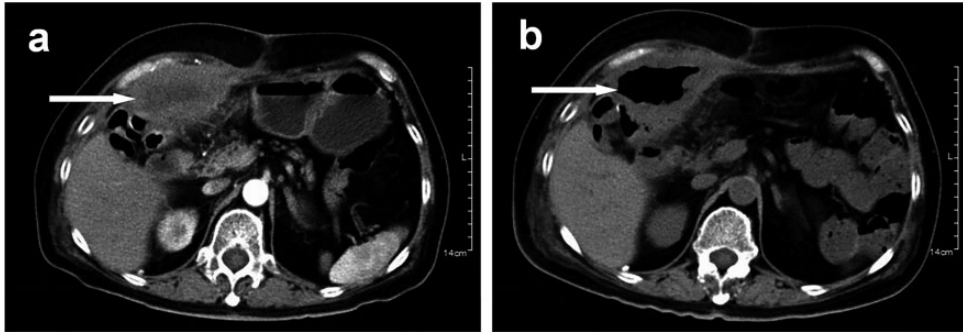


Figure 3. (a) Abdominal computed tomography scan on 16 August 2018 showed abdominal metastases before treatment with anlotinib. (b) Abdominal computed tomography scan on 4 September 2018 showed necrosis of metastatic tumors in the abdomen accompanied by cavity formation after treatment with one cycle of anlotinib.

gallbladder sarcomatoid carcinoma reportedly ranges from 45 to 91 years, and it is more commonly seen in women.⁶ The present case involved a 60-year-old woman, which is consistent with the literature. Sarcomatoid carcinoma is characterized by early lymphatic metastasis, rapid progression, a high short-term recurrence rate, and a worse prognosis than adenocarcinoma.⁷

The clinical manifestations for this type of gallbladder cancer are nonspecific and mainly involve right upper abdominal pain and an abdominal mass. Some patients may have fever, jaundice, nausea, and vomiting.⁸ Abdominal ultrasonography, CT, and magnetic resonance imaging are important imaging examinations in the diagnosis of gallbladder sarcomatoid carcinoma and can show the location, size, and characteristics of the tumor. However, because of the similar characteristics of gallbladder sarcomatoid carcinoma and adenocarcinoma, these cancers are difficult to distinguish by imaging examination. The final diagnosis depends on pathological and immunohistochemical examination. Histologically, sarcomatoid carcinoma of the gallbladder often exhibits two components: sarcomatoid carcinoma and epithelial carcinoma.¹ Sarcomatoid carcinoma is the main component of the tumor and is composed of

shuttle cells or pleomorphic cells arranged in intricate or intertwined bundles. The cells have obvious atypia and many mitoses. Immunohistochemistry shows cyokeratin expression in the sarcomatoid carcinoma cells and epithelial membrane antigen and vimentin expression in some of the cells. Ki-67 is highly expressed.⁷ In the present case, both the omental biopsy and the first post-operative pathologic examination showed poorly differentiated adenocarcinoma. The pathologists found that some of the poorly differentiated carcinoma had transformed into sarcomatoid carcinoma in the process of the pathological diagnosis after recurrence. The cells changed to a short fusiform morphology, the volume increased, the nucleus-to-cytoplasm ratio was high, and the heteromorphism increased. The reason for these changes may be that in the process of tumor recurrence, because of its heterogeneity, the cell phenotypes may be transformed.⁹

Surgery is the preferred treatment option.¹⁰ Radiotherapy, chemotherapy, and other treatments might also help to prolong the patient's survival time. Because of the low incidence rate and lack of data analysis of sarcomatoid carcinoma, no standard radiotherapy or chemotherapy methods have yet been proposed. In the

present case, the effect of chemotherapy for gallbladder sarcomatoid carcinoma was poor, and the effect of anlotinib was evaluated as PR. The findings of this case suggest that anlotinib has a certain therapeutic effect on gallbladder sarcomatoid carcinoma. The patient finally stopped taking anlotinib because of gastrointestinal bleeding; therefore, attention should be paid to the adverse effects of anlotinib.

Anlotinib is a new type of small molecule multi-targeted tyrosine kinase inhibitor developed independently in China. Unlike other tyrosine kinase inhibitors, it strongly inhibits many targets such as vascular endothelial growth factor receptor, platelet-derived growth factor receptor, fibroblast growth factor receptor, and c-Kit.¹¹ It has the effects of anti-angiogenesis and anti-tumor growth without inducing significant toxicity.¹² A series of clinical trials showed that anlotinib had survival benefits and good safety in the treatment of non-small cell lung cancer, medullary thyroid cancer, and soft tissue sarcoma after the failure of standardized therapy.^{13–15} In the present case, obvious tumor necrosis was observed after treatment with anlotinib. This provides an important reference for studying molecular-targeted therapies of gallbladder sarcomatoid carcinoma.

Conclusions

Sarcomatoid carcinoma of the gallbladder is rare and highly malignant. Extensive and careful pathological sampling and immunohistochemical examination are needed to establish the diagnosis. Surgery is the first-choice and main treatment method. Surgery combined with chemotherapy and target therapy may help to prolong the survival time. This report has described the whole process of diagnosis and treatment of a case of gallbladder sarcomatoid carcinoma, providing a reference for treatment.

Ethics

The study protocol was approved by the Ethics Committee of the Tongde Hospital of Zhejiang Province, Hangzhou, and the patient provided written informed consent.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

This study was supported by the Zhejiang Province Famous Traditional Chinese Medicine Experts Inheritance Studio Construction Project (GZS2017001), the Zhejiang Province Association of Traditional Chinese Medicine (2017ZB013, 2018ZA005), and the Science and Technology Department of Zhejiang Province (2018KY198).

ORCID iD

Xiufang Hong  <https://orcid.org/0000-0002-9789-982X>

References

1. Kataria K, Yadav R and Seenu V. Sarcomatoid carcinoma of the gall bladder. *J Surg Case Rep* 2012; 2012: 5.
2. Doval DC, Azam S, Mehta A, et al. A report of sarcomatoid carcinoma of the gallbladder treated with palliative deocetaxel and gemcitabine chemotherapy. *J Gastrointest Cancer* 2014; 45: 270–274.
3. Seok JY and Kim YB. Sarcomatoid hepatocellular carcinoma. *Korean J Hepatol* 2010; 16: 89–94.
4. Hamdani NH, Qadri SK, Aggarwalla R, et al. Clinicopathological study of gall bladder carcinoma with special reference to gallstones: our 8-year experience from eastern India. *Asian Pac J Cancer Prev* 2012; 13: 5613–5617.
5. Hundal R and Shaffer EA. Gallbladder cancer: epidemiology and outcome. *Clin Epidemiol* 2014; 6: 99–109.
6. Hu ZH, Li ZW, Shen L, et al. Surgical therapy and prognosis of sarcomatoid

- carcinoma of the gallbladder. *Hepatobiliary Pancreat Dis Int* 2010; 9: 175–179.
7. Qin Y, Ou Y, Ma L, et al. Gallbladder sarcomatoid carcinoma: six cases and literature review. *Chin J Clin Oncol* 2015; 42: 247–250.
 8. Chang X, Ma X, Li J, et al. Clinical analysis of 12 patients with sarcomatoid carcinoma of the gallbladder. *Shijie Huaren Xiaohua Zazhi* 2016; 24: 2063–2069.
 9. Takahashi Y, Fukushima J, Fukusato T, et al. Sarcomatoid carcinoma with components of small cell carcinoma and undifferentiated carcinoma of the gallbladder. *Pathol Int* 2004; 54: 866–871.
 10. Liu KH, Yeh TS, Hwang TL, et al. Surgical management of gallbladder sarcomatoid carcinoma. *World J Gastroenterol* 2009; 15: 1876–1879.
 11. Beedie SL, Mahony C, Walker HM, et al. Shared mechanism of teratogenicity of anti-angiogenic drugs identified in the chicken embryo model. *Sci Rep* 2016; 6: 30038.
 12. Sun Y, Niu W, Du F, et al. Safety, pharmacokinetics, and antitumor properties of anlotinib, an oral multi-target tyrosine kinase inhibitor, in patients with advanced refractory solid tumors. *J Hematol Oncol* 2016; 9: 105.
 13. Han B, Li K, Wang Q, et al. Effect of anlotinib as a third-line or further treatment on overall survival of patients with advanced non-small cell lung cancer: The ALTER0303 phase 3 randomized clinical trial. *JAMA Oncol* 2018; 4: 1569–1575.
 14. Sun Y, Du F, Gao M, et al. Anlotinib for the treatment of patients with locally advanced or metastatic medullary thyroid cancer. *Thyroid* 2018; 28: 1455–1461.
 15. Chi Y, Fang Z, Hong X, et al. Safety and efficacy of anlotinib, a multikinase angiogenesis inhibitor, in patients with refractory metastatic soft-tissue sarcoma. *Clin Cancer Res* 2018; 24: 5233–5238.