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RESEARCH ARTICLE

SQUAMOUS CELL CARCINOMA OF GALL BLADDER: A RARE CLINICAL ENTITY: MANAGEMENT EXPERIENCE OF A TERTIARY CARE CENTRE

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ABSTRACT

Background: Squamous cell carcinoma of gall bladder is a rare presentation with limited literature hence adjuvant treatment is still ill defined with under-powered studies showing controversial role of adjuvant treatment.
Aims: To analyse prognostic factors affecting outcome, role of adjuvant treatment and outcome.
Settings and Design: This was a retrospective analysis conducted from January 2010 to December 2013 in a tertiary care centre of North India.
Materials and Methods: It analysed patients of squamous cell carcinoma of gall bladder for clinical presentation, treatment, prognostic factors and outcome.
Results: Nine patients of pure squamous cell carcinoma were found. All patients had cholelithiasis and presented in locally advanced stage. Five patients were resectable while four were unresectable. Resectable patients underwent extended radical cholecystectomy followed by adjuvant chemotherapy and radiotherapy. Margin status post surgery was an important prognostic marker on multivariate analysis. Unresectable patients underwent palliative chemotherapy based on their eastern cooperative oncology group performance status. Resectable patients had a median survival of 18 months, while unresectable patients had a median survival of five months.
Conclusion: Surgery remains the main stay of treatment and adjuvant treatment has no proven benefit although there was a trend towards better survival in our cohort, especially in patients with positive margins.

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INTRODUCTION

Carcinoma (CA) Gall bladder is the most common neoplasm of the biliary tree and has a poor prognosis (Pavlidis *et al.,* 2012). It is two to six times more common in females than in males and its incidence increases with age. There is huge variation in demographical distribution with the highest incidence seen in South East Asian countries (Bartlet *et al.,* 2008). Adenocarcinoma is the most common histology. Pure primary squamous cell carcinoma accounts for less than 1% of all gallbladder malignancies (Roa *et al.,* 2011). Most of the reported cases have adenosquamous variant, while the pure squamous cell carcinoma is rarely reported. Moreover most of the reports are on clinico-pathologic correlation and surgical treatment, but adjuvant treatment (radiotherapy and chemotherapy) and its impact on survival are not well documented. According to our pubmed search this is the largest patient data on pure squamous cell carcinoma.

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MATERIALS AND METHODS

Departmental medical records of patients of CA gall bladder, who were on treatment in our department, were analysed from January 2011 to December 2015. Patients without a confirmed histological diagnosis and patients with history of any previous malignancy were excluded from the study. Out of 700 cases analysed nine cases of pure squamous cell carcinoma of Gall Bladder were found. All the relevant clinical details and treatment given were retrieved from the departmental records.

Statistics: SPSS Version 20 was used to analyse results and survival analysis.

RESULTS

Patient Characteristics

Details of 700 patients of gall bladder carcinoma were analysed out of which nine were found to be of pure squamous cell carcinoma. All the nine patients have died, due to disease

process, before the filing of this report. The patient and disease characteristics are highlighted in Table 1. The age range of patient cohort was from 30 to 70 years, with median age of presentation being 50 years. Females outnumbered males in the ratio of 2:1. Most of the patients had fair general condition with KPS of 70 or more present in 55% of the cohort. The most common presenting symptom was pain abdomen followed by lump abdomen and fever. The average duration of symptoms before diagnosis was four months. All nine patients in cohort had a diagnosis of cholelithiasis. Eight of the nine patients (88.9%) had direct liver infiltration at presentation. Seven patients had T3 disease while two patients had T4 disease. Seven patients (77.8%) had node positive disease at presentation while two patients had metastatic disease at presentation. All patients presented in locally advanced stage with two in stage IIIA, three in stage IIIB, two in stage IVA and two in stage IVB. All patients had squamous cell carcinoma of gall bladder.

Table 1. Patient & Disease Characteristics

Age	Median	50
	Range	30-70
Sex	Male	3
	Female	6
	Ratio (F:M)	2:1
KPS	≥70	5
	<70	4
T-Stage	T3	7
	T4	2
N- Stage	N0	2
	N1	7
AJCC- Stage	IIIA	2
	IIIA	3
	IVA	2
	IVA	2

Table 2. Treatment Characteristics

Serial No.	Age	Gender	Histology	Stage	Treatment	Os (in months)
1	70	F	SCC	IIIB	Sx – CCT – RT	18
2	42	M	SCC	IVB	CCT	6
3	56	M	SCC	IIIB	Sx – CCT – RT	20
4	56	M	SCC	IIIA	Sx – CCT – RT	12
5	38	F	SCC	IVA	CCT	9
6	50	F	SCC	IVB	CCT	4
7	52	F	SCC	IIIA	Sx – CCT – RT	11
8	56	F	SCC	IVA	ORAL CCT	2
9	30	F	SCC	IIIB	Sx – CCT – RT	18

Treatment characteristics

Patients with stage IIIA and IIIB were taken up for extended radical cholecystectomy. Out of the five patients taken up for surgery (Sx) three had R0 resection (negative margins) while two had R1 resection (positive margins). Adjuvant treatment after radical resection was adjuvant Chemotherapy (CCT) followed by Radiotherapy (RT). Chemotherapy used was Cisplatin + Gemcitabine, considering the squamous nature of histology, while radiotherapy was used in a dose of 45Gy/25#/5weeks by 3D conformal technique. Median number of chemotherapy cycles received in radical group was six. In unresectable patients (four) of stage IVA and IVB, the treatment was individualized considering the Eastern Cooperative Oncology Group (ECOG) performance status of the patient. All patients received palliative chemotherapy based on Cisplatin and gemcitabine combination or oral capecitabine. All unresectable patients were planned for six cycles of chemotherapy however they could only receive a median of three cycles and none of the patient could complete planned six cycles of chemotherapy.

Acute Toxicity

Gastrointestinal and Hematological toxicities were seen, mainly in patients who had undergone surgery. No patient had >grade II toxicity and treatment break was not warranted due to it.

Overall survival

Median survival in the cohort was 11months, while median survival for patients undergoing radical treatment was 18 months. Median survival for patients undergoing R0 resection was again 18 months while it was 11.5 months for patients undergoing R1 resection. Advanced stage patients on palliative treatment had a median survival of only five months. The relevant data along with the overall survival is enumerated in Table 2. Kaplan meier survival chart is depicted in Figure 1.

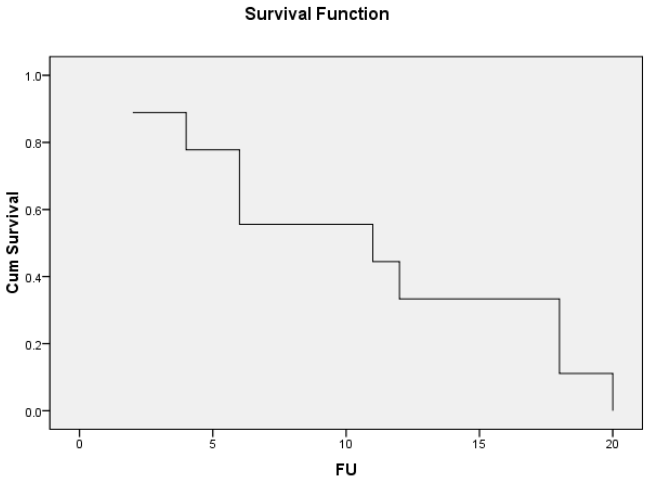

Figure 1. Overall Survival

DISCUSSION

Gallbladder cancer is the most common cause of death from biliary malignancies (Khan *et al.,* 2010). It is usually detected at an advanced stage due to its non-specific symptoms (Le *et al.,* 2011), even in our study all the cases presented in locally advanced stages. Etiology of gall bladder cancer is said to be some form of chronic inflammation, and the overwhelming inciting factor for inflammation is cholelithiasis (Bartlet *et al.,* 2008). In our study all the patients had cholelithiasis which probably makes it the etiological factor. Adenocarcinoma is the most common histology and Squamous histologic types (ASC and SCC) are rare, accounting for 1.4% to 10.6% of all cases of GBC (Henson *et al.,* 1992; Albores-Saavedra *et al.,* 1998). The wide variation in percentages may be due to clumping of the two histologies, while pure squamous cell carcinoma may be very rare as in our study it formed only 1.2% of all gall bladder malignancies (nine patients out of 700 analysed). The histogenesis of these tumors is still obscure. Squamous cell metaplasia may develop in response to irritation or originate from preexisting adenocarcinoma (Khaira *et al.,* 1995) though no adenocarcinoma component was found in any samples. Patients with ASC/SCC of the gallbladder are frequently diagnosed at an advanced stage with a bulky tumor and adjacent organ involvement (Chan *et al.,* 2007; Kim *et al.,* 2011; Oohashi *et al.,* 2002). It is reported that the growth rate of the squamous component (doubling time 81 days) was twice as fast as the adenocarcinomatous component (doubling time 166 days) (Charbit *et al.,* 1971). Thus SCC variants are

expected to be of more advanced stage and this is consistent with our study in which all patients presented in locally advanced stage with 44.4% patients being unresectable. Some authors have proposed that SCC variants have a lesser nodal and distal spread (Kim *et al*., 2011; Charbit *et al*., 1971) but the same could not be validated by this study as more than 50% of our patients had either nodal or distal spread. Liver infiltration is commonly reported for squamous cell carcinoma in various studies and is similarly found in our study, where 88.9% of patients had liver infiltration at presentation. Surgery is the mainstay of treatment for gall bladder malignancy with literature reporting improved survival with R0 resection as compared to R+ resection (Chan *et al.,* 2007). The reported resectability rate of these tumors in different series was around 50% (Chan *et al.,* 2007; Kim *et al.,* 2011), while some report it to be as low as 10 to 30%. In our series also 56% of patients could undergo surgery and out of five patients three achieved R0 resection while two achieved R+ resection. The role of adjuvant chemotherapy and radiotherapy for gallbladder carcinoma has been poorly defined because the available literature is derived from small, single-institution experiences in which heterogeneous treatment methods were used (Willcox and Chang, 1993). Adjuvant use of radiotherapy has improved survival as per one study (Houry *et al.,* 1999). Though most surgical series have heterogeneous data in terms of stage to account for median survival, it is known that median survival for stage III resectable patients is 12 months while for unresectable stage III and IV patients it is two to four months with one year survival of 5% only (Bartlet *et al.,* 2008). Considering this our patients who underwent surgery followed by adjuvant therapy had a median survival of 18 months while 4 unresectable patients had a median survival of five months; thus indicating towards the probable effectiveness of adjuvant therapy used. Patients undergoing R0 resection in our analysis had a better median survival, though number of patients was too less for any statistical significance, as compared to patients having R1 resection thus underlining the benefit of negative margins.

Conclusion

Squamous cell carcinoma of the gall bladder is a rare entity so in so that our nine patients represent the largest series of pure squamous cell carcinoma cases we could find. Surgery remains the main stay of treatment and although adjuvant treatment with chemoradiation has not shown any proven benefit, they trended towards improved median survival in our study. Patients with R1 resection had a poorer survival as compared to patients with R0 resection. Palliative chemotherapy has not shown any improvement in the median survival in unresectable cases, though it may help in palliation of symptoms.

Clinical significance

Carcinoma Gall Bladder has a much higher incidence in south-east Asian countries as compared to our western counterparts; this puts responsibility on our shoulders to perform research in this field. Our study highlights the importance of negative margins in surgery. Role of adjuvant treatment is still controversial; however it has shown some benefit in patients with positive margins. Patients on palliative treatment have a very poor outcome.

REFERENCES

Albores-Saavedra, J., Henson, D. E., Klimstra, D. S. 1998. Tumors of the Gallbladder, Extrahepatic Bile Ducts, and Ampulla of Vater. 3rd ed. Washington, DC: Armed Forces Institute of Pathology, 63–92.

Bartlet, D. L., Ramanathan, R. K., Josef, E. B. 2008. Cancer of the biliary tree. In: Devita, Hellman & Rosenberg editors. Cancer: Principles & Practice of Oncology. Lippincott Williams & Wilkins, P. 1172.

Chan, K.M., Yu, M.C., Lee, W.C., *et al*. 2007. Adenosquamous /squamous cell carcinoma of the gallbladder. *J Surg Oncol.,* 95:129–34.

Charbit, A., Malaise, E.P., Tubiana, M. 1971. Relation between the pathological nature and the growth rate of human tumors. *Eur J Cancer.,* 7:307–15.

Henson, D. E., Albores-Saavedra, J., Corle, D. 1992. Carcinoma of the gallbladder: Histologic types, stage of disease, grade, and survival rates. *Cancer*, 70:1493–7.

Houry, S., V. Haccart, M. Huguier, and M. Schlienger, 1999. "Gallbladder cancer: role of radiation therapy," *Hepato-Gastroenterology*, vol. 46, no. 27: 1578–1584.

Khaira, H. S., Awad, R. W., Thompson, A. K. 1995. Squamous cell carcinoma of the gallbladder presenting with a biliary-colic fistula. *Eur J Surg Oncol.,* 21:581—2a.

Khan, R. A., Wahab, S., Khan, M. A., Siddiqui, S., Maheshwari, V. 2010. Advanced presentation of Gallbladder cancer: epidemioclinicopathological study to evaluate the risk factors and assess the outcome. *J Pak Med Assoc*., 60: 217-9.

Kim, W.S., Jang, K.T., Choi, D.W., *et al*. 2011. Clinicopathologic analysis of adenosquamous/squamous cell carcinoma of the gallbladder. *J Surg Oncol.,* 103:239–42.

Le, M. D., Henson, D., Young, H., Albores-Saavedra, J. 2011. Is gallbladder cancer decreasing in view of increasing laparoscopic cholecystectomy? *Ann Hepatol*, 10:306-14.

Oohashi, Y., Shirai, Y., Wakai, T., *et al*. 2002. Adenosquamous carcinoma of the gallbladder warrants resection only if curative resection is feasible. Cancer, 94:3000–5.

Pavlidis, T. E., Pavlidis, E. T., Symeonidis, N. G., Psarras, K., Sakantamis, A. K. 2012. Current curative surgical management of gallbladder cancer: a brief review. *J Curr Surg.,* 2:81-3.

Roa, J. C., Tapia, O., Cakir, A., Basturk, O., Dursun, N., Akdemir, D., *et al*. 2011. Squamous cell and adenosquamous carcinomas of the gallbladder: clinicopathological analysis of 34 cases identified in 606 carcinomas. *Mod Pathol.,* 24:1069-78.

Willcox, J., Chang, F.C. 1993. Squamous cell carcinoma of the gallbladder. *Kans Med.,* 94:133–4.

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