Signet ring cell carcinoma of the gallbladder: a case report

S Pudasainin,[1] N Subedi,[2] KBR Prasad,[1] SK Rauniyar,[1] SK Bhattacharya,[2] R Koirala,[2] S Koirala,[1] A Aryal[1] and A Shrestha[3]

[1]Department of Pathology, [2]Department of Surgery, [3]Department of Radiology, Nepal Medical College and Nepal Medical College Teaching Hospital, Jorpati, Kathmandu, Nepal

Corresponding author: Dr. Sujata Pudasaini, Department of Pathology, Nepal Medical College, Nepal Medical College and Nepal Medical College Teaching Hospital, Jorpati, Kathmandu, Nepal; e- mail: sujatap2000@yahoo.com

ABSTRACT

Carcinoma of the gall bladder is the most common biliary tract tumor with higher incidence in females and increasing age. The risk is significantly higher in cholelithiasis. Signet ring cell carcinoma is a rare form of mucinous adenocarcinoma and has a worse prognosis. Early diagnosis is rare. We report a case of signet ring cell carcinoma of the gall bladder in a 70 years old female patient. The gross finding was yellowish white mass measuring 4 x 3.5 cm on cut surface of the gall bladder along with thickened wall. Histopathological examination of the specimen shows the sheets of signet ring cells with lateral spread through the lamina propria and large amount of extracellular mucin. There was metastasis in the retroperitoneum and mesenteric lymph node. The tumor was stage IV (according to TNM staging). Patient died 20th post operative day. Since very few cases have been reported, information regarding the behavior and prognosis of gall bladder carcinoma is limited. However it has been seen that stage III and IV carcinoma usually have worse prognosis.

Keywords: Gall bladder, signet ring cell carcinoma, histopathology.

Gallbladder carcinoma is the most common biliary tract tumor.[1,2] More than 80% cases of gall bladder carcinoma is associated with cholelithiasis.[2,3] Gall bladder carcinoma is more common in females than males and its incidence grows with age.[2]

Almost 90% of the gall bladder carcinoma is adenocarcinoma. Signer ring cell carcinoma is a rare and aggressive variant of mucinous adenocarcinoma with worse prognosis.[1,3]

CASE REPORT

A 70 years old female presented with pain in the abdomen for 5 days and vomiting for 3 days. Vomitus was bile stained. Patient has not passed urine for 3 days. Ultrasonography revealed gall bladder with marked irregular thickened wall and sludge suggestive of growth and mild left hydronephrosis. The patient underwent an open cholecystectomy. A thick walled gall bladder with mass, retroperitoneal mass and mesenteric lymph node was removed. With suspicion of carcinoma, surgeon sent the specimen for histopathology.

We received an already cut opened gall bladder in formalin measuring 6 x 3 x 2.5 cm. Outer surface was congested with areas of haemorrhage. Cut surface shows yellowish white mass measuring 4 x 3.5 cm in the mucosal surface. The wall of the gall bladder was thickened and measured 0.8 m in maximum thickness. No stones were identified (Fig. 1). Separate container

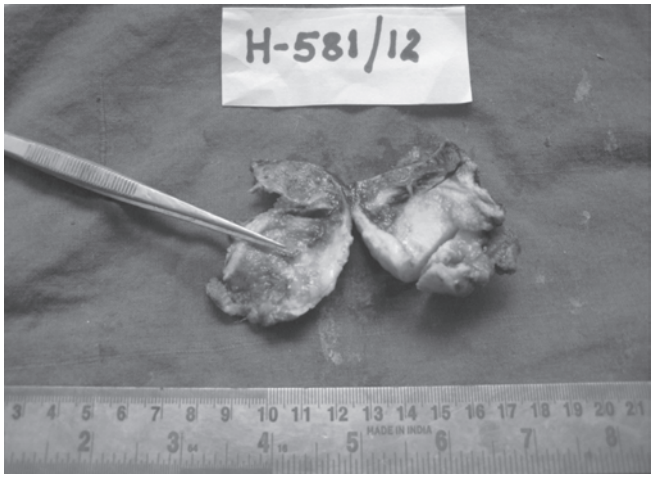

Fig. 1. Gross examination of the specimen showing irregular thickened wall and yellowish white mass

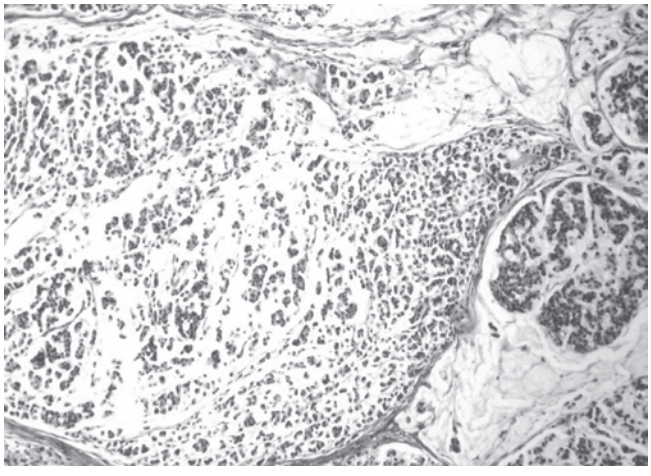

Fig. 2. Sheets of signet ring cells with extracellular mucin (40 X H and E stain)

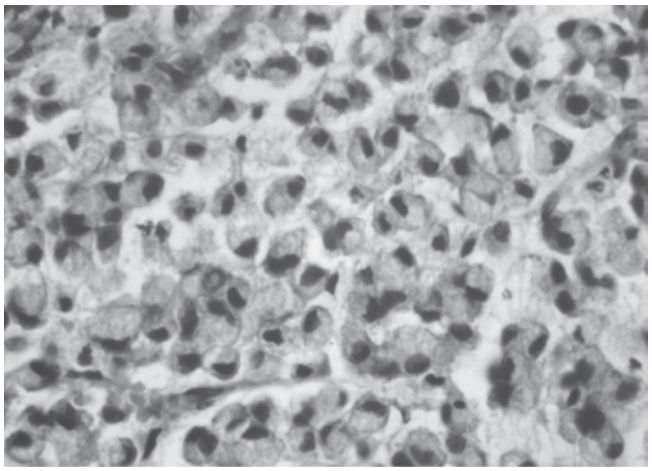

Fig. 3. Sheets of signet ring cells with eccentric nuclei (400 X, H and E stain)

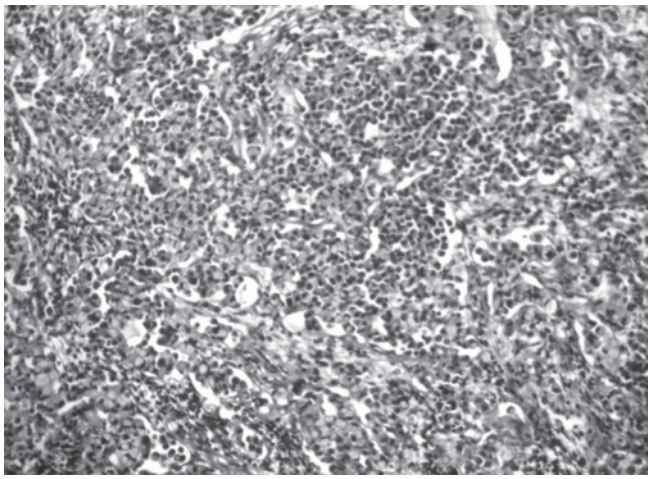

Fig. 5. Section form the lymph node showing sheets of signet ring cells infiltrating the lymphoid cells (40 X, H and E Stain)

labeled as retroperitoneal mass showed a fibrofatty tissue measuring 3 x 2 cm with focal grayish white areas and haemorrhagic areas. Another container labeled as mesenteric lymph node showed a grayish white nodular tissue measuring 1 x 0.8 cm. Represented sections were taken including the section from resected margins of the gall bladder.

Microscopic examination showed sheets of signet ring cells with lateral spread through the lamina propria. The tumor cells are infiltrating the wall of the gall bladder. The signet ring cell comprises of more than 90% of the tumor cells. Large amount of extra cellular mucin was also noted (Fig. 2,3). The resected margins were involved by the tumor. Sections from the retroperitoneal mass (Fig. 4) and mesenteric lymph node (Fig. 5,6) showed metastatic tumor deposit. The histopathological report was given as Signet ring cell carcinoma of the gall bladder (WHO classification), grade 3 (poorly differentiated) and stage IV (AJCC/UICC TNM classification, 6th edition).

Post operative period of the patient was critical with abdominal distension and respiratory distress. The patient expired on 20th post operative day.

DISCUSSION

Gall bladder carcinoma is the fifth most common malignant neoplasm of the digestive tract, adenocarcinoma being the most frequent histological type.[1] Patients usually do not have symptoms or have uncharacteristic symptoms even at later stage of the disease and it usually suggest gall baldder disease and not a carcionoma. The proper diagnosis is established comparatively late, often intraoperatively or on histopathological examination.[2]

Gall bladder carcinoma is more common in females than males and its incidence shows the tendency to increase with age.[2,4,5,6] Our case was a female of 70 years and almost the same finding was seen in a study of Pesic *et al*[2] where gall bladder carcinoma are more common in females and an average age of the patients was 71.3

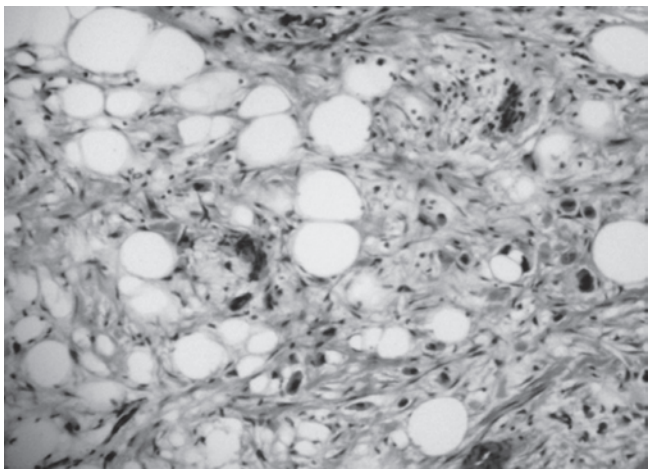

Fig. 4. Tumor cells infiltrating the retroperitoneal tissue (400 X, H and E Stain)

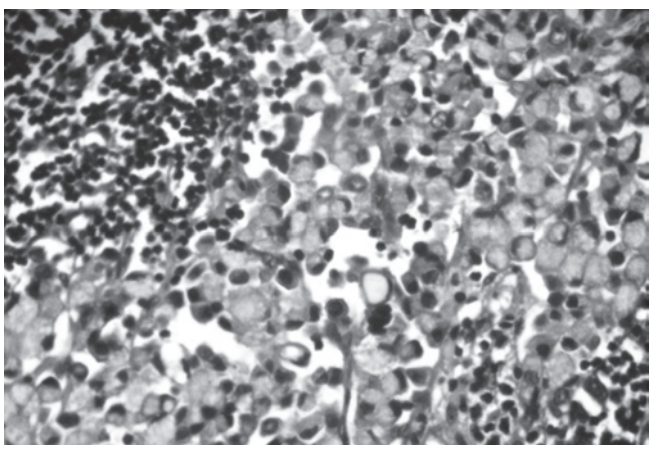

Fig. 6. Section form the lymph node showing sheets of signet ring cells (400 X, H and E Stain)

years. The presence of gall stone is one of the major risk factor of gall bladder carcinoma. However several other factors may be important in the development of gall bladder carcinoma because 10-25% of patients of gall bladder carcinoma do not have associated cholelithiasis.[6] Our cases also presented with gall bladder mass without gall stones. In a study done by Pandey *et al*[4] ultrasononngraphy provided a preoperative diagnosis of a gall bladder mass in 93.9% of the patients. In our case the ultrasononngraphy report was suggestive of growth with irregular thickened wall.

Adeno carcinoma is the most common histological type of gall baldder carcinoma. Signet ring cell carcinoma is a rare type and accounts for aggressive pathology.[1] It is commonly seen in stomach, colon and breast but can be seen in any other organ. It frequently metastasize to peritoneal surface, regional lymph nodes, ovaries and lungs.[1] Ahmad *et al*[7] reported a primary signet ring cell carcionoma of gall bladder where 90% of the tumor was composed of sheets of signet ring cells. In another case report, Bazan *et al*[1] reported signet ring cell carcinoma of gall bladder in a 63 years old man with multiple metastasis in the liver,lymphatic nodes, pleuras, peritoneum and subcutaneous tissue. In our case, the tumor was aggressive in stage IV with retroperitoneal and mesenteric lymph node metastasis.

Survival and prognosis of gall bladder carcinoma patients are improved by an early diagnosis, unfortunately its clinical characteristics appear at an advanced stage and this more characteristic feature worsens the prognosis.[1] Hence, survival of gall bladder carcinoma is directly related to the disease stage. The expected 5 year survival for grade I patients is reported as 75-100%.[3] With the involvement of lymph node or metastatic disease, 5 year survival rates range 0-15% with median survival of 6-12 months.[5] Pandey *et al*[4] in his study found out the mean survival of 3.7 months for stage IV gall bladder carcinoma and the 30 day post operative mortality was 8.7% for stage III and IV disease. In our case the carcinoma was stage IV and the survival of the patient was less than one month.

Primary carcinoma of the gall bladder is an unexpected histopathological finding in an elective cholecystectomy specimen done for benign gall bladder diseases. In spite of the modern diagnostic procedures, early diagnosis of gall bladder carcinoma is rare therefore a routine histopathological examination of all cholecystectomy specimens is a must. Histological type, grade and stage of the disease are the predictors of prognosis with highest postoperative survival in patients with early carcinoma and lowest in high grade and inoperable carcinoma.

REFERENCES

1. Bazan F, Sanchez J, Aguilar G *et al*. Metastatic gallbladder adenocarcinoma with signet ring cells: a case report. *J Med Case Reports* 2011, 5: 548-51.
2. Pesic M, Karanikolic A, Djordjevic N, Gmijovic D, Basic H. Clinical characteristics of primary carcinoma of the gall bladder. *Med Biol* 2002; 9: 227-30.
3. Karagulle E, Turk E, Kiyici H, Karadeli E, Moray G. Signet ring cell carcinoma of the gallbladder with skin metastasis: a case report. *Turkish J Pathol* 2010; 26: 162-4.
4. Pandey M, Pathak AK, Gautam A, Aryya NC, Shukla VK. Carcinoma of the gall bladder. A retrospective review of 99 cases. *Dig Dis Sci* 2001; 46: 1145-51.
5. Yalcin S. Carcinoma of the gall bladder. *Orphanet Encyclopedia* 2004: 1-5.
6. Singh S, Ansari MA, Narayan G. Pathobiology of gall bladder cancer. *J Sci Res*. 2012; 56: 35-45.
7. Ahmad Z, Qureshi A. Primary signet ring cell carcinoma of gall bladder: report of an extremely rare histological type of primary gall bladder carcinoma. *Brit Med J Case Reports* 2010; 10: 1136-9.