IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 21, Issue 11 Ser.7 (November. 2022), PP 01-04
www.iosrjournals.org

Synchronous Adenocarcinoma and Neuroendocrine Tumour Gall Bladder: A Case Report

Hmingthanzuali Ralte[1], Chawngthu Vanlalhlua[2], Laltlanzovi[3]
[1]*Assistant Professor, Department of Pathology, Zoram Medical College, Mizoram, India.*
[2]*Associate Professor, Department of Surgery, Zoram Medical College, Mizoram, India.*
[3]*Associate Professor, Department of Pathology, Zoram Medical College, Mizoram, India.*

Abstract
Introduction: Synchronous gallbladder tumors are uncommon. Simultaneous occurrence of two malignant tumours-Mixed neuroendocrine non-neuroendocrine neoplasms (MiNENs) represent a rare diagnosis of the gastro-entero-pancreatic tract. Evidence from the current literature regarding their epidemiology, biology, and management is of variable quality and conflicting. Based on available data, the MiNEN has an aggressive biological behaviour, mostly driven by its (often high-grade) neuroendocrine component, and a dismal prognosis. In most cases, the non-neuroendocrine component is of adenocarcinoma histology. Due to limitations in diagnostic methods and poor awareness within the scientific community, the incidence of MiNENs may be underestimated. In the absence of data from clinical trials, MiNENs are commonly treated according to the standard of care for pure neuroendocrine carcinomas or adenocarcinomas from the same sites of origin, based on the assumption of a biological similarity to their pure counterparts. However, little is known about the molecular aberrations of MiNENs.Material and methods: This is a case of a 66 yr old woman who presented with classical signs and symptoms of Cholelithiasis and cholecystitis. Laparoscopic subtotal cholecystectomy was done alongwithomental nodule biopsy. On histopathological examination and immunohistochemistry, two types of malignant tumours namely, adenocarcinoma and neuroendocrine tumour were present alongwith metastasis of Neuroendocrine element to omentum. Conclusion:Only few cases of gallbladder adenocarcinoma associated with neuroendocrine carcinoma has been reported in the medical literature.The prognosis of this association depends on staging based on the TNM classification (tumor size, tumor invasion, lymph node compromise, and metastasis) and the presence and extent of neuroendocrine component is the primary driver of behavior and clinical management.

Date of Submission: 10-11-2022 Date of Acceptance: 25-11-2022

I. Introduction

Gallbladder cancer is uncommon representing 80–95 % of biliary tract cancers worldwide [1, 2]. Adenocarcinoma is the most frequent, accounting for 98 % of gallbladder tumors and two thirds are moderately or poorly differentiated [3]. The diagnosis is an incidental finding in a late stage and may present with symptoms suggesting chronic cholecystitis [4]. Other gallbladder malignancies may be squamous cell carcinomas, neuroendocrine tumors, sarcomas, and lymphomas [4]. The frequency of the latter corresponds to 0.1 to 0.2 % of all the cases. Most of them correspond to extranodal marginal zone lymphomas of mucosa-associated lymphoid tissue (MALT) [5]. The presence of a synchronous gastrointestinal epithelial tumor associated with neuroendocrine tumour is rare, and this association within the gallbladder is exceedingly rare [6]. We report the case of a synchronous adenocarcinoma of the gallbladder associated with a neuroendocrine tumour with metastatic deposits in omentum.

II. Case Report

An 66-year-old woman from rural, Mizoram presented with severe abdominal pain in the right hypochondriac region since 3 months prior to consultation, with no other associated symptomatology. An abdominal ultrasonography evidenced the presence of cholelithiasis and normal bile ducts. A laparoscopic partial cholecystectomy was performed with no complications, peritoneal drainage tube intact.

On gross examination, the gallbladder in piecemeal measured 4x3x1 cm and showed a gray-brown and congested outer surface. On opening the gallbladder, an indurated wall 2 cm in thickness (Fig. 1) was evidenced. Mucosa had erosive and congested lesions showing no other macroscopic lesions, gall stone though present were not received in the Histopathology lab. Omental nodule measuring 4x3x1cm was also included.

The microscopic examination evidenced a welldifferentiated intestinal-type adenocarcinoma infiltrating upto the muscular layer (Fig 1), with no evidence of lymphovascular orperineural invasion. A dense diffuse monotonous small round cell infiltrate predominantly nodular with nodular formations extending from the mucosa to the perivascular adipose tissue was observed(Fig2 &3). Immunohistochemistry studies showed, positivity for adenocarcinoma with CK cocktail , the small round cell component elements were positive for NSE, and there was no apparent expression of the neoplastic cells for CD5,CD20 and CD 45(Fig 5,6,7,8,9). Sections from omental nodule showed metastatic disease of the neuroendocrine component(Fig4).

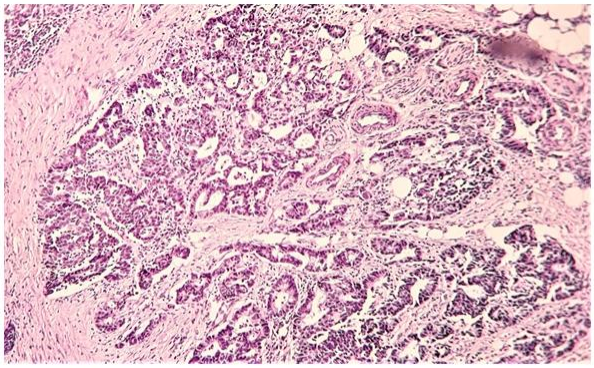

Fig1.Presence of intestinal type adenocarcinoma. H & E, 10 x

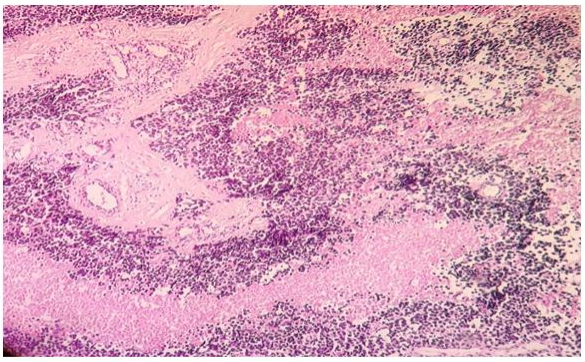

Figure 2 Diffuse infiltrates of monotonous round cells (neuroendocrine) component. H& E, 10x

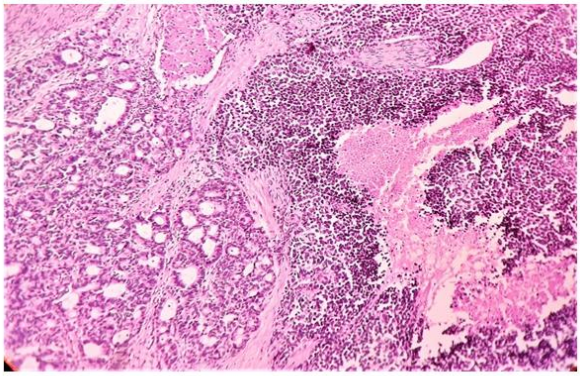

Figure3 depicting occurrence of adenocarcinoma and neuroendocrine component side by side. H&E, 10x

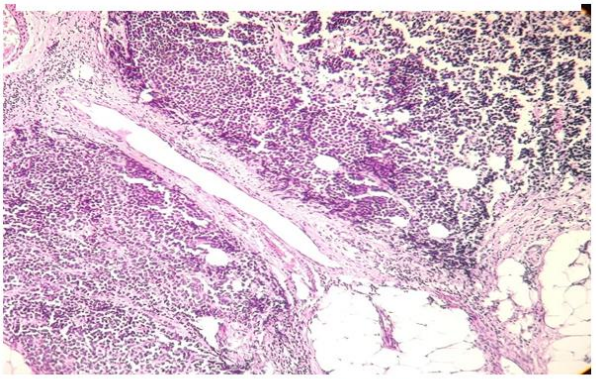

Figure4.Metastatic deposits in omentum, neuroendocrine component. H&E, 10x

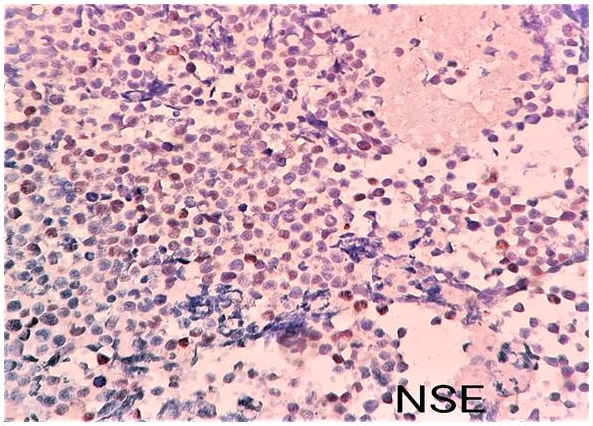

Figure 5. Immunohistochemical staining for NSE positive in neuroendocrine component.

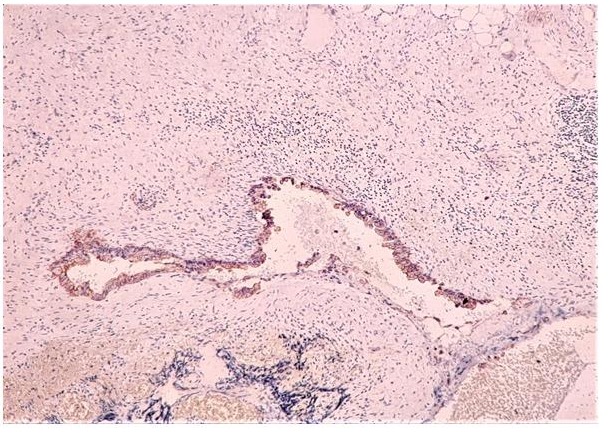

Figure 6. Immunohistochemical staining for cytokeratin positive in adenocarcinoma component.

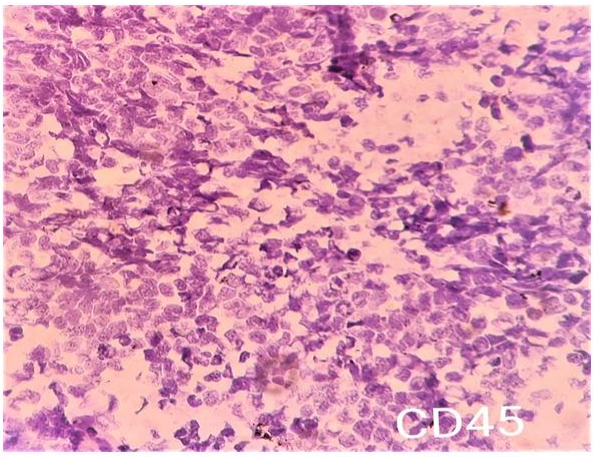

Figure 7. Immunochemical staining for CD45 negative in the round cells, rules out lymphoid element.

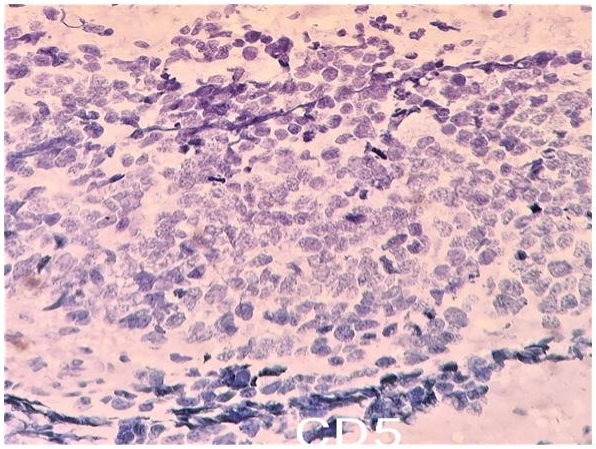

Figure 8. Immunohistochemical staining for CD5 is negative.

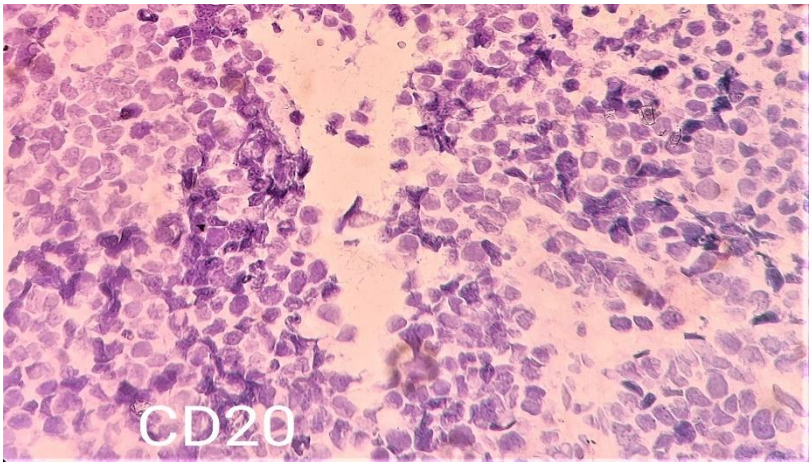

Figure 9. Immunohistochemical staining CD20 is negative.

Follow up of the patient: The peritoneal drainage tube was removed on 7th day of operation with no complications. The patient was referred to a Tertiary Cancer institute for further treatment.

III. Discussion

Gallbladder tumors are an uncommon clinical finding. Incidence varies worldwide depending on geographic zone or ethnic group such as Native Americans [1]. Diagnosis of this condition has increased in recent years, and it is the fifth most common gastrointestinal malignancy. This type of tumor is frequently found in women in their sixth or seventh decade of life [7], and associated risk factors are, presence of gallstones (RR: 3.01–23.8), size of gallstones (2.0–2.9 cm: RR: 2.4; > 3 cm: RR: 9.2–10.1),

length of time that the gallstones reside in the gallbladder (>20 years: OR: 6.2–12.1), increased body mass index (men RR: 1.8; women: RR: 2.1), infections: Helicobacter bilis (RR: 2.6–65), and chronic Salmonella typhi and paratyphoid fever infection (RR: 12.7–167) [1].

The etiology of gallbladder adenocarcinoma is unknown, but an association with chronic gallbladder inflammation, cholelithiasis, anomaluospancreatobiliary duct junction, porcelain gallbladder, and genetic predisposition [4] has been found. Like gastrointestinal adenocarcinomas, gallbladder adenocarcinomas develop from a pre-malignant precursor lesion such as the biliary intraepithelial neoplasia (BilIN) [8]. Clinically, gallbladder adenocarcinomas exhibit an unspecific presentation. They mostly manifest as chronic cholecystitis associated with pain in the right hypochondriac region. Diagnosis is established by histological features which usually are moderately or poorly differentiated. However, other histological subtypes such as papillary, mucinous, squamous, and adeno-squamous [4] subtypes may be observed. The number of gallbladder neoplasms diagnosed as an incidental finding ranges from 0.5 to 1.5 % [7].

On the other hand, gallbladder neuroendocrine tumours are rare. They correspond to 0.2 % of all neuroendocrine tumours. Neuroendocrine carcinomas account for 4% of all gallbladder malignancies and show female predominance and present at an average age in the early to mid-seventh decade of life. More than a third

of neuroendocrine carcinomas of Gall bladder are accompanied by an adenocarcinoma component (mixed neuroendocrine-non-neuroendocrine neoplasm MINEN)[8]

IV. Conclusion

Only few cases of gallbladder adenocarcinoma associated with neuroendocrine carcinoma has been reported in the medical literature.Synchronous gallbladder tumors are uncommon. An association of adenocarcinoma and choriocarcinoma, squamous cell carcinoma and angiosarcoma and mixed tumors such as carcinoid tumors and adenocarcinoma, carcinoma and sarcoma [9–11] has been described. The presence of synchronous adenocarcinoma and neuroendocrine tumors has been reported in the gastrointestinal tract, lung, and prostate [12–15]. The prognosis of this association depends on staging based on the TNM classification (tumor size, tumor invasion, lymph node compromise, and metastasis) and the presence and extent of neuroendocrine component is the primary driver of behavior and clinical management. The 5-year survival rate is less than 5 % [7].

Acknowledgments

The authors would like to express their gratitude to Dr. C.Lalchhandama ,Senior Pathologist, Civil Hospital, Aizawl and Lab technician Lalchhuanliana of Genesis Laboratory, Aizawl for their valuable contribution to this case report.

Compliance with Ethical Standards

Conflict of Interest

The authors declare that they have no competing interests.

References

[1]. Hundal R, Shaffer EA. Gallbladder cancer: epidemiology and outcome. ClinEpidemiol. 2014;6:99–109. 2. Zhu AX, Hong TS, Hezel AF, et al. Current management of gallbladder carcinoma. Oncologist. 2010;15:168–81.
[2]. Goldin RD, Roa JC. Gallbladder cancer: a morphological and molecular update. Histopathology. 2009;55:218–29.
[3]. Bosman FT, Carneiro F, Hruban RH, Theise ND. WHO classification of tumours of the digestive system. Lyon: International Agency for Research on Cancer; 2010.
[4]. Mani H, Climent F, Colomo L, Pittaluga S, Raffeld M, Jaffe ES. Gall bladder and extrahepatic bile duct lymphomas: clinicopathological observations and biological implications. Am J SurgPathol. 2010;34:1277–86.
[5]. Namikawa T, Munekage ERI, Fukudome IAN, Maeda H. Clinicopathological characteristics and therapeutic outcomes of synchronous gastric adenocarcinoma and gastric lymphoma. Anticancer Res. 2014;5074:5067–74.
[6]. Raki M, Patrlj L, Kopljar M, Kli R, Kolovrat M, Loncar B. Gallbladder cancer. Hepatobiliary SurgNutr. 2014;3:221–6.
[7]. WHO Classification of tumours 5edition Digestive System tumours 2019; 292-294.
[8]. Rooney TB, Schofer JM, Stanley MD, Banks SL. Biliary cystadenoma of the gallbladder. AJR Am J Roentgenol. 2005;185:1571–2.
[9]. Lada PE, Taborda B, Sánchez M, et al. Adenosquamous and squamous carcinoma of the gallbladder. Cir Esp. 2007;81:202–6.
[10]. Amador A, Hoyos S, Fuster J, et al. Biliary adenocarcinoma arising from atypical benign lesions. Cir Esp. 2005;78:192–4.
[11]. Nakamura S, Aoyagi K, Iwanaga S, Yao T, Tsuneyoshi M, Fujishima M. Synchronous and metachronous primary gastric lymphoma and adenocarcinoma: a clinicopathological study of 12 patients. Cancer. 1997;79:1077–85.
[12]. Argyropoulos T, Foukas P, Kefala M, et al. Simultaneous occurrence of colonic adenocarcinoma and MALT lymphoma: a series of three cases. World J GastrointestOncol. 2012;4: 89–93.
[13]. Kargi A, Gürel D, Akkoclu A, Sanli A, Yilmaz E. Primary pulmonary extranodal marginal zone lymphoma/low grade B-cell lymphoma of MALT type combined with well-differentiated adenocarcinoma. Tumori. 2010;96:168–71.
[14]. Kang JJ, Eaton MS, Ma Y, Streeter O, Kumar P. Mucosa-associated lymphoid tissue lymphoma and concurrent adenocarcinoma of the prostate. Rare Tumors. 2010;2:e54.

Hmingthanzuali Ralte, et. al. "Synchronous Adenocarcinoma and Neuroendocrine Tumour Gall Bladder: A Case Report." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 21(11), 2022, pp. 01-04.