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Case Report

A case of Gall Bladder Cancer with co-occurrence of Atrial Myxoma in a Healthy Woman

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ABSTRACT

Gall bladder cancer is an uncommon malignancy with high fatality rates. Incidence varies with geographic distribution, race, gender, and presence of risk factors. Gall bladder malignancies are often advanced at the time of diagnosis due to its silent clinical character and metastases at initial presentation is frequently seen. Treatment depends on staging of the cancer, with a combination of surgery, chemotherapy and radiation therapy. Intensive monitoring with ultrasound, liver function tests, and tumor markers like CEA, CA 19-9 is required after treatment. Co-occurrence of a benign and malignant tumor is extremely rare. Atrial myxoma is a benign primary cardiac tumor with a genetic predisposition and relatively common in women. Though occurrence of atrial myxoma with hepatocellular cancer has been reported, none were found with gallbladder cancer. Here, we present a unique case of metastatic gall bladder cancer with an incidental finding of atrial myxoma.

Keywords: Gall Bladder; Atrial Myxoma; Cancer

INTRODUCTION

Gallbladder cancer (GBC) is an uncommon but highly fatal malignancy. Globally the death rate due to GB cancer is about 1.7% and the incidence rate in US is about 1.4/100,000 in women and 0.8 in men[1]. Risk factors includes, gall stones, porcelain Gall bladder, sclerosing cholangitis, Gallbladder polyps, Congenital Biliary cystic dilatation, Abnormal pancreaticobiliary duct junction. Chronic infection (Salmonella, Helicobacter pylori), certain medications (Methyldopa, Isoniazid, oral contraceptive pills), carcinogen exposure, obesity and Diabetes [2].

Gall Bladder cancers are mostly adenocarcinoma from the secretory cells. Papillary adenocarcinoma is rare form of GB cancer from papillary cells which help promote motility of bile in gallbladder. They usually have better prognosis than other types of gall bladder cancer. Gall bladder cancers are highly fatal malignancies because it is usually diagnosed in the later stage where it has already been metastasized [1].

Prognosis is very poor with a survival rate of 12-14 months in patients undergoing resection and only six months for patients with palliative care. Transaminitis and hyperbilirubinemia can represent obstructive disease however they are not very sensitive tests in diagnosing GB cancer. Imaging and biopsy are mainstay in staging and diagnosing GB cancer.

Treatment is surgical and neoadjuvant chemotherapy based on staging of the cancer. Because it is highly fatal malignancy any modifiable risk factors should be addressed in the early stages to prevent from extensive disease and mortality.

Atrial myxoma is most common primary cardiac tumor that is present in patients ages between 30 to 70, common in women and with history of genetic predisposition. 85% occur in left atrium and 10% occur in right atrium and 5% in ventricles. They arise mostly from the atrial septum, common presentation is dyspnea, edema, syncope, arrythmias, thromboembolic events and sudden cardiac death [2]. Atrial myxoma has good prognosis if diagnosed and surgically treated early stages.

Here we are presenting a case of 69-yeaior-old female patient with only risk factors being Age and sex came in with complains of weight loss, early satiety and jaundice. Upon evaluation she found to have poorly differentiated GB carcinoma and an incidental finding of atrial myxoma.

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CASE PRESENTATION

A 69-year-old female with past medical history of well-controlled hypertension presented to the emergency department complaining of a three-week history of episodic, non-radiating, 6/10 intensity epigastric pain exacerbated by diet, unintentional weight loss of unknown amount, dark urine, and one-day history of yellowing of the eyes, early satiety, anorexia, occasional night sweats, and pale stools. Patient denies nausea, vomiting, use of herbal medications, melena, hematochezia, recent travel. No history of H. Pylori infection, cholelithiasis, family history of GB cancer. Patient emigrated to United states from Caribbean.

On presentation, the patient was afebrile with temperature of 97.8 F, Blood pressure 168/84, Hear rate 105 beats/min, Respiratory rate 17/min, saturating at 100% on Room air. On physical examination abdomen was soft, tenderness in epigastrium, no organomegaly, no masses felt. Negative for murphy's sign. Eyes were icteric, generalized jaundice was noted. No rashes, palpable lymphadenopathy. Cardiac exam, a faint 1/6 systolic murmur could be heard best at the left upper sternal border.

Initial laboratory evaluation showed Aspartate Transaminase(AST) 268 U/L, Alanine Transaminase (ALT) 291 U/L, alkaline phosphatase 938 U/L, albumin 2.7 g/dl, Total bilirubin 16.1 mg/dl, Direct bilirubin 13.3 mg/dl, BUN 11 mg/dl Creatinine 0.9 mg/dl, Lipase 285 U/L, Gamma Glutamyltransferase 1357 U/L, ethanol negative, calcium 8.6 mg/dl, WBC 9900, Hb 10.6 g/dl, Platelets 404000, PTT 29 seconds, INR 1.37, CRP 13.3 mg/dl, Alpha fetoprotein 20.2 ng/mL, CA 19-9 512 U/L, CEA 2.0 ng/mL, ANA negative. Urinalysis revealed dark yellow urine positive for trace blood, urobilinogen>/=8.0, +1 protein and bilirubin. Hepatitis panel A, B, C and HIV was negative.

CT abdomen pelvis with Intravenous contrast showed moderate to severely dilated intrahepatic and extrahepatic ducts with irregularly thickened gallbladder wall, concerning for malignant neoplastic process (Figure 1). It also demonstrated a filling defect in the right atrium, unable to determine if artifact, concerning for thrombus. Portocaval lymphadenopathy measuring upto 18 mm.

On Day 2 patient underwent MRCP (Magnetic Resonance Cholangiopancreatography) which showed Ill-defined, irregular enhancing gallbladder mass about 2.9 x 2.2 cm with central necrosis that is highly suspicious for gallbladder carcinoma with likely extension to liver. Intrahepatic biliary ductal dilation secondary to gallbladder mass, dilated cystic duct, and narrowed common bile duct (Figure 2). n the same day patient had Trans Thoracic Echocardiogram (TTE) to further evaluate the filling defect, which demonstrated a large 12 x 13cm mass in the right atrium, connected to the intra atrial septum with a narrow stalk, suggestive of an atrial myxoma (Figure 3). Cardiology recommended anticoagulation at this point to avoid thromboembolic events, and a therapeutic Heparin drip was started.

On day three, patient was sent for ERCP (Endoscopic Retrograde Cholangiopancreatography) for further evaluation, which showed a single localized biliary stricture in the middle third of the main bile duct, which was treated with plastic stent placement. The upper third of the main bile duct was dilated, with an obstruction in the middle of the common bile duct. A biliary sphincterotomy was performed. Common bile duct brushing was done, which revealed atypical cells, and cellular smears with scattered markedly dense clusters of atypical epithelial cells precluding a detailed cytomorphologic evaluation, identified admixed with ciliated columnar epithelial cells, degenerated cells, and inflammatory cells.

On day four, an Invasive Radiology guided biopsy of the gallbladder mass was performed. Biopsy results revealed poorly differentiated carcinoma, immunophenotypically consistent with pancreaticobiliary tract origin, favoring primary gallbladder malignancy (Figure 4-7).

Day 5 Transesophageal echocardiogram (TEE) was done to confirm the mass in left atrium. TEE showed which showed a 12 x 11cm homogeneous left atrial mass with connection to the septum with a narrow stalk consistent with left atrial myxoma without impairment of mitral valve function (Figure 4).Meanwhile patient had an elevated in WBC count of 12200 she was started on Zosyn to cover gram negative bacteria.

Despite ERCP and stent placement patient had persistent elevation in liver function tests with hyperbilirubinemia, so she had undergone ERCP with metal stent placement on Day 9 (Figure 7). Post ERCP patient had a spike in fever with T-max of 101.8 F, C-reactive Protein 22.8 mg/dL, Procalcitonin of 14.4 ng/mL, WBC 19900. Continued with Zosyn until the blood cultures grew

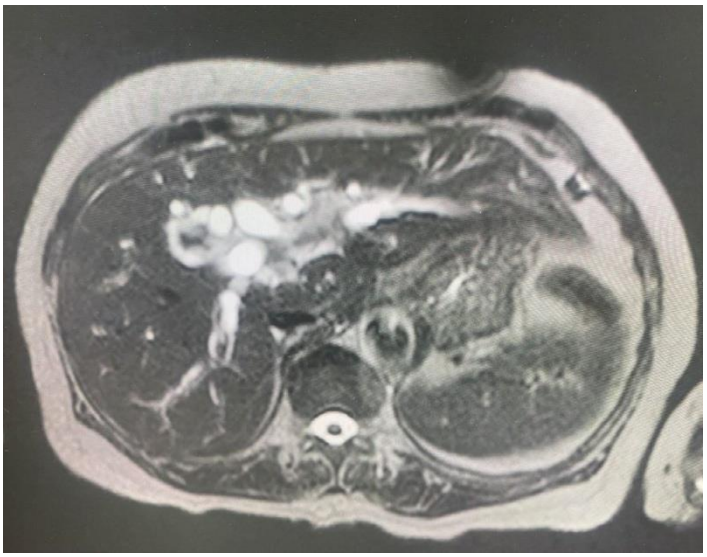

Figure 1: CT Abdomen: Arrow point out to the mass of Gall bladder .

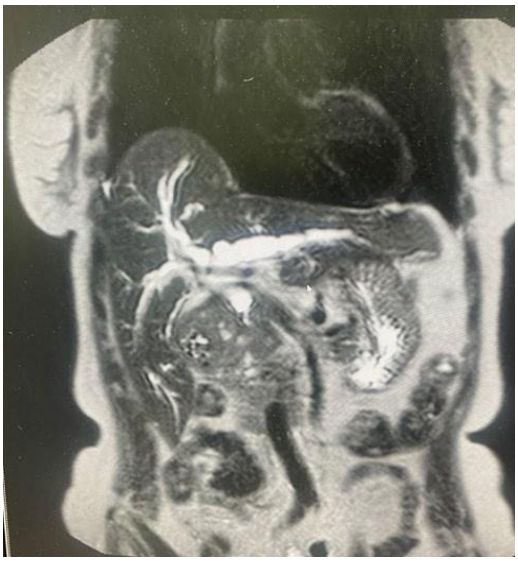

Figure 2: MRCP Arrow showing Gall bladder mass

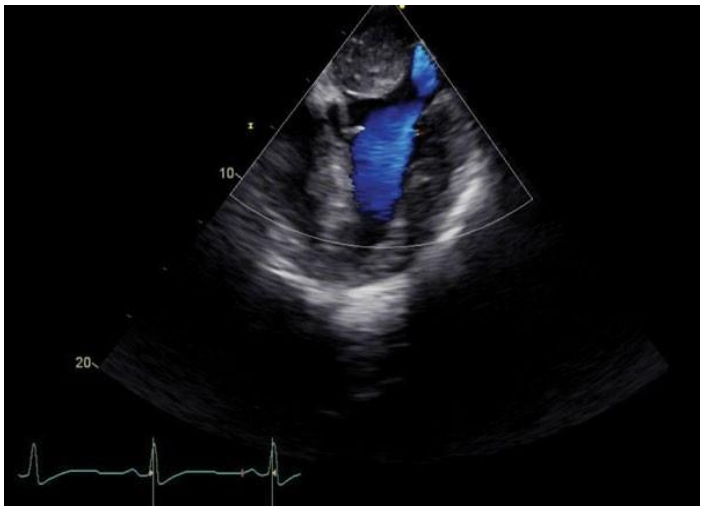

Figure 3: TTE: Showing Right atrial mass

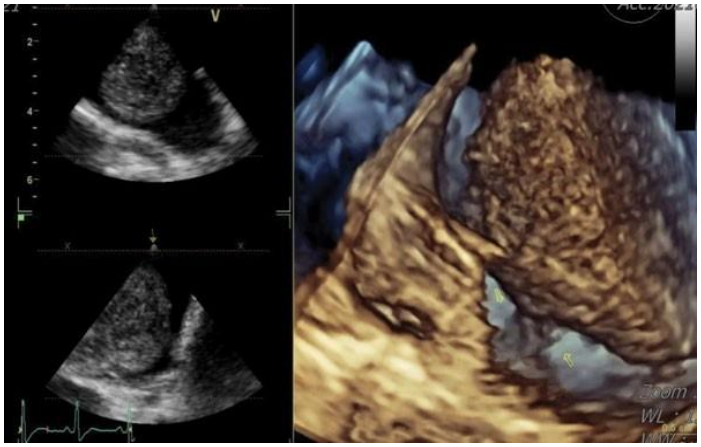

Figure 4: TEE showing Right Atrial mass

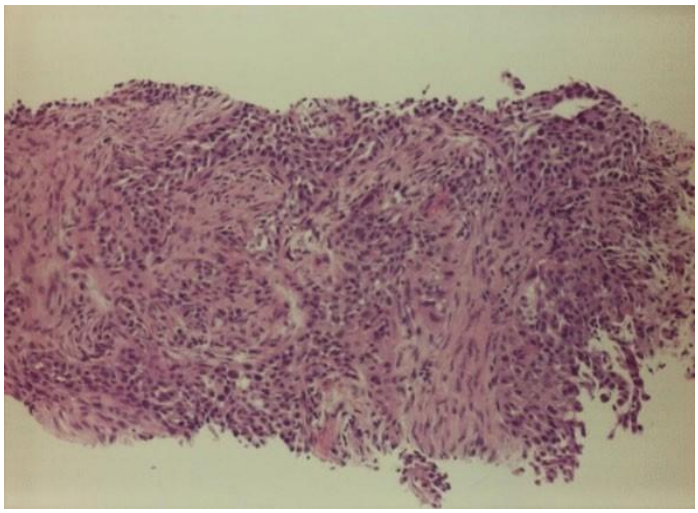

Figure 5: Gall Bladder mass showing malignant cells

ESBL Klebsiella pneumonia sensitive to Meropenem. Patient was then switched to IV meropenem for 7 days.

Thereafter patient improved symptomatically and clinically her jaundice came down. Liver function tests started trending down, AST 37 U/L, ALT 47 U/L, Alkaline phosphatase 237 U/L, Total bilirubin 3.0 mg/dL on discharge. Before discharge she had a portaCath placement for anticipation for outpatient chemotherapy. Once her gall bladder mass get shrunken from chemotherapy, the role for surgery was indicated.

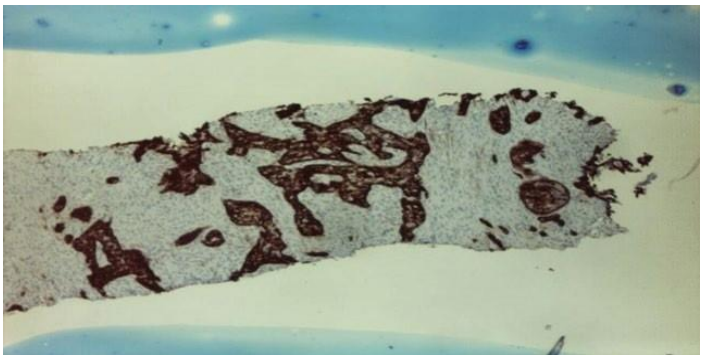

Figure 6: Immunohistochemistry (IHC) CK 7

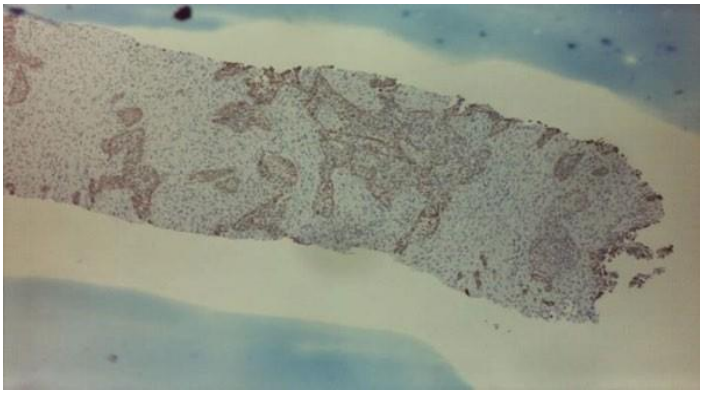

Figure 7: IHC CK 20

DISCUSSION

There are no case reports that were submitted so far where simultaneous occurrence of atrial myxoma, a benign primary cardiac tumor and Gallbladder carcinoma a malignant tumor. Occurrence of both benign and malignant tumors at the same time is extremely rare [3]. There have been case reports on hepatocellular carcinoma in associated with atrial myxoma however GB carcinoma and atrial myxoma has never been presented.

The incidence of GB cancer is only 1.2% among all cancers worldwide and it accounts to 1.7% of all cancer deaths. It is more common in women than in men because estrogen hormone in women causes saturation of cholesterol in bile causing gallstone formation which in turn causes chronic inflammation and disruption of cell signaling and growth. Gall bladder cancer has very poor prognosis because of its late presentation. Survival rate in US is 12-14 months in patients undergoing resection and only six months for patients with palliative care. GB cancer which is confined to gall bladder the survival rate is 60%, if it has spread to nearby lymph nodes the survival rate is 25% and distant metastases survival rate is below 2%. [1]

Chronic inflammation is the risk for Gall bladder cancer, inflammation causes mutations causing cancer. Most common mutations are K-ras, tumor suppressor beta-catenin (CTNNB1). [4] Gall bladder has no serosa which in turn lacks the limit of spread of the disease. Most common cancers of Gallbladder are adenocarcinoma. Risk factors are age, sex-female predominance, obesity, genetic, infections like typhoid and helicobacter pylori, porcelain Gall bladder, sclerosing cholangitis, polyps, medication like methyldopa, isoniazidand oral contraceptive pills [5]. Mirizzi syndrome which is obstruction of common hepatic duct due to impacted stone in neck of the gallbladder causing extrinsic

compression has been associated with gallbladder cancer with poo prognosis [4].

Most common symptoms presented are abdominal pain, nausea, anorexia, weight loss, jaundice with clay-colored stools and cola colored urine, which usually means poor prognosis as the cancer has spread to biliary tree. [4, 6] Patients with abdominal mass, hepatomegaly, obstructive symptoms indicate advance disease [4].

Laboratory analysis will show elevated alkaline phosphatase and bilirubin which suggests biliary obstruction however they are not very diagnostic as they lack sensitivity and specificity. Elevation in Ca19-9, CEA is can be diagnostic for GB cancers however they lack specificity, and they can be used as a marker for response to therapy [4,6].

Imaging studies like ultrasound and CT scan is limited in diagnosing GB carcinoma. More specific test in histologically diagnosing GB cancer is Endoscopic ultrasonography (EUS), it helps in diagnosing tumor invasion and involvement of lymph nodes. MRCP can be used in identifying the extend of the disease to detect unresectable candidates. GB cancer is positron emission tomography/computed tomography (PET) scan sensitive hence PET/CT is good in detecting advanced disease in order to prevent from unnecessary surgeries [4].

Treatment of gall bladder cancer is based on staging of the disease. There are four stages, stage 1- involvement up to muscularis, Stage 2 connective tissue involvement, stage 3 invading liver or other organ, stage 4 invading portal vein, hepatic artery or two extrahepatic structures. Stage 3 and 4 usually involves nodes around cystic duct, Common Bile Duct, hepatic artery, portal vein, aortic, caval and celiac nodes. [5] Surgical resection of gall bladder along with marginal hepatectomy, lymphadenectomy and common bile duct removal is indicated in patients with less than stage 2. In patients with Stage 2 or higher along with surgery adjuvant chemo is given for six months or four months of chemoradiation. Gemcitabine or 5-flurouracil (5FU) IV for six months has been shown to have median survival for 43.1 months. Another regimen four cycles of capecitabine plus gemcitabine every 21 days along with radio therapy has shown survival of 35 months. Regimen that showed 53 months survival was 5-FU based adjuvant chemotherapy that includes 5 fluorouracil with capecitabine and radiotherapy and this will be standard of care.

Locally advanced and metastatic gallbladder cancers, patients who are not candidate for surgery are to consider palliative therapy or chemotherapy. If cancer is locally advanced, they can be managed with external beam radiation. Patients who are fit for chemotherapy i.e., Eastern cooperative oncology group (ECOG) score <1, patients who are ambulatory who can perform their daily activities limited to household work can undergo chemotherapy. Gemcitabine plus cisplatin first-line option that is given on days 1 and 8 every three weeks has shown medical outcomes of 11.7 months.[4] Patients should get imaging done every 6 months up to 2 years then annually for 5 years. Liver function tests, CEA, CA19-9 done every three to four months for two years then every six months up to five years [4].

Prevention of GB cancer is by treating infections, reducing BMI, cholecystectomy especially in patients with large gallstone (size >2 cm), recurrent episodes of cholelithiasis, GB polyps (size > 6cm) [7].

Atrial myxoma is a benign tumor of atrium. They represent 50% of rare primary cardiac tumors. Myxomas are from the endocardium of atrial septum, they are more common in women ages 30-70 years. Most commonly it is found in left atrium and they usually present with dyspnea, syncope, arrythmias, edema, sudden cardiac death, only 10-15% are asymptomatic like our patient who had no cardiac symptoms. CT scan of abdomen done for her abdominal pain and jaundice showed some filling defect in the atrium which led us to do and TTE followed by TEE which then confirmed left atrial myxoma [3]. There has been a case study where acalculouscholecystitis has misled the diagnosis of right atrial myxoma. Right atrial myxoma can present with right heart failure causing ascites, dyspnea, hepatic congestion, right upper quadrant pain.This should be on back of her mind when a patient comes in with right heart failure symptoms but imaging points towards acalculouscholecystitis, myxoma should be in differential and treated accordingly.

Myxomas are usually diagnosed by TTE, TEE and MRI. Mainstay of treatment is surgical and should be done immediately as it has high chance of thromboembolic events and sudden cardiac death. It has an excellent prognosis after surgical resection of the tumor. Because of the rarity of the combination of benign and malignant tumor association our case is unique with rare presentation in a female patient with GB carcinoma and incidental finding of atrial myxoma.

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