A Unique Case of Abdominal Pain

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Abstract

Gallbladder cancer is rare type of cancer with a long-term poor prognostic outcome. Gallbladder cancer reportedly makes up < 1% of all cancers and about 10% of all hepatobiliary cancers. Due to patients remaining asymptomatic in the early stage of disease, the prognosis at diagnosis is quite poor, due to most cases being diagnosed in advanced stages, with the ten-year survival rate being around 13%. The majority of cases are diagnosed by an incidental mass finding on imaging completed for other reasons, or most often, detected incidentally during cholecystectomy for presumed benign gallbladder disease during pathologic review. This case study aims to bring attention to this rare type of cancer.

In this case a 40-year-old Hispanic female presented with epigastric abdominal pain for 10 days. There was no back or flank pain, nor changes in bowel habits, dysphagia, odynophagia, vomiting, hematochezia, melena, or jaundice. The pain was characterized as burning epigastric pain, and with radiation "to the back of the mouth", with no worsening or alleviating factors. The patient had no cough, chest pain, shortness of breath, palpitations, dizziness, headache, fatigue, rash, or edema.

She had been on no new medications, no new food exposure, or recent travel. The patient's last menstrual period was the previous week. Physical examination revealed epigastric tenderness to palpation with light and deep palpation, and additionally she had a fullness/mass-like sensation in the epigastrium with palpation.

The patient was initially treated with PPI therapy, and laboratory evaluation was completed including a CBC, CMP, UA, lipase, and urine Hcg, as well as a CT scan of the abdomen and pelvis was ordered due to the abdominal fullness on examination. There were no abnormalities seen on laboratory workup. Patient returned to the clinic 6 weeks later with no improvement with PPI therapy; however, patient did not complete her initially ordered CT scan. At this time H. pylori serum antibody testing was completed which was positive, as well as the CT scan of the abdomen and pelvis which revealed cholelithiasis without evidence of cholecystitis and a moderate sized hiatal hernia. Patient was treated for her H. pylori, and referred to general surgery, and underwent a laparoscopy cholecystectomy. Pathologic evaluation of the gallbladder revealed well-differentiated adenocarcinoma invading the perimuscular connective tissue.

Surgical oncology evaluated patient who recommended staging CT scan of the chest and dedicated liver CT imaging along with CEA and CA 19-9 testing which were normal without any evidence of distance metastasis. Segment 4B/5 liver resection and portal lymphadenectomy was completed which showed no histologic abnormality. Patient was seen by medical oncology who recommended adjuvant chemotherapy with capecitabine for 6 months.

This case exemplifies the unexpected nature of gallbladder cancer, and the importance to remain diligent in our goal for early diagnosis and improved prognosis.

Case Presentation

Setting: Outpatient Internal Medicine Office

Patient Demographics: 40-year-old, Hispanic female

Chief Complaint & History of Present Illness:

- Central/epigastric abdominal pain for the last 10 days; no back pain, change in bowel habits, chest pain, constipation, diarrhea, dysphagia, flank pain, hematemesis, hematochezia, jaundice, melena, nausea, or odynophagia.
- Associated Symptoms: burning epigastric pain, reflux-like symptoms
- Aggravating Factors: None
- She had not tried anything OTC for her symptoms
- Patient denied any urinary changes, cough, shortness of breath, dizziness, headaches, nor any new medications, food changes, or recent travel. LMP: 8/8/2020 (3 days prior to visit)

Past Medical History:

- Irritable bowel syndrome
- Cosmetic abdominoplasty

Medications:

- None

Social History:

- Never a cigarette smoker
- One alcohol beverage consumption weekly
- No illicit drug abuse

Family Medical History:

- Father: Unaware of any medical conditions
- Mother: Pre-eclampsia/eclampsia

Physical Examination:

- Vital Signs:
  - Height: 5'4"
  - Weight: 164 pounds
  - BMI: 28.2 kg/m²
  - Blood Pressure: 122/88 mmHg
  - Pulse: 84 bpm
  - Respirations: 12/minute
- HEENT:
  - Head: Normocephalic and atraumatic.
    Eyes: Extraocular Movements intact.
    Conjunctiva/sclera: Conjunctivae normal.
    Pupils: Pupils are equal, round, and reactive to light.
    Neck: Normal range of motion and neck supple with no masses or LAD appreciated
- Cardiovascular:
  - Rate and Rhythm: Normal rate and regular rhythm.
    Pulses: Normal pulses.
    Heart sounds: Normal heart sounds.
- Pulmonary:
  - Effort: Pulmonary effort is normal.
    Breath sounds: Normal breath sounds.
- Abdominal:
  - General: Bowel sounds are normal. Comments: **Epigastric tenderness to palpation with light and deep palpation, in addition she has a fullness/mass-like sensation in the right epigastrium with palpation**
- Skin:
  - General: Skin is warm and dry. Capillary Refill: Capillary refill takes less than 2 seconds.
- Neurologic:
  - General: No focal deficit present.
    Mental Status: She is alert and oriented to person, place, and time.
- Psychiatric:
  - Mood and Affect: Mood normal. Behavior: Behavior normal. Thought Content: Thought content normal. Judgment: Judgment normal

Differential Diagnoses

- GERD
- Gastritis
- PUD
- H. pylori infection
- Eosinophilic/esophagitis
- Hiatal Hernia
- Diastasis recti/Ventral hernia
- Pancreatitis
- Cholelithiasis
- Gastric/Intra-abdominal Mass/Malignancy
- Aortic dissection
- Mesenteric ischemia
- Myocardial ischemia
- Other?

Case Presentation

Course of Care:

- Day 1
  - Labs ordered: **CBC, CMP, Hcg, UA, Lipase** (See results below)
  - **EKG**: NSR, normal PR, QRS, QT intervals, normal RWP, no TWI, no pathologic Q waves, no ST segment changes, no evidence of LVH
  - **CTAP with contrast ordered**
  - Started on **pantoprazole** therapy
- Day 59
  - Returned to internal medicine clinic for follow up 2 months later
  - Patient did not complete CTAP
  - No improvement with pantoprazole; would like to proceed with CTAP now
  - **H. pylori serum antibody testing** ordered (See results below)
- Day 61
  - Patient seen in office to review results
  - **H. pylori antibodies positive**
  - Started on **quadruple therapy** (Bismuth, Tetracycline, Metronidazole, PPI)
  - CTAP noted: **cholelithiasis without cholecystitis, moderately sized hiatal hernia**
  - Patient requested **referral to general surgery** for consideration of elective laparoscopic cholecystectomy; referral placed
- Day 72
  - Seen by general surgery
  - Elected to undergo **laparoscopy cholecystectomy**
- Day 81
  - Underwent successful laparoscopic cholecystectomy without complication
  - Pathology returned as: **gallbladder with well differentiated adenocarcinoma invading the perimuscular connective tissue; margins uninvolved**
- Day 96
  - Patient was seen by **surgical oncology** who noted that patient underwent a unremarkable laparoscopic cholecystectomy without spillage.
  - She was unexpectedly found to have stage **T2b gallbladder adenocarcinoma**
  - Recommended **CT scan of chest and dedicated CT liver** to be completed
  - Recommended **CEA, CA19-9** levels and subsequently scheduled for a **segment 4B/5 liver resection and portal lymphadenectomy**
  - Staging CT scans completed which were **unremarkable for any evidence of metastasis**
  - **CEA and CA19-9 were within normal limits (See results below)**
- Day 100
  - Seen in office by **medical oncology** who noted that the patient would likely require adjuvant therapy
  - Whether chemotherapy or chemotherapy and radiation would likely require multidisciplinary evaluation and review of her final pathology
- Day 132
  - Patient underwent **exploratory laparotomy with partial hepatectomy (segments IVB and V) with portal lymphadenectomy** successfully without complication
  - Pathology returned as: **pericholecystic hepatic tissue with reactive fibrosis and foreign body giant cells consistent with previous surgery, no evidence of residual malignancy. Periportal lymph nodes negative for malignancy**
- Day 150
  - Patient followed up with surgical oncology and was doing well post-operatively without complication
- Day 161
  - Patient saw medical oncology who recommended starting **6 months of chemotherapy with capecitabine**

Lipase	114 (N)		**CMP**			**CBC**		
Hcg	Undetectable			Na	140		WBC	7.1
UA	Color	Yellow		K	140		RBC	4.60
	Bilirubin	Negative		Cl	4.6		Hgb	13.3
	Ketones	Negative		CO2	106		Hct	42.1
	SG	1.020		Anion Gap	10		MCV	91.5
	Blood	Large		Glucose	81		MCH	28.9
	pH	5.0		BUN	15		MCHC	32.6
	Protein	0		Creatinine/GFR	0.75/>90		RDW	14.7
	Urobilinogen	0.2		Ca	9.3		Plt	366
	Nitrite	Negative		Total Bilirubin	0.4		Neut	56%
	Leukocyte Esterase	Negative		AST	14		Lymp	34%
				ALT	19		Mono	6%
				ALP	57		Eosino	3%
				Albumin	3.9		Baso	1%
				Globulin	3.4			
				Total Protein	7.3			

H. pylori abs	**Positive**

CEA	**<0.5**
CA 19-9	**17 (Normal 0-35 U/mL)**

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Pathologic Diagnosis :

A: Gallbladder:
- Gallbladder with well-differentiated adenocarcinoma invading perimuscular
connective tissue; margins uninvolved (see comment).
- Focal perineural invasion present.
- Cholelithiasis.
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Pathologic Diagnosis

A. Liver, segment 4B/5, resection:
-Pericholecystic hepatic tissue with reactive fibrosis and foreign body giant cells compatible with previous surgical site changes and no evidence of residual malignancy.
-Remaining liver tissue with no significant histologic abnormality.

B. Periportal lymph node:
-Four lymph nodes, negative for malignancy (0/4).

Discussion: Gallbladder Cancer

Introduction:

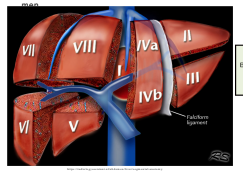
- Gallbladder cancer is an uncommon but highly fatal malignancy with fewer than 5,000 new cases yearly in the United States
- Adenocarcinoma makes up around 76% of cases of gallbladder cancer
- Majority of cases are found incidentally in patients undergoing laparoscopic cholecystectomy for cholelithiasis, in which cancer is found in 1-2% of cases
- The poor prognosis associated is thought to be related to advanced stage disease at the time of diagnosis, which is due to the location of disease and the vagueness of symptoms at presentation

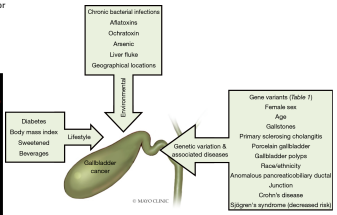
Epidemiology:

- Higher rates of gallbladder cancer is seen in South American countries, particularly Chile, Bolivia, and Ecuador, as well as some areas of India, Pakistan, Japan, and Korea
- In Chile, the mortality rates are the highest in the world with both genetic factors and socioeconomic factors that delay access to care (cholecystectomy for gallstones) thought to contribute
- In the U.S. the incidence is 1-2 cases per 100,000 persons annually with an increased risk in Southwestern Native Americans and Mexican Americans, and 3x more common in women than men

Risk Factors:

- Gallstone disease
- Porcelain gallbladder
- Primary sclerosing cholangitis
- Chronic infection and inflammation
  - Salmonella
  - Helicobacter
  - Chronic typhoid infection
- Congenital biliary cysts
- Abnormal pancreaticobiliary duct junction
- Medications
  - Methyldopa
  - Oral contraceptive
  - Isoniazid
- Carcinogen exposures
  - Dyes, papers, oil, textiles, cigarette smoke, aflatoxin, (in corn, soybeans, and peanuts), Thorotrast
- Obesity, elevated blood glucose levels, higher gravidity and parity



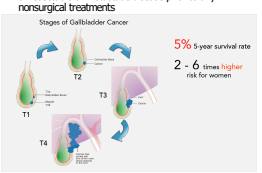


Presentation:

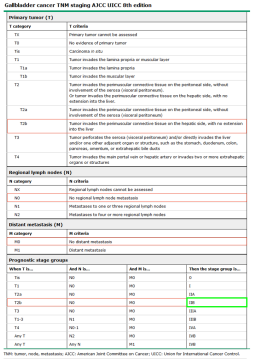
- Patients are usually asymptomatic in early stage carcinoma
- Gallbladder cancer should be suspected in those patients with a suspicious gallbladder mass on imaging
- However, most cases are caught incidentally during cholecystectomy for presumed benign gallbladder disease, where pathology review confirms the diagnosis
- If a patient presents with jaundice, RUQ pain, consider cholangiography, preferably a MRCP for evaluation and potential diagnosis

Diagnosis:

- Biopsy is not recommended prior to surgery with high index of suspicion based on imaging results or if deemed suitable for surgery
- Biopsy can be recommended in patients with unresectable or metastatic disease prior to any nonsurgical treatments



Staging:



Treatment:

- In all patients with resectable gallbladder cancer, consider adjuvant chemotherapy if there is evidence of locoregionally advanced disease (large mass invading/abutting liver, and/or nodal disease), mainly to rule out rapid progression and avoid futile surgery
- In patients with ≥ T1b tumors detected on pathologic review, subsequent **hepatic resection and lymphadenectomy**, with or without bile duct excision for malignant involvement is recommended

Prognosis (Surveillance, Epidemiology, and End Result Data):

SEER stage	5-year relative survival rate
Localized	69%
Regional	28%
Distant	2%
All SEER stages combined	19%

Stage:	5-Year Survival Rate
0	80%
I	50%
II	28%
IIIa	8%
IIIb	7%
IVa	4%
IVb	2%

References

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