Medical Nutrition Therapy

for Complications Associated with

Gallbladder Adenocarcinoma

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Introduction

Gallbladder adenocarcinoma is an aggressive biliary neoplasm of the digestive tract. Gallbladder adenocarcinoma has high incidence in certain ethnic groups such as Pima Indians and Mexicans. The tumor occurs in older patients with several other comorbidities. It is more common in females than males.[1] Although high prevalence of cholelithiasis is an associated finding, less than 1% of individuals develop gallbladder carcinoma.[2] Gallbladder carcinoma causes 2000-3,000 deaths every year.[3] In 2012, the estimated mortality rate in the United States with Gallbladder and other biliary carcinoma was 3,200. [2]

Pathophysiology

Gallbladder adenocarcinoma originates from the surface epithelium of the gallbladder. Initially it is localized to the gallbladder but eventually tumor grows through the wall of the gall bladder and infiltrates the liver. In later stages tumor may invade the extra hepatic bile ducts and it can also infiltrate the duodenum. It is often incidentally diagnosed during histological examination of gallbladder. Clinical symptoms are similar to those caused by cholelithiasis such as abdominal pain, jaundice, nausea, vomiting and fever.[1] Cholelithiasis is the primary cause of biliary obstruction where gallstones, passed from gallbladder, lodge into common bile duct thus causing inflammation. Cholangitis is the inflammation of the biliary duct secondary to obstruction of the common bile duct due to gallstones or disease. Cholangitis causes the infection affecting hepatic ducts, biliary canaliculi, hepatic veins, perihepatic lymphatics and may lead to sepsis.[3]

Associated Factors

Studies have shown nutritional factors associated with increased gallbladder cancer risk. A review of research demonstrated various factors such as genetics, ethnicity, age, chronic

inflammation, congenital biliary abnormalities, gallbladder polyps,gender, obesity and other lifestyle factors elevating the risk. [4] Other studies consider typhoid, diet, poverty and geographical location as risk factors. An ecological study revealed that Chilean women have the highest gallbladder cancer rate in the world. The study among Chilean women revealed an association among higher incidence of gallbladder cancer and poverty and lack of healthcare.[5]

Diagnosis/Signs/Symptoms

As previously stated, diagnosis is often incidental due to the symptoms mimicking cholelithiasis. Most often gallbladder adenocarcinoma is diagnosed after it metastases to other organs such as liver or duodenum, exhibiting symptom such as upper right abdominal pain, jaundice, fever and vomiting.[1]

Treatment

If it is diagnosed early enough, the most effective treatment is surgical removal of the gallbladder known as cholecystectomy. Treatment also includes surgical resection of part of the liver and associated lymph nodes for the patients with T2, where tumor invades perimuscular connective tissue, or greater stage of the disease. Preoperative percutaneous transhepatic biliary drainage is performed to reduce jaundice. The disease is considered unresectable after it spreads beyond the gallbladder fossa and regional lymph nodes within the hepatoduodenal ligament.[2] With early treatment patients may have the best chance of long term survival. Even though there are limited options for adjuvant therapy; radiation therapy with fluorouracil radio sensitization is the most commonly used postoperative treatment.[6]

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Prognosis:

Research has shown poor prognosis due to delayed diagnosis. The 5 year survival rate is only 5% in patients with advanced gallbladder carcinoma.[1] Recent research identifies several prognostic factors such as radical surgery with hepatic resection and hilar lymphadenectomy, T stage, lymphatic embolization, and gallbladder perforation. Gallbladder perforation displays worse prognosis with a median survival time of seven months. Radical surgery with hepatic resection and hilar lymphadenectomy may have slightly improved prognosis. However in most cases, due to delayed diagnosis, it is too late for the tumors to be resected surgically. Nevertheless, with gallbladder carcinoma's extremely poor prognosis, most patients may have a poor survival rate.[7]

A Case Study of Gallbladder Adenocarcinoma

Mr.HR was presented to Veterans Hospital with severe nausea, vomiting and diarrhea. His skin was jaundiced. Upon further investigation, his liver function tests (LFT's) were found abnormally elevated. A right upper quadrant (RUQ) sonogram was ordered and results revealed a Hilar hepatic mass with intrahepatic biliar dilation. Hepatic mass was associated with a possible hepatocarcinoma or adenocarcinoma. Gallbladder was found decompressed with multiple posterior stones. Later that day patient was transferred to University Hospital for ERCP; a diagnostic and therapeutic test that provides radiographic and endoscopic visualization of biliary tree. ERCP is typically performed with dilated common bile duct and elevated LFT'S.

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Mr. HR's vital signs were presented as following at admission:

Temperature	**B/P**	**O_2 Saturation**
98.1F	110/48	100%

Mr. HR was an 85 years old Caucasian single male who lived alone. He was legally blind due to a left eye enucleation and was hard of hearing from his left ear. He independently lived next door to his relatives. He reported to be a non-smoker and an occasional drinker without any history of drug abuse. Patient denied any allergies and reported to have never received any vaccines or immunizations. He had a history of Hypertension, Hyperlipidemia and Chronic Kidney Disease (CKD). He did not have any family history of kidney disease. He reported to take Simvastatin for his hyperlipidemia, Hydrochlorothiazide and Atenelol for his blood pressure at home.

Upon admission at University Hospital patient was initially kept NPO and provided Intra Venous (IV) fluids to maintain hydration. Initially patient was diagnosed with cholangitis. Patients diagnosed with cholangitis are kept NPO until the surgical procedure is performed. It is also speculated that patient's nutritional status may be altered and oral intake may decrease due to indigestion, decreased ability to digest fat and abdominal gas.[3]

Next day he was given Ondansetron for his nausea and vomiting and Piperacillin, an antibiotic to fight soft tissue infection, for cholangitis. His vital signs were stable and he denied any abdominal pain. Upon admission some of his lab values were elevated. Following is a brief overview of the lab values:

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Labs	**Ca** (mg/dL)	**Cl** (mEq/L)	**CO_2**	**BUN** (mg/dL)	**Cr** (mg/dL)
Normal Range	9.0-10.5	98-106	23-30	10-20	0.6-1.2
Values	8.6 ↓	115 ↑	22 ↓	59 ↑	1.64 ↑
Labs	**Alb**(g/dL)	**AST**	**ALT**	**Alk Phos**(IU/L) Adults>60yrs	**Billi**
Normal Range	3.5-5.0	0-35	4-36	51-153	0.3-1.0
Values	2.0 ↓	202 ↑	178 ↑	1040 ↑	8.7 ↓

Given patient's NPO status with a concurrent infection, it is vital to monitor his lab values in order to ensure optimal organ functions and electrolytes balance. Creatinine (Cr) is an indicator of renal function. Elevated Cr was associated with dehydration secondary to nausea and vomiting patient had experienced earlier. ALT, AST and Alk Phos are markers of liver function and detect liver disease and malignancies. Low Albumin is an indicator of chronic liver disease, inflammation, infection and nephrotic syndrome. It is recommended to monitor albumin if the patient is kept NPO or has a concurrent infection.[3] Since the patient was both NPO and was treated for infection his albumin was closely observed. Billirubin is a marker of extra-hepatic duct obstruction. Electrolytes such as Na, K, Cl and Ca are vital for fluid balance, acid base status and homeostasis in the body. They are considered as markers for kidney's function.[8] CO_2 measures level of carbon dioxide in the blood and low levels are typically associated with metabolic acidosis secondary to kidney dysfunction.[3]

Next day patient had a successful stent placement in his left biliary duct. As a result of drainage from biliary duct his LFT's showed a slight improvement. Patient was kept NPO in order to keep the gallbladder inactive. Even though hydration improved, patient had fluid deficit and he started to show signs of slight hypernatremia with Na at 152 mEq/L. Hypernatremia was addressed with IV fluids and oral intake. Slow administration of fluids often assists in decreasing serum sodium levels. Percutaneous liver biopsy was performed on right liver lobe mass to confirm the diagnosis of carcinoma.

On the third day, patient showed a slight improvement in his LFT's but they were still not within normal limits. Patient expressed the desire to eat and he was ordered Adult regular diet. Patient reported to eat well and his condition improved clinically.

On day four, patient's LFT's demonstrated a little improvement from the previous days. Patient's high LFT's and low Alb was indicative of compromised liver function. However his BUN and electrolytes imbalance suggested decreased kidney function. Decreased lab values of Mg, PO_4 and Ca, as well as increased BUN suggested increased renal loss and hypomagnesaemia; often associated with renal disease and acute kidney injury secondary to CKD. Phosphate is also indicative of kidney function and decreased level may signify renal losses.[8] However his Cr was within normal limits.

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Following is a brief overview of patient's lab values on day four:

Labs	**Mg** (mEq/L)	**PO_4** (mg/dL)	**Cl** (mEq/L)	**CO_2**	**Ca** (mg/dL)	
Normal Range	1.6-2.4	2.5-4.5	98-106	23-30	9.0-10.5	
Values	1.4 ↓	1.9 ↓	118 ↑	19 ↓	8.4 ↓	
Labs	**BUN** (mg/dL)	**Alb** (g/dL)	**AST**	**ALT**	**Alk Phos**	**Billi**
Normal Range	10-20	3.5-5.0	0-35	4-36	30-120	0.3-1.0
Values	28 ↑	1.7 ↓	96 ↑	107 ↑	985 ↑	3.8 ↑

At that point patient was given Ondansetron, Ciprofloxacin , Magnesium oxide and Morphine for his nausea/vomiting, infection, renal loss and as sedative respectively. Patient was still on Adult Regular Diet per doctor's diet order. At that point patient's fluid intake and output, for past 24 hours, were as follows:

Intake: 3960cc

Output: 1425cc

Net: 2535cc gain

Assessment

Patient had been in the hospital for more than 72 hours and per hospital's protocol initial nutrition intervention was required. Initial dietary assessment was performed by the intern on day four. Patient was alert at the time of visit and family was present as well. His nephew reported that patient had a very good appetite at home and he consumed regular diet. The patient reported

to have not eaten his breakfast due to a test earlier in the morning. At the time of visit patient had only eaten a few bites of chicken and applesauce; ~25% of his lunch. His niece stated that she stayed with the patient in order to encourage him to eat. At the time of visit patient denied any nausea or vomiting, but stated that he had decreased appetite due to nausea and vomiting earlier. Considering his age and dentition patient was asked if he had any chewing or swallowing difficulty to which he denied. The patient reported his usual body weight at 150lbs and denied any recent weight loss. Upon inquiry, patient reported drinking, "a lot of fluids". The patient denied using any multivitamins at home. Since the patient was legally blind, his family was asked if they would prefer any help at mealtimes for him, but the family denied and stated that the patient could self feed and family was available to help as well. The niece also reported that at home they make sure that the patient eats well. To ensure caloric intake patient was offered Boost supplement twice a day. In order to ensure optimal meal consumption the supplement was recommended as a snack between meals only. The importance of optimal food intake and its association with normal lab values for overall well being was reiterated with the patient and the family.

Following anthropometric measurements were recorded for the nutritional assessment:

Height	Weight(admit)	Weight(IBW)	IBW%	Weight(UBW) Pt reported	BMI	BMI Classification
165.1cm	77.2kg	61.8kg	124.9	68.04kg	28.3	Overweight (25-29.9)
65''	170.19#	136#		150#		

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The patient's ideal body weight was calculated using the Hamwi equation for males. Following method was used: IBW=106#for first 60 inches +6 # for each inch +- 10%

IBW=106+ (6x5) =136# + -10%

IBW%=Current weight/IBWX100 IBW%=77.2/61.8X100=124

The patient's caloric needs of 1500-1800 kcals were estimated based on 25-30 kcal/kg per his ideal body weight since patient was elderly and on the lower end of overweight BMI classification. His protein needs of 62-92 g were estimated based on 1-1.5g per his ideal body weight as well. His protein needs were calculated considering his abnormal LFT's and decreased renal function. His fluid needs were recommended as 1mL/kcal or as recommended by his team. Assessment of protein needs for patients with both renal and liver failure requires precision and clinical judgment. There is a very fine balance between the two conditions that requires a moderate level of protein; hence not further compromising the liver or renal function by selecting either low or high amount of the nutrient. His age and overall condition was another factor that helped determine his needs.

Diagnosis

Patient was nutritionally diagnosed at moderate risk based on University Hospital's risk criteria protocol. Patient was diagnosed with increased nutrient needs related to compromise liver function as evidenced by abnormal labs and increased LFT's. Patient was diagnosed with increased nutrient needs based on his compromised liver function and his concurrent infection. Even though Patient was also diagnosed nutritionally with decreased oral intake related to altered GI function as evidenced by patient reported poor appetite. During the visit, patient was observed

with poor intake and he confirmed it as well. In addition, his metabolic state and medications also played a role in decreasing his appetite.

Intervention

Nutrition intervention was initiated with the goal of patient's meal consumption >75% prior to discharge from the hospital. Based on abnormal electrolytes and elevated BUN, a recommendation was made to advance diet to renal, as tolerated, after physician's approval. Boost Plus was requested as a supplement between meals twice a day to address nutritional deficit. One serving of Boost plus provided, 360kcal, 14 g protein, 14 g fat and 45g CHO. The Boost Plus was recommended between meals in order to ensure optimal meal intake. Multivitamins and minerals were also requested if not contraindicated pharmacologically.

Monitoring and Evaluation

To monitor and evaluate nutritional intervention input and output was requested. Patient was also informed of a follow up with the dietetic intern, within next few days, to evaluate his nutritional status. Nutrition care and ADIME was discussed with and approved by registered dietitian.

Over the weekend another percutaneous cholangiography was performed for external biliary drainage catheter placement. Patients LFT's showed a slight improvement but his potassium and Cr were elevated at 6.0 (mEq/L) and 3.47(mg/dL) respectively. Patient was ordered a liver failure diet by his physician. The hospital's liver failure diet provides nutrients limiting sodium and protein in order to prevent hepatic encephalopathy. Patient's blood pressure increased and Hydrochlorothiazide was added to patient's existing medications in order to control it.

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Assessment

After the weekend, patient developed hyperkalemia and metabolic acidosis per his physician's report. Patient was followed up by the dietetic intern. During the visit, the patient was slightly drowsy and not very well oriented. In addition, family was not present. Patient stated improvement in his appetite and eating all his breakfast and "drinking enough fluids; more than 3 cups/day." Patient denied any nausea, vomiting and stated to feel better overall. Patient denied constipation even though his chart note documented him missing bowel movement for past two days. His caloric needs did not change from the initial assessment.

Diagnosis

Nutritional diagnosis remained somewhat consistent with the initial diagnosis of increased nutrient needs related to compromised liver function as evidenced by abnormal labs.

Intervention

Diet advancement to renal was recommended again by the dietetic intern based on patient's hyperkalemia and compromised renal function. Hyperkalemia is commonly observed in renal failure due to inadequate excretion of potassium. However it was recommended that patient may benefit from a renal diet that reduces the symptoms of uremic toxicity and electrolyte imbalance. It was a relief to observe that later during the day patient's diet order was altered from liver failure to renal failure diet with potassium restriction. Continuation of Boost Plus until optimal PO intake was recommended. Multivitamins and minerals were recommended again if not contraindicated pharmacologically.

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Monitoring and Evaluation

Strict input and output was requested in order to monitor and evaluate nutritional intervention. Dietetic intern documented in patient's chart to meet the family during the next visit, given patient's mental orientation, to discuss his diet and monitor intake.

The physician ordered Senna and Docusate for patient's constipation. Furosemide was also initiated at that point. Later that day, the patient's urine output decreased. His total input and output was measured at 1120 and 900cc respectively in 24 hours. Following labs were measured:

Labs	**K** (mEq/L)	**Cl** (mEq/L)	**Ca** (mg/dL)	**BUN** (mg/dL)	**Cr** (mg/dL)
Normal Range	3.5-5.0	98-106	9.0-10.5	10-20	0.6-1.2
Values	6.0 ↑	112 ↑	8.2 ↓	66 ↑	4.28 ↑
Labs	**Alb** (g/dL)	**CO_2**	**ALT**	**Alk Phos**	**Billi**
Normal Range	3.5-5.0	23-30	4-36	30-120	0.3-1.0
Values	1.5 ↓	18 ↓	54 ↑	738 ↑	2.5 ↑

Lab results revealed an improvement in patient's LFT's with AST at normal level and significant improvement in ALT and Billirubin. However there was a significant increase in his Cr and BUN. Elevated BUN is suggestive of hypercatabolism, dehydration and also associated with kidney dysfunction.[3]

Later during the day nephrology consult was sent and patient's primary problem was altered to acute kidney injury secondary to CKD. The nephrologist discontinued Hydrochlorothiazide to

avoid further kidney damage due to toxicity. Magnesium oxide was also discontinued in order to avoid magnesium toxicity in renal impairment. Recent research has demonstrated high incidence of renal insufficiency in cancer patients. This is an important issue in clinical practice for drug management in cancer patients. The studies suggest that reduction in renal clearance may result in accumulation of potentially toxic species and over dosage. Thus the usual dosage in renal compromised patients frequently requires dosage reduction to avoid severe toxicities.[9] During his consults, the nephrologist consistently either discontinued or reduced the dosage of certain drugs based on patient's kidney function. The nephrologist did not recommend patient for long term dialysis since patient's medical condition was compromised due to metastatic cancer, but approved treatment with short term hemodialysis if needed.

During the course of the next day patient's biopsy results were received which confirmed positive gallbladder adenocarcinoma. A renal failure diet was continued. His renal function and acidosis improved with potassium at 4.6 (mEq/L) and HCO_3 at 23, respectively. Another nephrology consult indicated slight hypervolemia in the presence of ascites. The nephrologist's diagnosis was stage 3 CKD with developing AKI due to bladder outlet obstruction and possible benign prostatic hypertrophy with some contribution from cholangitis. Patient's renal function improved with post obstructive diuresis.

Discharge Summary

Next morning the patient was discharged to VA hospital in stable condition. The dietetic intern was unable to follow up due to his discharge. The patient was discharged with renal failure/liver failure diet. Patient's labs were significantly improved upon discharge. His billirubin had gradually decreased from initial 8.6 to 2.4 on discharge. At discharge patient's reported weight

was 77 kg with a loss of 0.2 kg during the hospital course. Patient was discharged with active diagnosis of gallbladder adenocarcinoma, acute/chronic kidney disease, urinary obstruction, hyperlipidemia and hypertension. An oncology follow up was made at VA hospital.

Mr HR had a diagnosis of gallbladder adenocarcinoma with complications involving cholangitis, decreased liver and renal function. During the course of the treatment patient's labs consistently displayed the nutritional consequences. Accurate diet order combined with pertinent medications and adequate intake improved outcome and ensured well being. Even though fat intake is highly associated with gallbladder complications, it was not addressed during the case study, since the main focus was to treat his complications arising from liver/renal failure and infection. In addition, due to patient's frail condition and poor prognosis of the disease, the main focus remained to address the existing issues in order to maintain the patient on a stable state.

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Following is a brief overview of drug nutrient interaction of the medications used: [10,11]

Name	Common Use	Interaction
Furosemide, Hydrochlorothiazide	A diuretic, used to help reduce edema through urination of sodium and excess fluids	Increases excretion of electrolytes (potassium, magnesium and calcium). Avoid natural licorice. Caution is used with calcium &/or vitamin D supplement.
Ciprofloxacin/CIPRO	A quinolone to treat bacterial infection	Interacts if taken with dairy or calcium-fortified products alone. May increase caffeine levels if taken with caffeine-containing products, leading to excitability and nervousness.
Morphine	Narcotic analgesic for pain relief	May decrease motility. Alcohol may increase the sedative affects.
Senna, Ducosate	Laxatives used for constipation	Excessive use may cause dehydration and electrolyte imbalance.
Ondansetron	Prevents and treats nausea and vomiting due to neoplasm or after surgery. It works by blocking serotonin that causes vomiting.	May cause stomach pain and constipation. Alcohol may be limited to reduce dizziness
Piperacillin	An antibiotic to fight infection	May cause diarrhea.
Magnesium Oxide	Mg supplement	Toxicity may be experienced in renal failure due to decreased clearance

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