
Palliative Care Clinical Rounds

Presented by
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Objectives

This session will provide participants with an opportunity to review best practices with other primary-care providers and local experts. The goal is to help each other better manage challenging palliative cancer cases in Northern Ontario and create a community of practice.

Learning Objectives:

By the end of the program, participants will be able to:

- Discuss outcome of cases with malignant ascites
- Analyze outcomes and determine additional options for treatment



Declarations

- We have no conflicts of interest to declare

Agenda

- Presentation of case
- Overview of malignant ascites
- Discussion period
- Feel free to make comments or ask questions at any time in the chat

Introduction to the Case

May 2020: The patient is a 68yo female with history of breast cancer being followed by the Palliative Symptom Management Clinic who is complaining of abdominal discomfort.

Past medical history

2007

- Detected lump to left breast
- Diagnosed with breast cancer → T2 N1, ER/PR+, HER2- lobular carcinoma
- Completed chemotherapy and bilateral mastectomy → remission x 10 years
- Type 2 diabetes, obesity
- Social: rarely smokes, no etoh



Past medical history cont'd

2017

- Presented with: Pain (neck, ribs, hip), abdominal distension, and anemia
- Diagnosis: Stage IV Breast cancer w/ mets to bone and peritoneum
- No lung, brain, or liver mets
- Treatment: Denosumab, Palbociclib, and Letrozole
 - Letrozole: Aromatase Inhibitor; indicated as hormonal therapy for ER/PR+ breast ca in post-menopausal women
 - Denosumab: Monoclonal antibody; for bone mets from breast cancer
 - Palbociclib: CDK Inhibitor for ER+ breast cancer
- Outcome: Symptoms improved + disease controlled with tx

History of Presenting Illness

May 2020: A 68yo female with history of breast cancer was being followed by the Palliative Symptom Management Clinic complaining of abdominal discomfort.

- Presentation:
 - Abdominal pain, orthopnea, early satiety
 - No bowel changes, weight loss, jaundice
 - Continues to be on letrozole/palbociclib with denosumab
- CA-15-3 (tumor marker) levels
 - Aug 2019: 161
 - March 2020: 357
- LFTs: Stable
- Ultrasound revealed:
 - Liver changes consistent with steatohepatitis
 - Small amount of ascites
 - No liver metastases or carcinomatosis

What are your next steps?

Investigations

	12/6/20 14:32
Fluid Source	Abdominal
Fluid Volume	50.0
Fluid Color	Yellow
Fluid Appearance	Slightly Cloudy
Fluid RBC	< 2000
Flid Tot Nucleated Cell	100
Fluid Neutrophils	0.03
Fluid Lymphocytes	0.37
Fluid Other Cells	0.60
Fl Pathologist Review	^
Fluid Glucose	5.9
Fluid Albumin	26
Fluid LDH	418
Fluid Amylase	< 30

Transudative (or “systemic”): Low protein count and low specific gravity. Caused by heart failure, renal failure or cirrhosis of the liver.

Exudative (or “local”): High protein count and high specific gravity. Caused by peritoneal carcinomatosis, pancreatitis, bowel obstruction, etc.

Cytology: Negative
Culture: Negative
Gram Stain: Negative

CT: Normal liver, moderate ascites, no carcinomatosis

Serum-to-ascites albumin Gradient

- Serum-to-ascites albumin gradient
 - Serum albumin - ascitic fluid albumin = SAAG
 - >11 g/L → portal hypertension (97% accuracy)
 - <11 g/L → r/o portal hypertension

	June	September
Serum Albumin	42	45
Ascitic Fluid Albumin	26	30
SAAG	16 (HIGH)	15 (HIGH)

Serum-to-ascites albumin gradient (SAAG)

Classification of ascites by the serum-to-ascites albumin gradient

High albumin gradient (SAAG ≥ 1.1 g/dL)
Cirrhosis
Alcoholic hepatitis
Heart failure
Massive hepatic metastases
Heart failure/constrictive pericarditis
Budd-Chiari syndrome
Portal vein thrombosis
Idiopathic portal fibrosis
Low albumin gradient (SAAG < 1.1 g/dL)
Peritoneal carcinomatosis
Peritoneal tuberculosis
Pancreatitis
Serositis
Nephrotic syndrome

Graphic 81696 Version 5.0

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Summary of Investigations

Test	June	July	August
Hgb	99	98	97
WBC		3.3	2.6
CA 15-3	322	207	215
Paracentesis	No malignant cells or infxn		
LFT's		WNL	
Ultrasound	Ascites		
CT abdo/pelvis	Moderate ascites, no carcinomatosis, no liver mets		

How would you manage this patient's symptoms?

Interventions


Plan	Outcome
Therapeutic paracentesis	Required every 3-4 weeks
Consider indwelling peritoneal catheter	Not inserted over the summer- would she need further chemo? + pt. preference
Diuretic (Spironolactone and Furosemide)	Decreased frequency of paracentesis to 8 week intervals
Consulted Internal Medicine for ascites	Seen in August
Oncology monitoring	Ongoing

November 2020

Symptom management

- Paracentesis q8 weeks
- Ongoing diuretics → Tenckhoff inserted for ease of drainage → diuretic d/c'd
- Referred to GI to investigate anemia → further mets at antrum

Cancer management

- Repeat ultrasound → ?metastatic disease to liver
- Restaging CT of chest, abdo, pelvis revealed liver and peritoneal metastases
- MRI revealed >10 hypoechoic lesions on the liver
- CA-15-3: 425 

Did management change after finding mets?

December

Chemo reassessed → initiated palliative hormonal therapy (Tamoxifen)

- No malignant cells in ascitic fluid
- CA 15-3 decreased modestly
- Carcinoembryonic antigen: normal (2.5)
- 3L drained/week

March

- CA 15-3: 425 → 267
- Improvement in bony mets
- Growing hepatic and peritoneal mets
- Initiated Fulvestrant (third line)
- Carcinoembryonic antigen: normal (3)
- 2.5L drained/week

Malignancy-related ascites

Definition: Pathologic accumulation of fluid within the peritoneal cavity

Etiology of ascites:

- Cirrhosis (80%)
- **Cancer (10%)**
- Heart failure (3%)
- TB (2%)
- Dialysis, pancreatic disease (1%)
- Other: chronic etoh, IVDU, obesity, hypercholesterolemia, Type 2 DM, nephrotic syndrome, malnutrition, pancreatic ascites, and ovarian lesions

Etiology + Pathophysiology

- **Cirrhosis, heart failure, etc:** imbalance in volume and hormonal dysregulation in the setting of portal hypertension → ascites
- **Malignancy-related ascites:**
 - Peritoneal carcinomatosis
 - Liver mets
 - Peritoneal carcinomatosis + massive liver mets
 - Hepatocellular carcinoma + cirrhosis
 - Chylous ascites d/t malignancy
 - Budd-Chiari syndrome (occlude hepatic veins)

Peritoneal carcinomatosis
tumor cells produce fluid,
blocked lymphatics, and inc.
vascular permeability →
ascites

Liver metastases
Obstruction/compression of
portal veins leading to portal
hypertension → ascites

Malignancy-related ascites

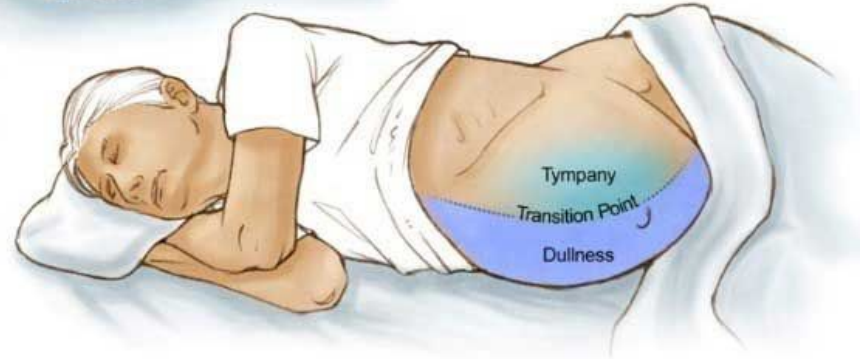
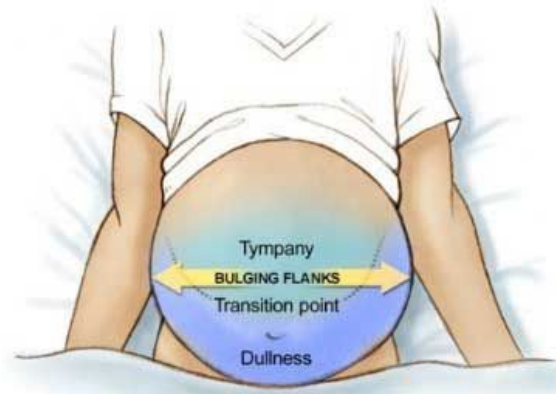
Tumor types

- Ovarian, bladder, peritoneal mesothelioma → peritoneal carcinomatosis
- Colonic, gastric, breast, pancreatic, lung cancers → peritoneal carcinomatosis and/or massive liver mets
- Lymphoma → LN obstruction → accumulation of chylous ascites

History + Physical Exam

History: Nausea, vomiting, dyspnea, early satiety, abdominal discomfort RT distension

Physical exam (>500mL): bulging flanks, shifting dullness, fluid-wave test, peripheral edema



Diagnostic Imaging

- Ultrasound:
 - Can detect small volumes of fluid
 - Fluid type may be seen with floating debris or septations indicating malignancy or loculated ascites
- CT
 - Can detect the smallest volumes of fluid
 - Can differentiate fluid types
 - Can detect peritoneal mets, liver lesions, etc.
- MRI
 - Greatest sensitivity for peritoneal metastases

Diagnostic Paracentesis

Why? Determine cause of ascites and r/o spontaneous bacterial peritonitis

Assess:

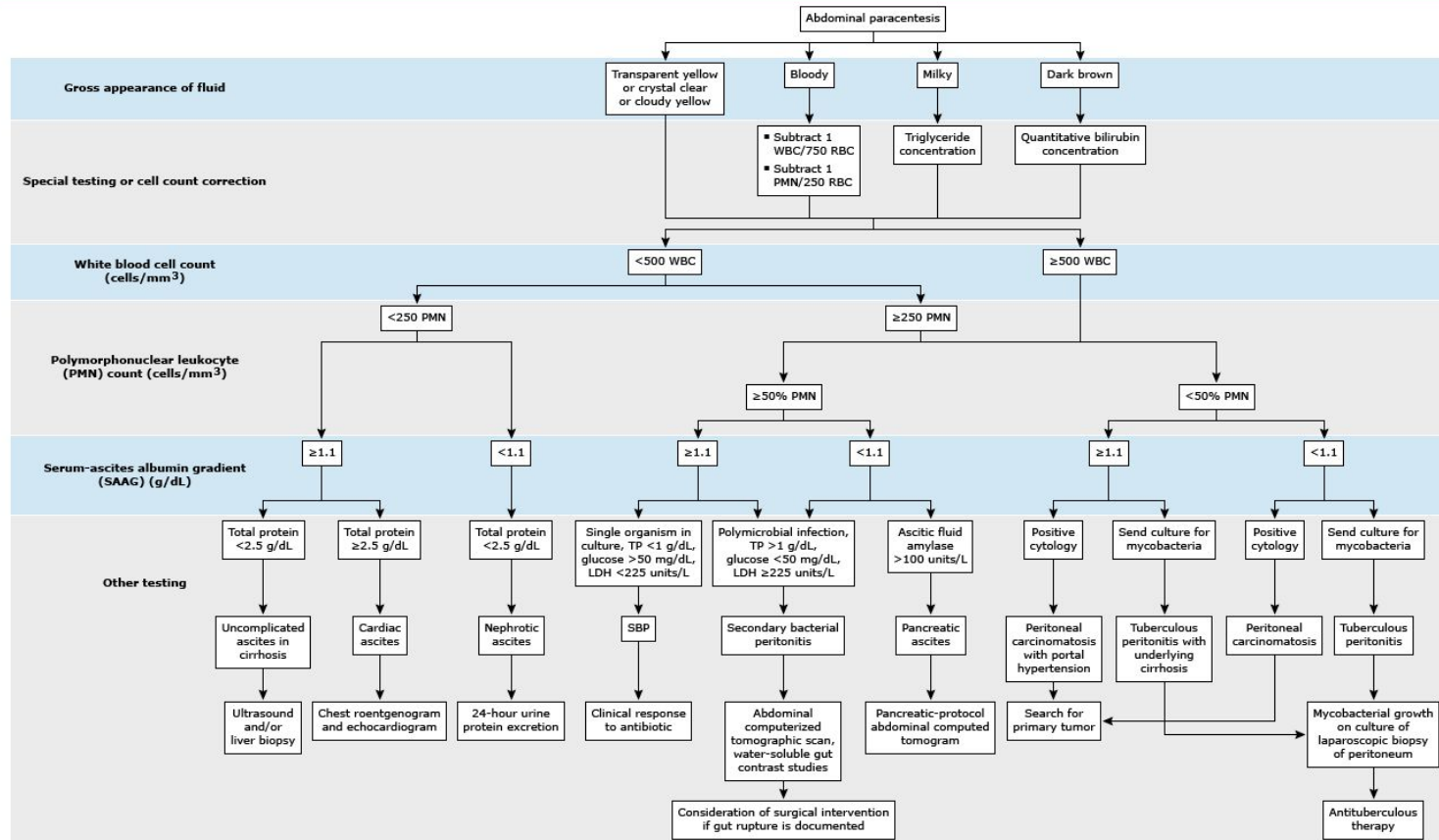
- Appearance
 - Clear, straw-coloured → uncomplicated ascites
 - Cloudy → infection, malignancy
 - Bloody → traumatic tap, cirrhosis, malignancy
 - Milky → cirrhosis, malignancy (inc. triglycerides)
- Serum-ascites albumin gradient
 - Serum albumin - ascitic fluid albumin = SAAG
 - >11 g/L → portal hypertension (97% accuracy)
 - <11 g/L → r/o portal hypertension

Diagnostic Paracentesis cont'd

Test	Notes
WBCs, differential, C&S, gram stain	Infection, spontaneous bacterial peritonitis
Total protein	>25g/L in peritoneal carcinomatosis (95%) <25g/L in liver mets or HCC-complicating cirrhosis (100%)
Cytology	58-75% sensitivity Volume: 50mL-200mL ++ sensitive for peritoneal carcinomatosis only → will not be + for other causes of malignant ascites
Glucose	Low in peritoneal carcinomatosis (consumed by WBCs, bacteria, malignant cells, etc)
Lactate Dehydrogenase	Fluid-to-serum ratio >1.0 → LDH being produced in or released into peritoneal cavity d/t tumor cells or infection

Runyon, 2019; Zhang et al., 2019

Differential diagnosis of ascites



WBC: white blood cell; RBC: red blood cell; PMN: polymorphonuclear leukocyte; TP: total protein; LDH: lactate dehydrogenase; SBP: spontaneous bacterial peritonitis.

Source: UptoDate

Treatment of Malignant Ascites

- Therapeutic paracentesis
- Diuretics
- Shunts
- Tumor-targeted treatments

Goals of treatment

- Mitigate/decrease discomfort

Therapeutic Paracentesis for Malignant Ascites

Indications: Symptomatic management of tense or diuretic-resistant ascites.

*Exception: ovarian cancer

Frequency: guided by symptoms (generally every 1-2 weeks)

Volumes: No limits → start with 4-6L

Setting: office, endoscopy unit, interventional radiology suite (u/s indicated if loculated)

Goals: Limit interventions (albumin, fluid), time, imaging, etc. Immediate relief in 90% of pt's



Runyon, 2019; Stephenson & Gilbert, 2002

Peritoneal drainage catheter

Indications: Palliative management of recurrent ascites-
permit removal of fluid at home by nurse, patient, or family

Contraindications: Peritonitis, uncorrectable
coagulopathy, loculated ascitic fluid

Common complications/risks:

- Catheter dysfunction- 39/687 (leakage, occlusion, dislodgement → managed by flushing)
- Infection- 37/687

Frequency: No more than 500mL q12h

Types:

- Non-tunneled: Central line, Pigtail
- Tunnelled: PleurX, Tenckhoff



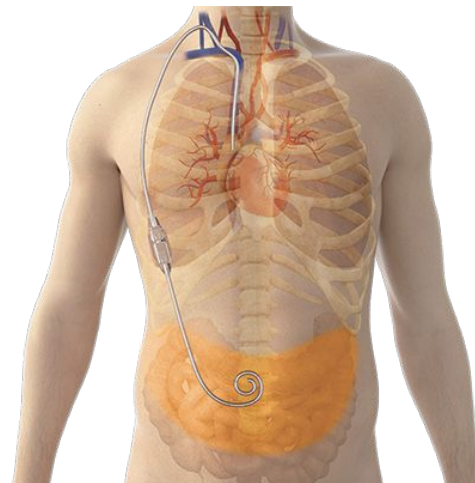
Caldwell, 2018; Runyon, 2019; Tapping, 2012

Types of Peritoneal Drainage Catheters

Type	Notes
Non Tunnelled (Central Line, Pigtail)	<p>Simple and temporary</p> <p>Ideal in institutional setting with shorter life expectancy</p> <p>Prone to complications over extended duration (peritonitis, accidental removal, leakage, occlusion)</p>
Tunnelled catheter (PleurX, Tenckhoff)	<p>Low(er) risk of infection and leakage</p> <p>Beneficial for pt's with longer life expectancy (i.e. gyne cancers)</p> <p>"The tunnelled peritoneal catheter is feasible and safe and causes minimal complications. Its use results in significant improvement in dyspnea and improvement in overall quality of life for a small number of patients." (Wong, 2015)</p>

Medical Management

- Diuretics
 - Indications:
 - Portal hypertension
 - SAAG >11
 - Cirrhosis with hepatocellular carcinoma
 - Dosing:
 - Starting: 100mg/day Spironolactone and 40mg/day furosemide
 - Not contraindicated in PC, but less likely to be effective
- Peritoneovenous shunt- ?
 - Contraindications: hemorrhagic, high protein, loculated, portal hypertension, bleeding disorders, cardiac or renal failure
 - Limited utility in malignant ascites
- Nutrition
 - Na⁺ restriction not recommended if QOL a concern



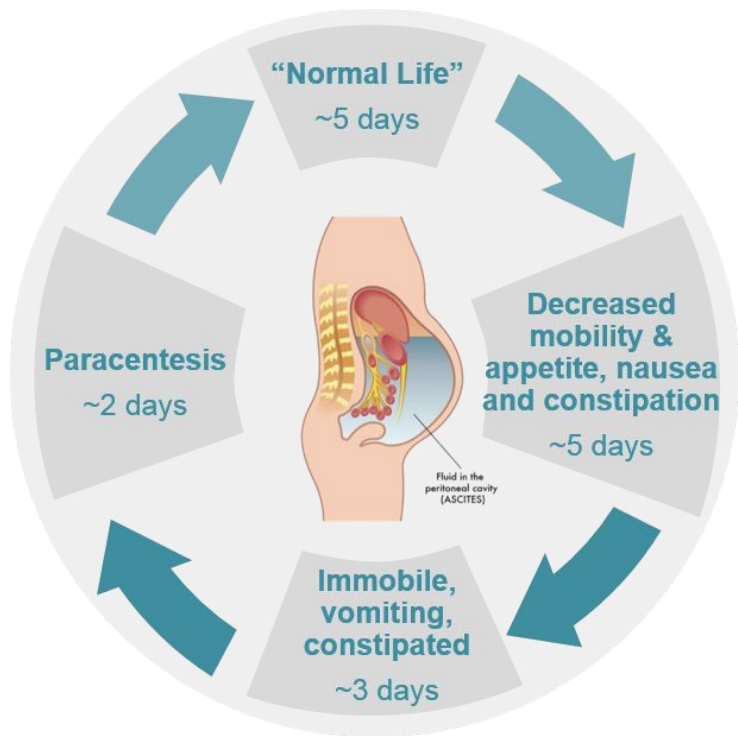
Medical Management cont'd

- Tumor-targeted treatment
 - Epithelial ovarian, fallopian tube, or peritoneal carcinoma → operative candidate?
 - Peritoneal mesothelioma or some pt's with isolated peritoneal carcinomatosis from appendiceal or colorectal adenocarcinoma → intraperitoneal chemo and/or cytoreductive therapy
 - For all other solid tumors with malignancy-related ascites + poor prognosis → consider palliative systemic therapy in line with tolerance and goals of care.
 - Role of intraperitoneally administered chemotherapy for malignancy-related ascites in causes other than ovarian cancer is not well-established.



Symptom Management

- **Pain and discomfort:** remove fluid, consider other sources of pain
- **Early satiety, nausea:** Consider prokinetic agent (Metoclopramide 10mg q4h)
- **Fatigue:** Consider short trial of glucocorticoid or methyphenidate
 - Ex: Dexamethasone 4-8mg daily
- **Dyspnea:** remove fluid



Lessons learned?



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