

Complications of Gallstones

Surgical Skills Network Education Program

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Case 1

- 45 year old female
- Presents to outpatient clinic with recurrent episodes of upper abdominal pain
- Outpatient US shows gallstones

Case 1

- Patient has lots of questions:
 - What are gallstones?
 - Why do I have them?
 - What is the pain that I get after eating pizza?
 - How do you remove the stones?
 - Can I just leave them alone? What could happen?
 - Do I need another ultrasound? Or any other tests?

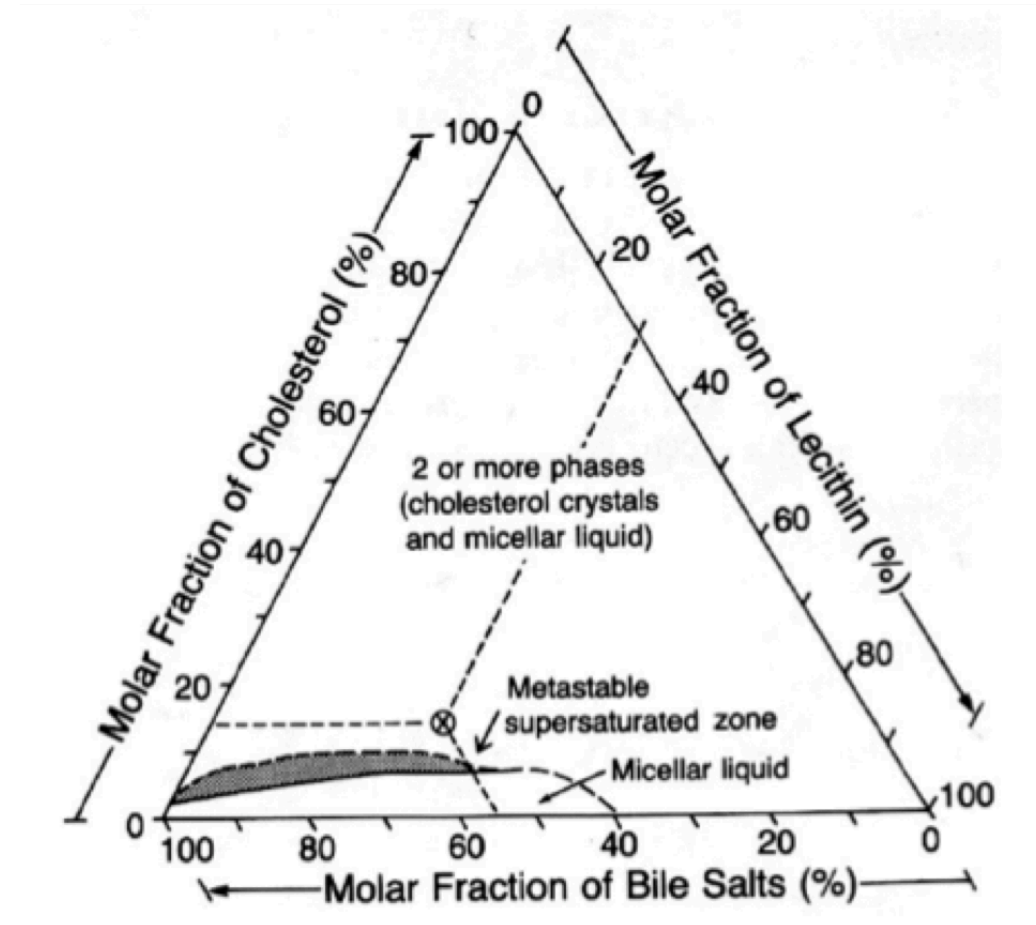


Gallstones- Epidemiology

- Prevalence 10-15%
 - Men 12%
 - Women 24%
 - Symptomatic in ~20%
 - 15-25% of asymptomatic patients will become symptomatic over next 10-15 years
 - annual risk of recurrent symptoms 2-3%
 - choledocholithiasis or pancreatitis 1-2% per year
 - Risk of recurrent complications ~30% per year following episode of complicated GS disease
- Risk Factors
 - age
 - obesity
 - female gender
 - pregnancy
 - ethnicity- China, Japan, India, Thailand
 - rapid weight loss
 - cirrhosis
 - Crohn's disease
 - genetics
 - dyslipidaemia

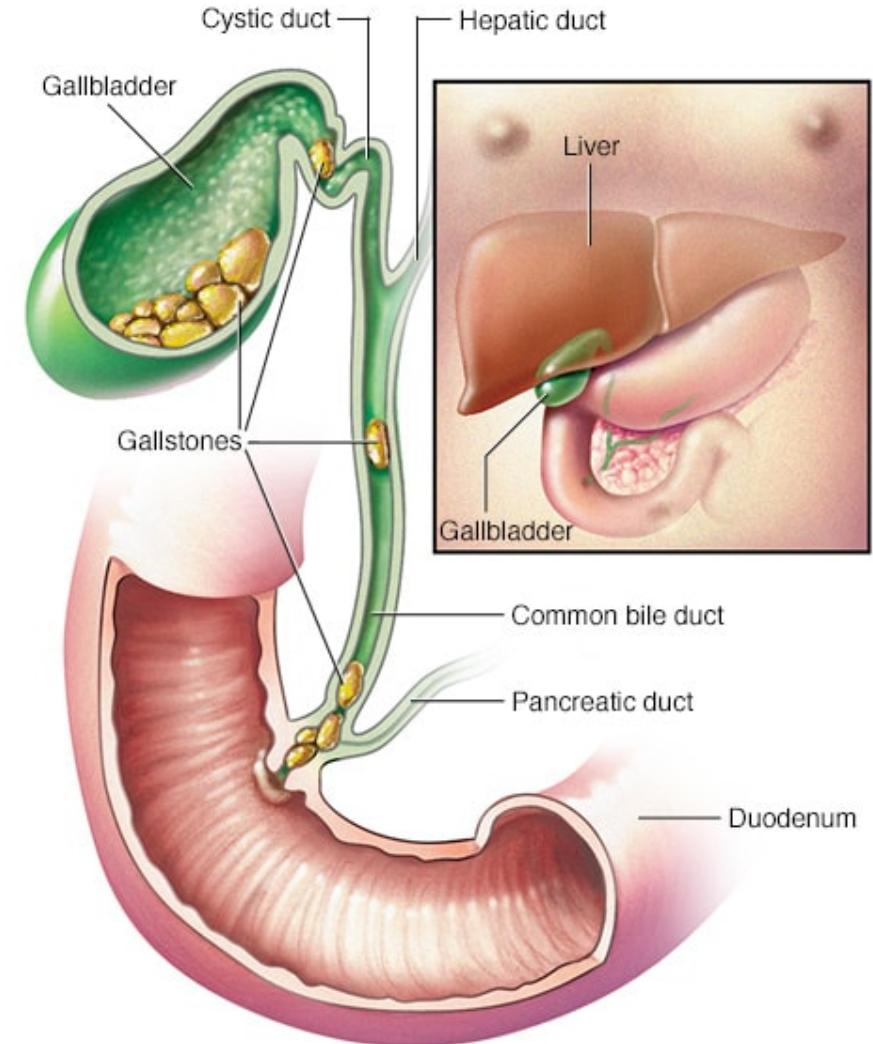
Gallstones- Pathogenesis

- Normal bile allows high concentration (~20mM) of cholesterol to be soluble
 - bile salts and phospholipids form mixed micelles
 - ideal ratio bile acid: phosphatidylcholine: cholesterol = ~10:3:1
- Supersaturation of cholesterol in bile
 - oestrogen
 - increases hepatic synthesis and secretion of cholesterol in bile
 - increases gut absorption of cholesterol
 - progesterone
 - bile salt supersaturation
 - gallbladder hypomotility
- Nucleation
 - supersaturated cholesterol forms a new vesicle conformation
 - recruitment of additional cholesterol molecules leads to accumulations of crystals
 - facilitated by mucin (secreted by GB mucosa)



Gallstones- Complications

- Biliary colic
- Cholecystitis
 - Phlegmon
 - Empyema
 - Mirizzi's syndrome
- Fistula
 - Cholecystogastrostomy (Bouveret's syndrome)
 - Cholecystoduodenostomy (gallstone ileus)
 - Cholecystodochostomy (Mirizzi's syndrome)
 - Cholecystocolostomy
- Choledocholithiasis
- Cholangitis
- Pancreatitis
- Gallbladder cancer
- Gallbladder failure



Gallstones- Investigation Ultrasound

- Echogenic foci within gallbladder
- Highly reflective
- Posterior acoustic shadow
- Mobile (rolling stone)

- Sensitivity 84% (95%CI 76-99%)
- Specificity 99% (95%CI 97-100%)



Case 2- Clinical

- 75yo man
- Presents to ED with RUQ and fevers
- Known gallstones
 - Previous gallstone pancreatitis
- Unwell: HR 140, BP 100/50
- Background:
 - IHD- previous CABG, on clopidogrel
 - COPD- ex-smoker, puffers
 - AF- apixaban

Describe your approach to this patient including:

- *provisional diagnosis*
- *immediate concerns*
- *further work-up and immediate management*
- *definitive management*

Case 2- Imaging



Case 2- Diagnosis and Management

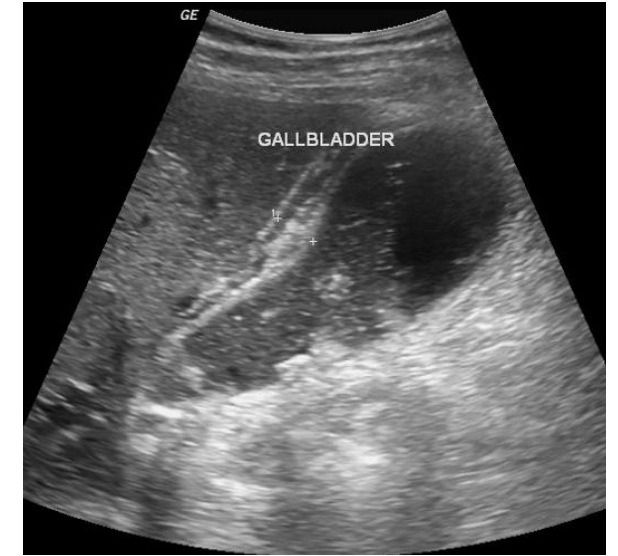
- What is the diagnosis?
- What are some advanced/ complicated presentations of this pathology
- Describe the pathophysiology of this condition
- Management options

Cholecystitis- Pathophysiology

- Results from chemical irritation and inflammation following obstruction of the gallbladder
- Mucosal injury
 - impacted stone causes trauma, leading to release of phospholipases
 - lecithin converted into toxic lysolecithin
 - disruption of protective glycoprotein mucus layer
- Gallbladder hypomotility and progressive distension
 - Mediated by release of prostaglandins
 - raised intraluminal pressure compromises venous and lymphatic drainage -> oedema and inflammation
 - progression to ischaemia/ necrosis
- Secondary bacterial infection
 - e. coli, klebsiella, enterococcus, enterobacter

Cholecystitis- Investigations

- Bloods:
 - FBC, CRP, procalcitonin
 - LFTs
- Ultrasound
 - presence of gallstones
 - GB wall thickening >4-5mm or oedema
 - ddx GB cancer, adenomyomatosis, cirrhosis, right heart failure, spread of inflammation from adjacent organ
 - Pericholecystic fluid
 - GB wall hyperaemia
 - sonographic Murphy's sign
- CT abdo
 - Assessment of anatomy and complicated cholecystitis
- Cholescintigraphy (HIDA scan)
 - 99m-technetium-labelled hepatic iminodiacetic acid
 - contrast usually visualised in CBD, GB and duodenum within 1 hour; >4 hours suggest obstruction of cystic duct
 - CCK or fat stimulation to assess ejection fraction
 - <35% suggestive of GB dyskinesia



Cholecystitis- Diagnosis and Staging (Tokyo Guidelines 2018)

Acute Cholecystitis- Tokyo Guidelines 2018

Table 1 TG18/TG13 diagnostic criteria for acute cholecystitis

A. Local signs of inflammation etc.
(1) Murphy's sign, (2) RUQ mass/pain/tenderness

B. Systemic signs of inflammation etc.
(1) Fever, (2) elevated CRP, (3) elevated WBC count

C. Imaging findings
Imaging findings characteristic of acute cholecystitis

Suspected diagnosis: one item in A + one item in B

Definite diagnosis: one item in A + one item in B + C

Table 7 TG18/TG13 severity grading for acute cholecystitis

Grade III (severe) acute cholecystitis

"Grade III" acute cholecystitis is associated with dysfunction of any one of the following organs/systems:

1. Cardiovascular dysfunction: hypotension requiring treatment with dopamine ≥ 5 $\mu\text{g}/\text{kg}$ per min, or any dose of norepinephrine
2. Neurological dysfunction: decreased level of consciousness
3. Respiratory dysfunction: $\text{PaO}_2/\text{FiO}_2$ ratio < 300
4. Renal dysfunction: oliguria, creatinine > 2.0 mg/dl
5. Hepatic dysfunction: PT-INR > 1.5
6. Hematological dysfunction: platelet count $< 100,000/\text{mm}^3$

Grade II (moderate) acute cholecystitis

"Grade II" acute cholecystitis is associated with any one of the following conditions:






1. Elevated WBC count ($> 18,000/\text{mm}^3$)
2. Palpable tender mass in the right upper abdominal quadrant
3. Duration of complaints > 72 h^a
4. Marked local inflammation (gangrenous cholecystitis, pericholecystic abscess, hepatic abscess, biliary peritonitis, emphysematous cholecystitis)

Grade I (mild) acute cholecystitis

"Grade I" acute cholecystitis does not meet the criteria of "Grade III" or "Grade II" acute cholecystitis. It can also be defined as acute cholecystitis in a healthy patient with no organ dysfunction and mild inflammatory changes in the gallbladder, making cholecystectomy a safe and low-risk operative procedure

Cholecystitis- Complications

- Empyema
- Perforation
- Mirizzi syndrome

Type	Figure	Description
I		External compression of the common hepatic duct due to a stone impacted at the neck of the gallbladder or at the cystic duct.
II		The fistula involves less than one-third of the circumference of the common bile duct.
III		Involvement of between one-third and two-thirds of the circumference of the common bile duct.
IV		Destruction of the entire wall of the common bile duct.
V		Cholecystoenteric fistula together with any other type of MS.

Case 3- Clinical

- 66yo woman presents to ED
- Epigastric pain, fever 39.8⁰, vomiting
- B/G: smoker, PVD (previous SFA stent, on aspirin)
- Investigations:
 - WCC 17.3
 - Creat 120, eGFR 65
 - Bilirubin 73
 - ALP 305
 - GGT 291
 - AST 136
 - ALT 201
 - INR 1.7

Describe your approach to this patient including:

- *provisional diagnosis*
- *immediate concerns*
- *further work-up and immediate management*
- *definitive management*

Cholangitis

- Charcot's triad
 - Right upper quadrant pain
 - Fever
 - Jaundice
- Reynold's pentad
 - Confusion
 - Shock

Diagnostic Criteria- Tokyo Guidelines 2018

Table 2 TG18/TG13 diagnostic criteria for acute cholangitis [4]

A. Systemic inflammation	
A-1. Fever and/or shaking chills	
A-2. Laboratory data: evidence of inflammatory response	
B. Cholestasis	
B-1. Jaundice	
B-2. Laboratory data: abnormal liver function tests	
C. Imaging	
C-1. Biliary dilatation	
C-2. Evidence of the etiology on imaging (stricture, stone, stent etc.)	

Suspected diagnosis: one item in A + one item in either B or C
Definite diagnosis: one item in A, one item in B and one item in C

Thresholds:

A-1	Fever		BT >38°C
A-2	Evidence of inflammatory response	WBC count ($\times 1,000/\mu\text{L}$) CRP (mg/dL)	<4 or >10 ≥ 1
B-1	Jaundice	(bili >34 $\mu\text{mol/L}$)	T-Bil ≥ 2 (mg/dL)
B-2	Abnormal liver function tests	ALP (IU)	>1.5 \times STD ^a
		γ GTP (IU)	>1.5 \times STD ^a
		AST (IU)	>1.5 \times STD ^a
		ALT (IU)	>1.5 \times STD ^a

Cited from Kiriya et al. [4]

ALP alkaline phosphatase, ALT alanine aminotransferase, AST aspartate aminotransferase, CRP C-reactive protein, *r-GTP (GGT)* r-glutamyltransferase, WBC white blood cell

^aSTD: upper limit of normal value

Cholangitis- Severity grading Tokyo Guidelines 2018

Table 4 TG18/TG13 severity assessment criteria for acute cholangitis [4]

Grade III (severe) acute cholangitis

“Grade III” acute cholangitis is defined as acute cholangitis that is associated with the onset of dysfunction at least in any one of the following organs/systems:

1. Cardiovascular dysfunction: hypotension requiring dopamine ≥ 5 $\mu\text{g}/\text{kg}$ per min, or any dose of norepinephrine
2. Neurological dysfunction: disturbance of consciousness
3. Respiratory dysfunction: $\text{PaO}_2/\text{FiO}_2$ ratio < 300
4. Renal dysfunction: oliguria, serum creatinine > 2.0 mg/dl
5. Hepatic dysfunction: PT-INR > 1.5
6. Hematological dysfunction: platelet count $< 100,000/\text{mm}^3$

Grade II (moderate) acute cholangitis

“Grade II” acute cholangitis is associated with any two of the following conditions:

1. Abnormal WBC count ($> 12,000/\text{mm}^3$, $< 4,000/\text{mm}^3$)
2. High fever ($\geq 39^\circ\text{C}$)
3. Age (≥ 75 years old)
4. Hyperbilirubinemia (total bilirubin ≥ 5 mg/dl)
5. Hypoalbuminemia ($< \text{STD}^a \times 0.7$)

Grade I (mild) acute cholangitis

“Grade I” acute cholangitis does not meet the criteria of “Grade III (severe)” or “Grade II (moderate)” acute cholangitis at initial diagnosis.

Early diagnosis, early biliary drainage and/or treatment for etiology, and antimicrobial administration are fundamental treatment for acute cholangitis classified not only “Grade III (severe)” and “Grade II (moderate)” but also “Grade I (mild)”.

Therefore, it is recommended that patients with acute cholangitis who do not respond to the initial medical treatment (general supportive care and antimicrobial therapy) undergo early biliary drainage or treatment for etiology (see flowchart).

Cited from Kiriya et al. [4]

^aSTD: lower limit of normal value

Case 4

- 65yo man with upper abdominal pain
- Febrile 38.9, tachycardic HR 140
- Abdomen generally tender; guarding upper abdo and right para-umbilical region
- B/G: deaf, mild developmental delay, independent ADLS
- Bloods:
 - WCC 24.1, CRP 2
 - Creat 160 (eGFR 51)
 - LFTs: bili 37; ALP/ GGT/ AST/ ALT 2-3x ULN
 - Lipase 9,061
- Imaging

Outline

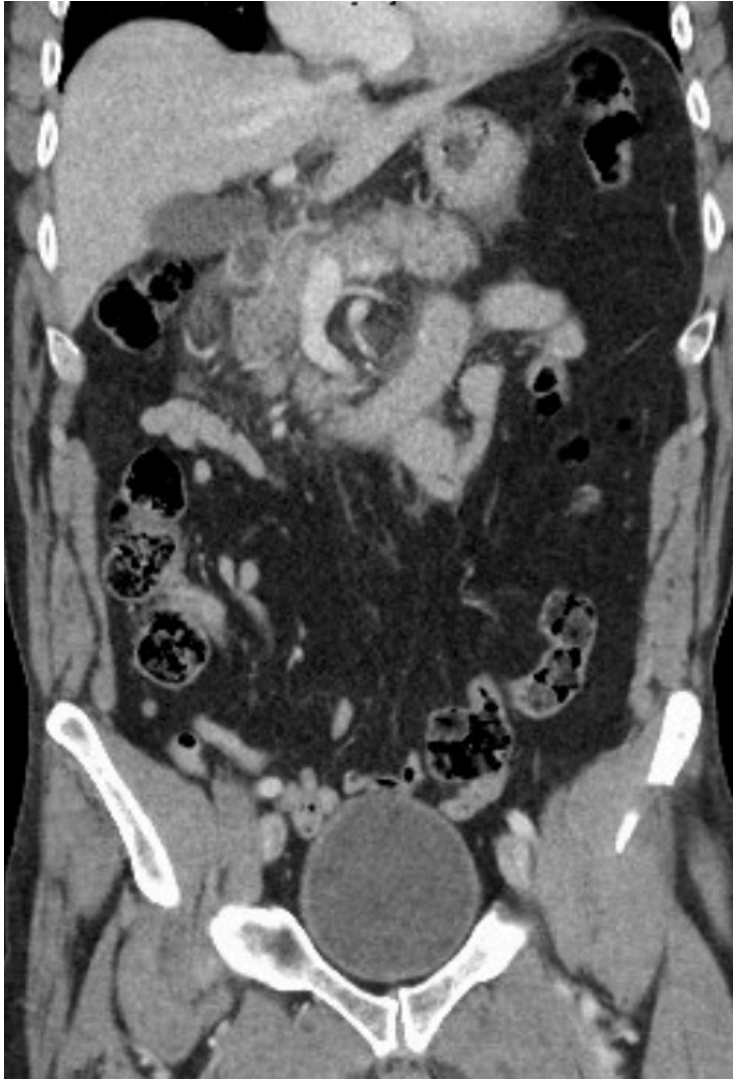
- *differential diagnoses*
- *investigation*
- *initial management*

Pathophysiology

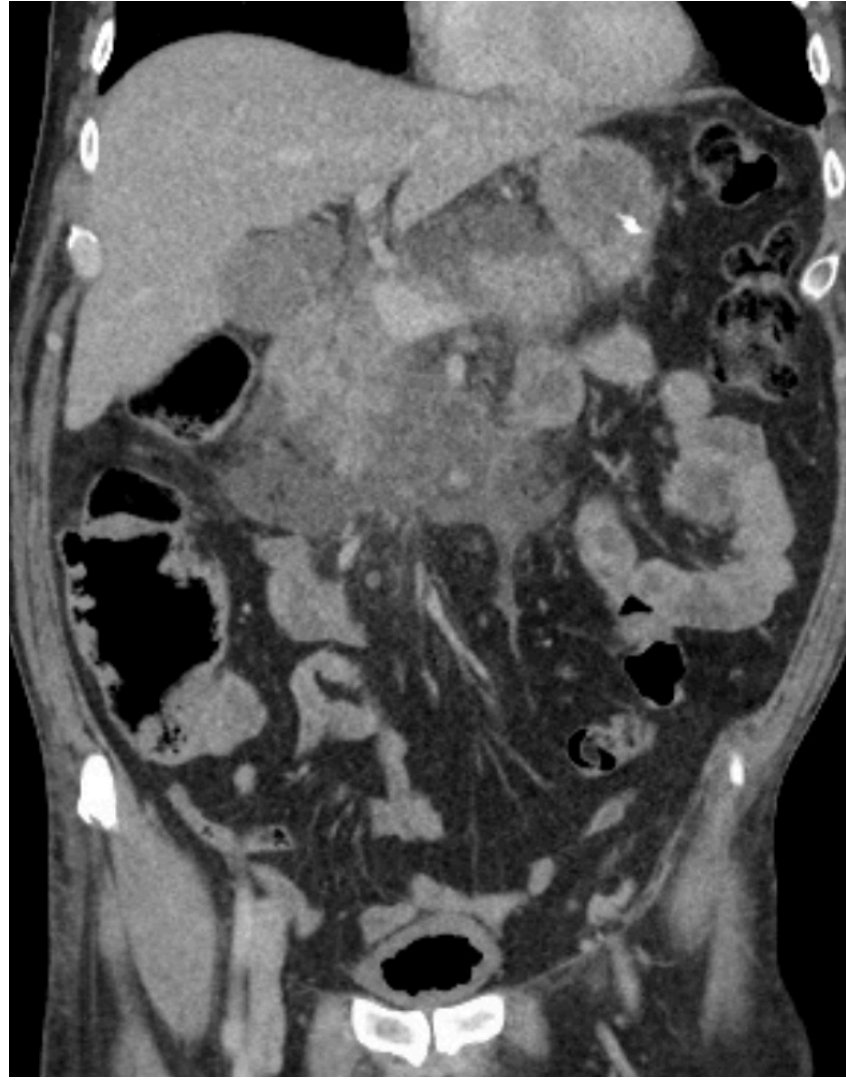
Clinical considerations

- *definitions*
- *complications*
- *severity grading*
- *ongoing management*
- *role of surgery*

Case 4- Imaging



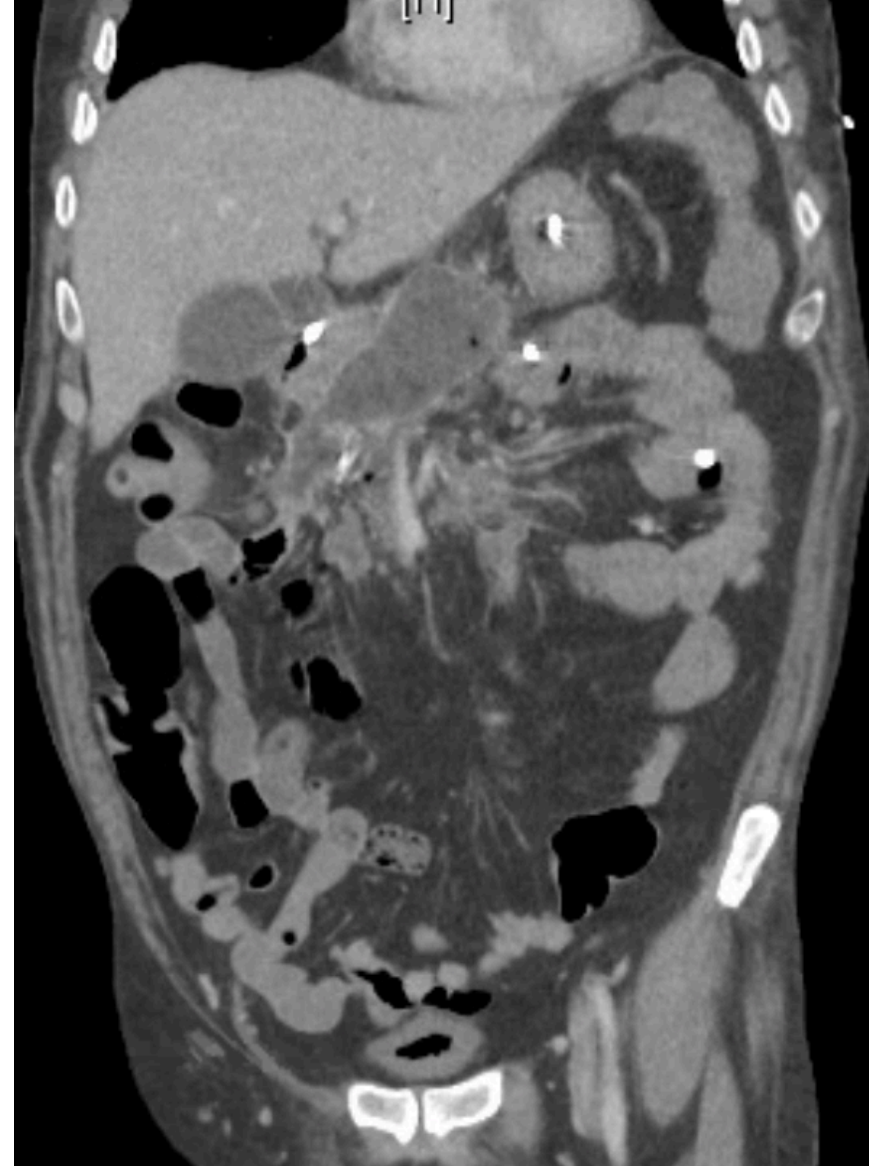
Presentation CT



1 Week Progress CT



Case 4- Imaging



Pancreatitis- Pathophysiology

- Aetiology
 - I GET SMASHED
- Pathogenesis
 - Ductal hypertension due to obstruction, or direct cellular toxicity
 - Co-localization of lysosomes and zymogens, mediated by influx of calcium
 - Intra-cellular activation of trypsin
 - Auto-activation of proteolytic enzyme cascade
 - Exacerbated by disruption of para-cellular junctions
 - Local inflammatory response, compensatory responses
 - Infiltration of macrophages, neutrophils, lymphocytes
 - Systemic Inflammatory Response Syndrome (SIRS)
 - TNF- α , IL-1, IL-2, IL-6, IL-8
 - Leukotrienes, prostaglandins
 - Activation of complement cascade
 - Fever, increased vascular permeability, vasodilation, hyperdynamic circulation
 - Compensatory Anti-inflammatory Response Syndrome (CARS)
 - IL-4, IL-10, TGF- β
- Multitude of down-stream end-organ effects due to:
 - Tissue oedema
 - Endothelial damage
 - Cellular apoptosis
 - Catabolism
 - Neuroendocrine activation
 - Pituitary: ACTH, ADH
 - Adrenal: Cortisol, catecholamines
 - Renal: RAAS activation
 - Pancreas: glucagon, decrease insulin
- Multiple Organ Dysfunction Syndrome

Pancreatitis- Definitions

- Sepsis-1 (1991) and Sepsis-2 (2001) consensus meetings:
 - SIRS:
 - Dysregulated immune response to a non-infective stimulus
 - 2 or more of:
 - Temp <36 or >38
 - HR >90
 - RR>20 or paCO₂<32mmHg
 - WCC <4 or >12
 - Sepsis
 - SIRS in the presence of an infective stimulus
- Sepsis-3 (2016)
 - Sepsis
 - Life-threatening organ dysfunction due to a dysregulated host response to infection
 - Severe sepsis: qSOFA score 2 or more
 - Septic shock: sepsis + persistent hypotension MAP<65mmHg and lactate >2mmol/L
- Shock
 - Physiological state in which perfusion of oxygen to end-organs is insufficient to meet cellular requirement for oxidative metabolism

Pancreatitis- Grading of Severity

- Glasgow- Imrie (PANCREAS)
- APACHE II
- Ranson
- BISAP
- Revised Atlanta
- Organ failure
 - Modified Marshall score
 - Cardiovascular
 - Respiratory
 - Renal
 - qSOFA
 - Hypotension: SBP <100mmHg
 - Altered mental state: GCS<15
 - Tachypnoea: RR>22
 - SOFA

Complications

- Local

- Oedematous
 - Acute peri-pancreatic fluid collection
 - Pseudocyst
- Necrotising
 - Acute necrotic collection
 - Walled off necrosis
- +/- secondary infection

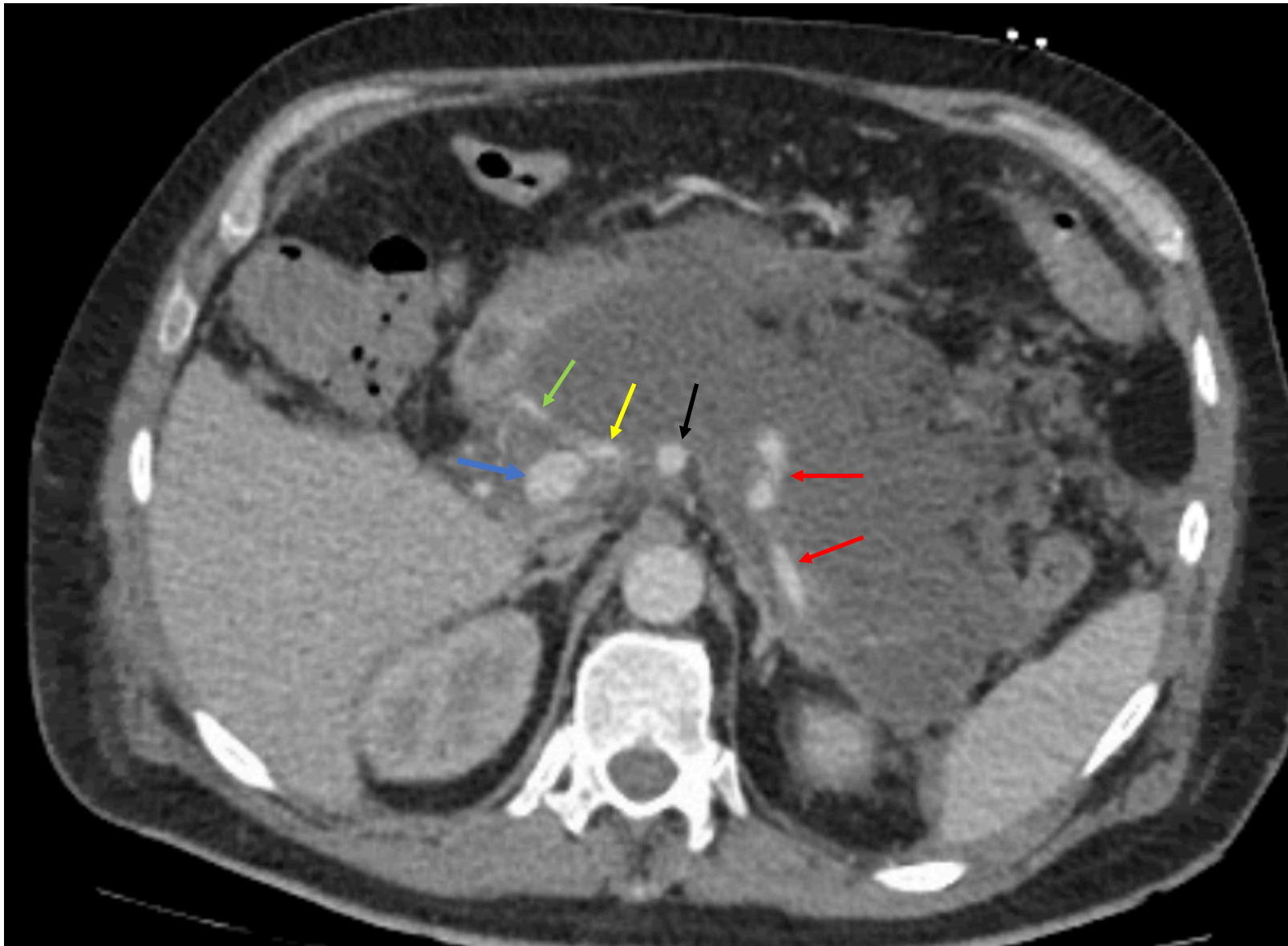
- Regional

- Gastric outlet obstruction
- Biliary obstruction
- Cholangitis
- Ileus
- Abdominal compartment syndrome
- Pseudo-aneurysm
- Infarction: spleen, transverse colon, pancreas

- Distant

- SIRS/ Sepsis/ Shock
- End-organ dysfunction/ failure
 - Cerebral
 - Renal
 - Pulmonary
 - Cardiac
 - Gastro-intestinal
 - Pancreatic
- Malnutrition
- Metabolic
 - Hyperglycaemia, hypertriglyceridaemia, hypocalcaemia
- VTE/ PE

Complications- Vascular



Pancreatitis- Key References

- Revised Atlanta Classification 2012
 - Gut 2013; 62:102-111
- IAP/APA evidence-based guidelines for the management of acute pancreatitis
 - Pancreatology 2013; 13: e1-e15
- PANTER trial
 - A Step-Up Approach or Open Necrosectomy for Necrotizing Pancreatitis.
 - NEJM 2010; 362: 1491-502
- Vascular complications of pancreatitis
 - ANZJS 2005; 75: 1073-1079