

Introduction

- Drug-induced pancreatitis (DIP) accounts for 0.1 to 2% of all acute pancreatitis (AP)
- Several medications including mesalamine, azathioprine, simvastatin, and tetracycline antibiotics have been implicated in AP
- Mechanism by which doxycycline causes pancreatitis is unknown.
- Doxycycline use has increased in recent years
- Careful history, with special attention to the onset of symptoms in association with the start of doxycycline is key to diagnosis
- We report two cases of patients diagnosed with doxycycline induced AP (DIAP) after careful exclusion of other causes of AP.

Case 1

- **60-year-old woman presented with 2-days N/V and epigastric pain**
- **PMH** -> Crohn's disease, T2DM, and HTN
- **PSH**-> Hemicolectomy, ileostomy, and CCY
- **SH** -> quit smoking 3 years prior. No ETOH or illicit drug use
- **Med hx**-> gabapentin, hydrocodone-acetaminophen, bupropion, atorvastatin, aspirin, cyclobenzaprine, dicyclomine, esomeprazole, fenofibrate, glimepiride, hydroxyzine, levothyroxine, metoprolol tartrate, mirabegron, quetiapine, ondansetron, furosemide, famotidine, celecoxib, vedolizumab, ceftriaxone, doxycycline
- **VS**-> afebrile, otherwise wnl
- **PE**-> epigastric and RUQ tenderness
- **Labs**-> lipase 6,699 u/l (normal 73 to 393 u/l), creatinine 1.94 mg/dl (normal 0.60 to 1.30 mg/dl), blood glucose 174 mg/dl (normal 70 to 100 mg/dl), calcium 9.6 mg/dl (normal 8.5 to 10.5 mg/dl). LFTs, lipid panel, triglycerides, and IgG subclasses were wnl
- **Imaging**-> CT A/P confirmed AP (Figure 1)

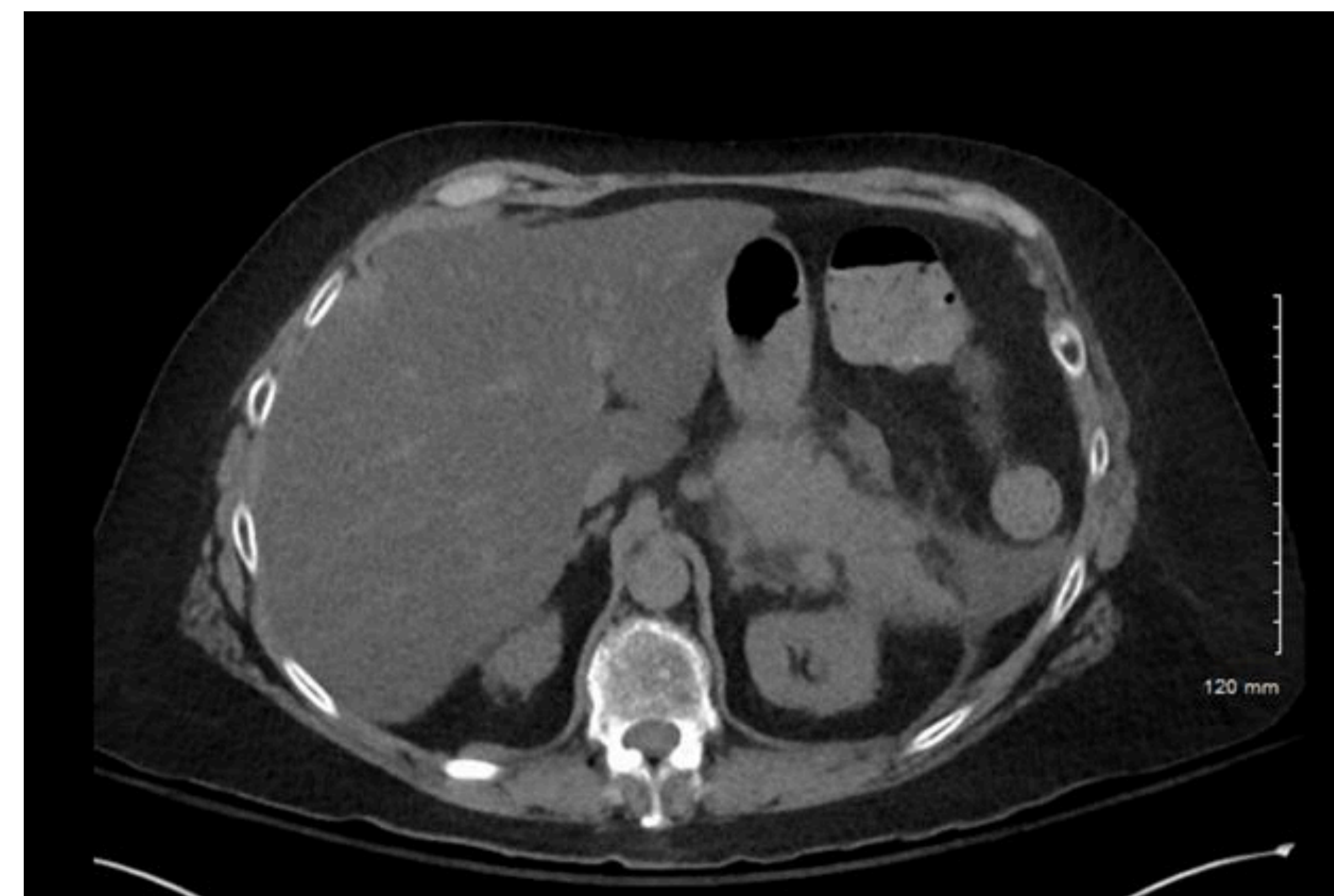


Figure 1: CT A/P. Acute interstitial pancreatitis. No obvious necrosis or peripancreatic fluid.

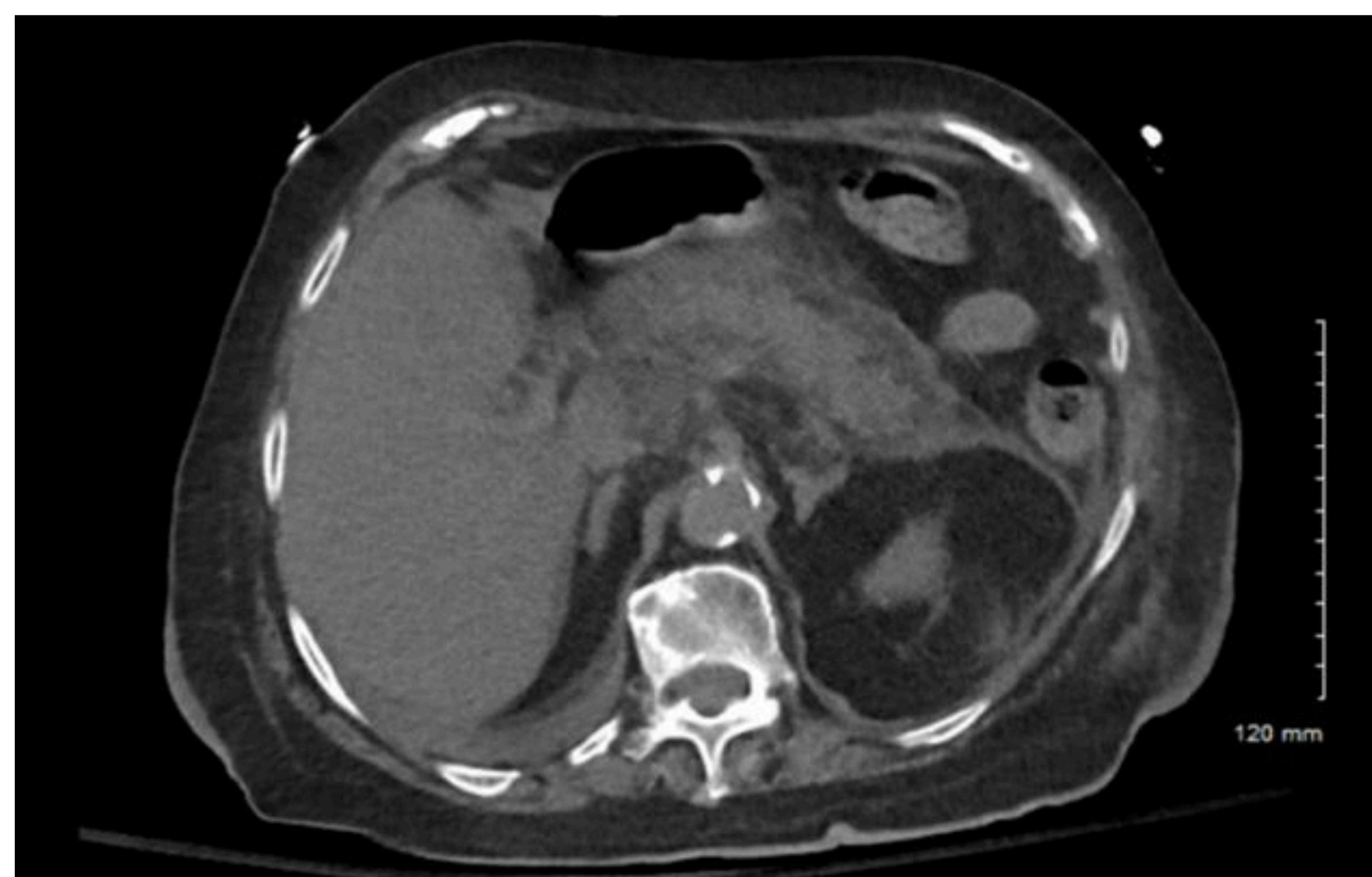


Figure 2: CT A/P. Severe peripancreatic and pancreatic edema.

Case Resolution and Discussion:

- BISAP score 2
- Latency of vedolizumab is short (vedolizumab started 2 months prior)
- Ceftriaxone latency 2 – 7
- Furosemide (Class Ia), acetaminophen (Class 2), and atorvastatin (Class III) which are known to cause acute pancreatitis; however, she had been taking these medications for several years prior to her developing AP
- Patient recovered with discontinuation of doxycycline, fluid resuscitation

Case 2

- **91-year-old woman presented with 2-days of severe epigastric abdominal pain w/o N/V**
- **PSH**-> CCY, 4 weeks prior to the admission, she underwent ORIF of her left elbow fracture that was complicated by wound dehiscence. Wound cultures were + for MRSA and *Enterobacter ludwigii*. She was treated with doxycycline 100 mg twice daily for 22 days.
- **SH**-> No tobacco, alcohol, or recreational drug use.
- **Med hx**-> acetaminophen, bisacodyl, bumetanide, digoxin, docusate sodium, gabapentin, isosorbide dinitrate, levofloxacin, metoprolol tartrate, pantoprazole, rivaroxaban, senna-docusate, sertraline, simvastatin, tramadol, doxycycline
- **VS**-> Afebrile, HR 105, BP 80/32, R 21. She appeared ill, mucous membranes dry. There was no jaundice and she had diffuse tenderness on the abdominal exam.
- **Labs**-> BUN 56 mg/dl (6 - 24 mg/dl), creatinine 2.35 mg/dl (0.60 to 1.30 mg/dl), ALP 223 u/l (33 to 138 u/l), leukocyte count 26.7 k/ul (4.0 to 12.0 k/ul), platelet count 156 k/ul (140 to 440 k/ul), calcium 6.4 mg/dl (8.5 to 10.5mg/dl), lactic acid 2.8 mmol/l (0.4 to 2.0 mmol/l), lipase 301 u/l (73 to 393 u/l). Triglycerides, AST, ALT, total bilirubin, and IgG subclasses were wnl.
- **Imaging**->CT A/P was notable for extensive intra pancreatic and peripancreatic edema (Figure 2).

Case Resolution and Discussion:

- BISAP score 5
- No obvious cause of AP
- acetaminophen (Class II), sertraline (Class IV), and simvastatin (Class Ia) which are known to cause pancreatitis; however, she had been taking these medications for several years prior to the development of AP making these medications less likely causes
- Given her recent doxycycline use and no other identifiable cause, DIAP was diagnosed
- Transferred to the ICU for hypovolemic shock. She required fluid resuscitation with vasopressors and discontinuation of doxycycline which resulted in full recovery

Conclusions

- At risk -> Elderly, women, advanced HIV, IBD
- 8/11 cases occurred in women
- Severity variable (4/9 required ICU care)
- Severe AP noted in the elderly & young patients
- Determining culprit medication can be difficult given patients are often on several causative meds
- Understanding latency can help. DIAP has variable latency (1-22 days)
- Naranjo scale may downgrade severity
- Rechallenge can be ethically difficult to perform
- Consider DIAP as doxycycline prescriptions have increased in recent years