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Rosai-Dorfman Disease in the Setting of Post-Transplant Lymphoproliferative Disorder

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*Names in bold type indicate presenting author.

Establishing the Problem: Identifying Barriers to Workflow Among Internal Medicine Resident Physicians within the VA Medical Center

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Mentor: Evan Symons

Program: Internal Medicine

Type: Original Research

Background: Workflow inefficiencies, particularly those related to the electronic health record 'CPRS', have been a major focus in feedback from Internal Medicine (IM) resident physicians working at the Omaha Veterans' Affairs (VA) facility. We surveyed current IM resident physicians to elucidate which factors have been especially cumbersome to daily workflow at the Omaha VA facility.

Methods: We drafted a list of CPRS components and institutional variables, which were then formulated into a Likert-style questionnaire. Participants were asked to gauge how frequently they had difficulty using each item. Additionally, participants ranked their level of agreement with statements regarding daily tasks essential to medical practice. These questions were distributed to current IM residents using Microsoft Forms. A public link was used to preserve anonymity.

Results: A total of 21 responses were obtained (91 participants total, 23% response rate) which is comparable to established survey response rates. Locating intake and output data is challenging for most respondents (50% responding 'constant issues'; 35% responding issues occur 'frequently'). Difficulty logging onto a workstation was experienced 'occasionally' or greater in 90% of survey participants. (Figure 1). By comparison, patient list selection, reviewing notes, and forwarding pagers cause less frequent impediments.

Conclusion: A majority of IM resident physicians experience disruptions to daily workflow by potentially modifiable factors at the Omaha VA facility. Interventions to mitigate these factors can be prioritized based on the percentage of residents affected and the relative event frequency.

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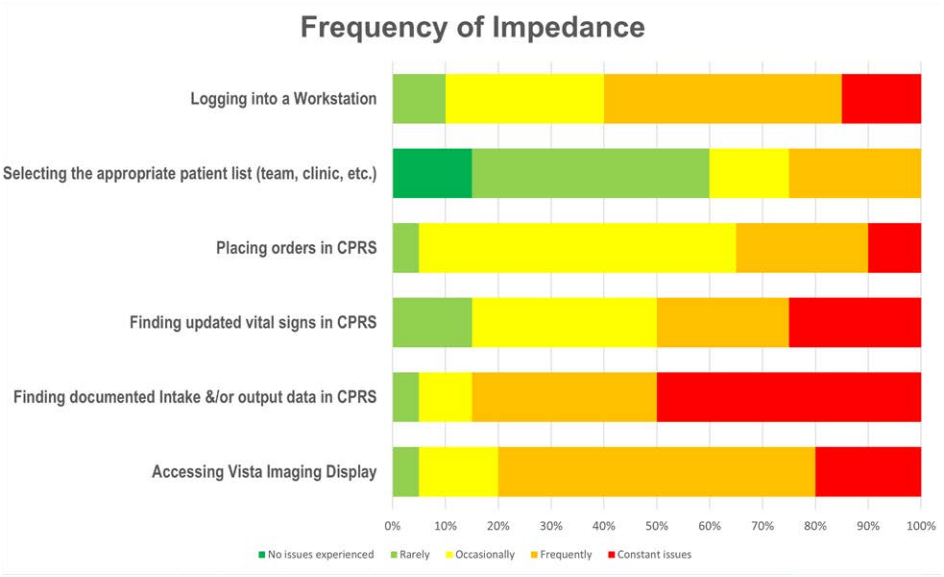

Figure 1. Participant responses to the prompt: "Please estimate how often you have experienced difficulty when using each of the following items

Immunotherapy-Induced Glomerulonephritis: Whodunit?

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Mentor: Ketki Tendulkar

Program: Nephrology

Type: Case Report

Background: Kidney immune-related adverse events are well recognized side effects of immune checkpoint inhibitor therapy.

Case: A 72-year-old man was referred for evaluation of acute kidney injury (AKI) after being treated with adjuvant nivolumab for melanoma. Serum creatinine increased from 1.0 mg/dL to 3.1 mg/dL with 300 mg of proteinuria. A presumed diagnosis of interstitial nephritis was made based on eosinophiluria. Nivolumab was stopped and he was started on prednisone and lisinopril and his kidney injury resolved. Six months later he was started on talimogene laherparepvec (T-VEC) for progressive disease. Four months into treatment, he developed edema, 10 g of proteinuria, and AKI. Kidney biopsy showed mesangio- and focal endocapillary proliferative glomerulonephritis. Immunofluorescence (IF) was positive for C3 and trace C1Q and electron dense mesangial deposits were present. T-VEC was discontinued, he was treated with rituximab, and prednisone for immune complex glomerulonephritis. He achieved resolution of kidney injury and proteinuria.

Conclusion: Programmed death 1 inhibitors (PD1i) have been described to cause AKI, most commonly due to tubulointerstitial nephritis (TIN). The improvement after stopping nivolumab and onset of proteinuria after T-VEC administration raises the possibility of a T-VEC induced immune

mediated effect as opposed to TIN. T-VEC is an oncolytic virus that can be used in melanoma and immune mediated adverse events are less common. Although delayed onset kidney injury from nivolumab cannot be excluded in this case, our findings could be due to T-VEC. T-VEC should be considered a cause of immune adverse events.

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Rosai-Dorfman Disease in the Setting of Post-Transplant Lymphoproliferative Disorder

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Program: Dermatology

Type: Case Report

Background: Rosai-Dorfman disease (RDD) is a rare non-Langerhans cell histiocytosis. RDD must be distinguished from juvenile xanthogranuloma (JXG).

Case: A 6-year-old male with history of short gut syndrome status post small bowel transplant 3 months prior presented to clinic with 1-4 mm pink, firm, edematous, painful and pruritic papules on the face, buttocks, extensor arms, and legs for 4-5 weeks. Punch biopsy showed a lymphoid infiltrate composed of variably-sized reniform cells, intermixed histocytes and eosinophils. Histology raised concern for post-transplant lymphoproliferative disorder (PTLD); however, EBV stain was diffusely negative. One month later, he presented to an outside dermatologist with worsening of his rash and diffuse lymphadenopathy of cervical, inguinal, and submandibular areas. Skin biopsy confirmed a histiocytic infiltrate, and the right inguinal lymph node showed reactive lymphoid hyperplasia of T cells and histiocytes with negative EBV. A diagnosis of JXG was rendered with plans to treat with chemotherapy.Before commencing treatment, cutaneous nodules significantly improved spontaneously; however, lymphadenopathy worsened. PET-CT discovered a hypermetabolic lymph node with central necrosis. Cervical node biopsy showed EBV+ monomorphic PTLD with diffuse large B cell lymphoma. Prior skin biopsies were reviewed and revealed S100+ and CD207+ cells with emperipolesis, consistent with Rosai-Dorfman disease in the setting of PTLD.1 The patient's RDD resolved without specific treatment, and he was initiated on chemotherapy per ANHL0221 for his PTLD.

Conclusion: While cutaneous RDD often presents with absence of systemic symptoms, it has been reported in the setting of lymphoproliferative disorders and can thus represent a diagnostic challenge.

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Sporadic Hypokalemic Periodic Paralysis Likely Induced by Kratom (Mitragyna speciosa)

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Mentor: Erin L. Smith

Program: Neurological Sciences

Type: Case Report

Background: Hypokalemic periodic paralysis (HPP) is the most common periodic paralysis but is still rare with a prevalence of 1 in 100,000. In severe cases seizures, respiratory depression, cardiac arrhythmias or arrest, and coma might occur. Dietary triggers, strenuous exercise, and prescription medications have been known to precipitate HPP attacks. Here we describe a case of an HPP attack suspected to be triggered by Kratom, an over-the-counter supplement derived from the tropical evergreen tree (Mitragyna speciosa) that has gained recent popularity for its use in chronic pain, sleep, and psychiatric symptoms.

Case: A thirty-year-old male with a significant past medical history of bipolar type 1 disorder presented with acute onset bilateral proximal upper and lower extremity weakness, muscle cramps, and difficulty climbing the stairs. His thyroid levels and renal profile were normal. He reported having a similar episode five years ago related to hypokalemia that resolved after replacement. His potassium serum level was 3.3 mEq/L (normal range: 3.5 to 5.2 mEq/L). The complete resolution of his neuromuscular symptoms observed after correcting low potassium serum levels. We advised him to stop Kratom herbal supplements, and the patient reported no further episodes of recurrent neuromuscular weakness.

Conclusion: Kratom's effects on the nervous or cardiovascular systems and potassium homeostasis are not well recognized. The literature has not reported Kratom-induced HPP, and the exact mechanism for its role in inducing hypokalemia is unclear in this case. Clinicians need to inquire about the use of recreational and over-the-counter medications triggering the HPP attacks.

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The Kneed for Stability: Posterior Knee Pain in a Recreational Soccer Player

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Program: Family Medicine

Type: Case Report

Background: A sensation of instability following knee injuries is a concerning symptom requiring further imaging. We present a case of a soccer player with right knee pain.

Case: A 25-year-old female presented to clinic with right knee pain. Ten days prior, she suffered a hyperextension injury during a recreational soccer game after a defender "knocked knees" with her while she was kicking a ball. She experienced immediate pain, redness, warmth, and difficulty walking. She continued to experience pain, stiffness, and sensation of instability despite using an OTC knee brace. Exam revealed mild effusion, tenderness over the lateral posterior joint line and popliteal fossa, and limited active ROM due to pain. Apley compression, McMurray, and Thessaly tests were positive, as well as increased external rotation on Dial test. MRI showed partial injury to the distal insertion of the LCL and biceps tendon. Given partial injury, orthopedic surgeon recommended trial of non-operative management. Patient was placed in Reddie Brace and started physical therapy. At 3-month follow-up, patient was pain free with no sensation of instability, and was cleared to return to sports.

Conclusion: The posterolateral corner (PLC) of the knee consists of several major lateral knee stabilizers including the lateral collateral ligament (LCL) and biceps femoris. Mechanism of injury classically involves hyperextension, twisting mechanism, or anterior or valgus blow to a flexed knee. Primary symptoms are pain and instability, especially in full knee extension. PLC injuries typically present with concurrent ACL or PCL injury — only a quarter of PLC injuries occur in isolation.

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An Unusual Cause of Diastolic Murmur

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Program: Internal Medicine

Type: Case Report

Background: Atrial myxoma is a rare primary cardiac tumor, part of a heterogenous group of intracardiac masses which includes metastatic disease and thrombus. Presentation varies from incidental discovery to life-threatening cardiac tamponade, arrhythmia, valvular obstruction, and systemic embolization.

Case: An asymptomatic 55-year-old male with hypertension and hyperlipidemia presented with ventral hernia. Computed tomography (CT) incidentally found a large left atrial mass. A soft holodiastolic murmur was variably heard. Vitals, blood tests, ECG, and chest x-ray were normal.

TTE was normal except for a round, mobile left atrial mass attached to the interatrial septum by a stalk, with severe diastolic prolapse into the LV. With findings diagnostic of atrial myxoma, biopsy was foregone to avoid risk of embolism due to tumor friability. The patient was referred for surgical resection. TEE was performed to confirm TTE findings (Figure 1A, 1B & 1C) and guide hemodynamic management perioperatively. Doppler analysis revealed severe mitral valve (MV) obstruction, with resting MV gradients of 10 (max) and 5 (mean) mmHg, and effective MV area 0.82 cm2. Based on TEE findings, the patient underwent resection of the mass en bloc (Figure 1D). Post-op TEE showed restoration of normal MV structure and function.

Conclusion: The pearl of confirming atrial myxoma is focused imaging to identify tumor stalk and absence of intrinsic MV disease. Once confirmed, biopsy can be avoided, and direct surgical consultation obtained. TEE adds value to perioperative hemodynamic management.

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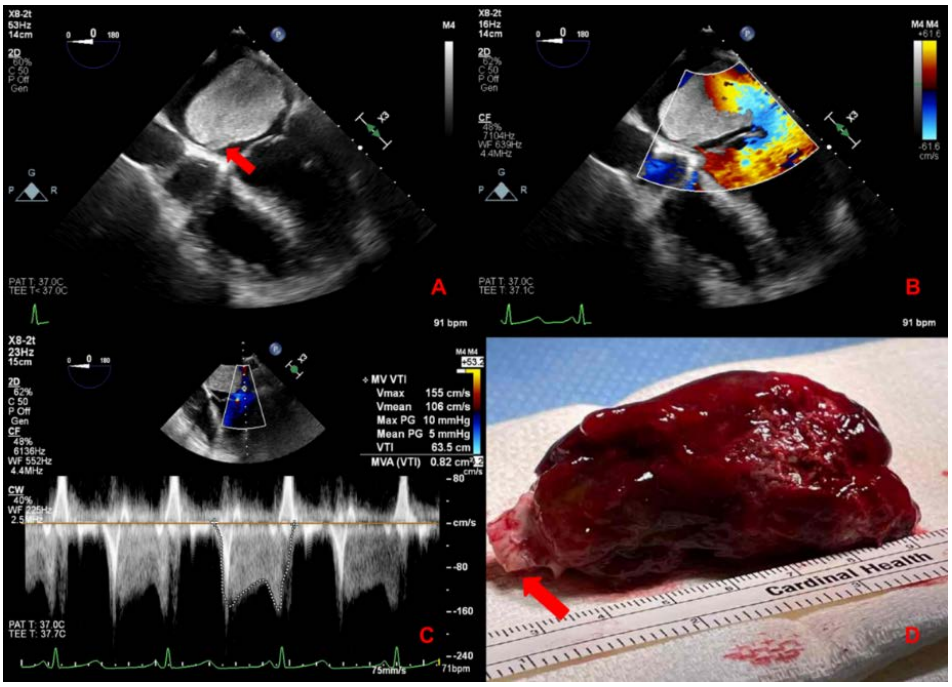

Figure 1. Left atrial myxoma TEE findings and gross pathology. (A) Left atrial myxoma attached to interatrial septum by stalk as seen on TEE; (B) TEE color flow imaging showing high-velocity flow around myxoma; (C) TEE Doppler showing severe obstruction through normal mitral valve; (D) gross pathology of friable myxoma with stalk.

Gastroenteritis Leading to Multiorgan Failure in a Young Adult

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Program: Internal Medicine

Type: Case Report

Background: Acute Liver Failure (ALF) is a severe, potentially reversible form of liver injury defined by development of hepatic encephalopathy within eight weeks of symptom onset without pre-existing liver disease. To our knowledge, this is the first case of ALF attributable to Escherichia coli gastroenteritis in a previously healthy young adult without pre-existing liver disease.

Case: A 36-year-old female with recent heavy alcohol use presented with four days of progressive abdominal pain, vomiting, and diarrhea. She was afebrile, hypotensive, and tachycardic. Exam demonstrated generalized abdominal tenderness without peritoneal signs. Significant laboratory investigations included AST 489 U/L, ALT 143 U/L, bilirubin 2.6 mg/dL, creatinine 0.95 mg/dL, and LDH 18,522 U/L. Imaging was unremarkable. She received intravenous fluids and Zosyn empirically. Two days later she became obtunded and developed scleral icterus, jaundice, and anasarca. AST had skyrocketed to 12,516 U/L, ALT 3,381 U/L, bilirubin 6.6 mg/dL, and Cr 3.08 mg/dL. Evaluation for infectious, autoimmune, and toxin-mediated causes of ALF were unrevealing except positive testing for Enteropathogenic Escherichia coli (EPEC). She briefly required dialysis but within a week her liver and kidney function normalized. She was diagnosed with ischemic hepatitis secondary to EPEC.

Conclusion: Severe transaminitis >1000 has a limited differential including ischemic hepatitis, acute viral hepatitis, and toxin-mediated hepatitis. The rapid rise and fall in liver enzymes and marked LDH elevation is specific for ischemic hepatitis. Liver enzymes take weeks to normalize after viral or toxin-mediated hepatitis. Physicians must readily identify and treat underlying causes of ALF to prevent progression to multiorgan failure or death.

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Fluid-Resistant Hyponatremia in Active Inflammatory Bowel Disease: A Case Report

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Mentor: Andrew Huang

Program: Pediatric Gastroenterology

Type: Case Report

Background: Role of intestinal permeability in inflammatory bowel disease. The intestinal inflammation and permeability can cause impaired epithelial function affecting transport of electrolytes, enzymes, and nutrients.

Case: A 14-year-old male presented with 3 weeks of generalized abdominal pain, bloody diarrhea, and weight loss. Evaluation revealed elevated lipase, inflammatory markers, hyponatremia (Na+ 127), and normal abdominal ultrasound. He was admitted for acute pancreatitis and subsequently diagnosed with Crohn's Disease. Despite hypertonic intravenous fluids and enteral sodium supplements, hyponatremia persisted for several days. Nephrology workup was unrevealing. Upon initiation of prednisone and infliximab for IBD, serum sodium level responded and normalized within two weeks.

Conclusion: Electroneutral NaCl and electrogenic Na absorption are predominant mechanisms of gut sodium retention. The observed hyponatremia in active IBD is attributed mainly to decreased sodium absorption, rather than increased secretion, as proinflammatory mediators reduce expression and function of transporters involved in sodium uptake. Mucosal healing with restored epithelial function from prednisone and infliximab combined with a mild mineralocorticoid effect from prednisone stimulating sodium retention likely explain resolution of hyponatremia. Separately, we ponder the initial diagnosis of acute pancreatitis. Without characteristic epigastric pain or abnormal imaging, only one diagnostic criteria (elevated lipase) is truly fulfilled. Pancreatic abnormalities in IBD are common with AP being the most prevalent. However, other causes of hyperlipasemia in IBD include systemic inflammation affecting the pancreas, abnormal reabsorption of lipase from the inflamed, hyperpermeable gut, and macrolipase formation. We consider that this patient's hyperlipasemia may be attributed to intestinal inflammation rather than true AP.

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Pancytopenia: Horse, Zebra, or Something Else

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Mentors: Thomas Perry, Shaun Thompson

Program: Anesthesiology

Type: Case Report

Background: Often masquerading as sepsis, hemophagocytic lymphohistiocytosis (HLH) presents a major challenge for diagnosis by intensivists. Characterized by dysregulated interactions between T-cells and target cells, HLH leads to profound cytokine release secondary to genetic or immunogenic factors. The treatment is cytotoxic therapy and immunosuppression, both contraindicated in sepsis, highlighting the importance of delineating HLH from other etiologies of multiorgan failure.

Case: A 71-year-old male was admitted to the ICU for shock after recieving hyperthermic intraperitoneal chemotherapy (HIPEC) with carboplatin for mesothelioma. On admission, he was critically ill on vasopressors and mechanical ventilation. His hemodynamics continued to worsen with no etiology identified prompting HLH to be considered on the differential. Workup identified an

*Names in bold type indicate presenting author.

H-score of 218 indicating 93-96% chance of HLH. Based on the 2004 diagnostic criteria, 5 out of 8 criteria were met indicating a probable diagnosis. Despite these findings, hematologists declined to diagnose HLH due to multiple confounding variables, with his pancytopenia likely due to myelotoxicity secondary to decreased carboplatin clearance used in the HIPEC in the setting of an acute kidney injury. The elevated ferritin/soluble interleukin -2 receptor was explained by critical illness postoperatively. Nonetheless, dexamethasone was initiated, but cytotoxic therapy was withheld given neutropenia. His condition improved, and he was transferred out with the diagnosis of undifferentiated shock.

Conclusion: This case illustrates the elusiveness of diagnosing HLH, as infection and malignancy are often etiologies of both sepsis and HLH, indicating need for more diagnostic clarity. The ambiguity of this diagnosis also highlights the importance of early hematology consultation in treating these patients.

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A Case of Agitated Catatonia Improved by Electroconvulsive Therapy in a Patient with Schizophrenia

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Mentor: Ashish Sharma

Program: Psychiatry

Type: Case Report

Background: Catatonia is a psychomotor disturbance that is most often associated with mood disorders, but is also observed in up to 35% of patients with schizophrenia (Table 1). The variability in presentation makes prompt diagnosis difficult and increases the risk of serious morbidity and mortality. Benzodiazepines are traditionally used as first line, however they only have a remission rate in acute catatonia of 70% vs. 80-100% for ECT. Clinicians should quickly switch to ECT if symptoms are refractory or there is concern for decompensation.

Case: 62-year-old female with history of schizophrenia, heart failure, hypertension, and seizures who had been stable on outpatient weekly maintenance ECT and regimen of Olanzapine, Valproic acid, Lorazepam, and Phenobarbital (for seizures). She missed 1 month of ECT due to port malfunction that triggered ED visit for agitation. No catatonia/psychosis noted and delirium workup was negative at that time. Overnight she developed refractory agitation and hallucinations that required restraints and transfer to ICU for etomidate drip. We promptly started bilateral ECT M/W/F initiation after observation of catatonic features (mutism, mannerisms, sterotypies, and internal agitation). After 5 treatments and restarting home regimen, improvement was noted and she was back to baseline with no catatonic features after 6 weeks of inpatient ECT. She was discharged back to ALF on home regimen with new port and maintenance ECT.

Conclusion: This case demonstrates the variability in catatonia presentations, emphasizes importance of having a rapid treatment plan if high clinical suspicion, and reinforces the effectiveness of ECT in treating schizophrenia with agitated catatonia.

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Table 1. Reviewing the diagnostic criteria for catatonia syndrome in the DSM V.

DEFINITION OF CATATONIA PER DSM-V		
Presence of 3 or more of the following 12 psychomotor features (1):		
1	Catalepsy	Passive inducton of postures held against gravity
2	Waxy Flexibility	Slight and even resistance to repositioning
3	Stupor	No psychomotor activity or reactivity to environment
4	Agitation	Not influenced by external stimuli
5	Mutism	No or minimal verbal response
6	Negativism	Opposing or not responding to external stimuli
7	Posturing	Spontaneous/active maintenance of posture against gravity
8	Mannerisms	Odd caricatures of ordinary actions
9	Stereotypies	Repetitive, frequency, non-goal directed movements
10	Grimacing	Facial grimacing
11	Echolalia	Repeating words spoken to them
12	Echopraxia	Mimicking movements of others

Unmasking the C3ulprit

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Mentor: Prasanth Ravipati

Program: Nephrology

Type: Case Report

Background: C3 glomerulonephritis (C3GN) is a rare disease with pathology findings typically showing a proliferative pattern with C3 deposition on immunofluorescence (IF) and negative immunoglobulin (Ig) staining. In certain cases, it is important to pursue paraffin IF, which can unmask deposited Ig, differentiating C3GN from immune complex GN.

Case: A 22-year-old man with no chronic medical history presented with complaints of arthralgias and sore throat and was found to have acute kidney injury. He was without rash, synovitis, or peripheral edema. Serum creatinine was 4.37 mg/dL, urinalysis showed numerous dysmorphic red blood cells, and spot protein to creatinine ratio was 2.5. Serologic evaluation showed low C3, low C4, and a positive anti-nuclear antibody. Additional antibody testing, serum protein electrophoresis with immunofixation, and infectious diseases evaluation were negative. Kidney biopsy showed mesangioproliferative glomerulonephritis involving all glomeruli, with IF staining positive only for C3 in the glomerular capillary walls. A preliminary

diagnosis of C3GN was made. However, electron microscopy (EM) showed fibrillary-like substructure within subendothelial deposits and intracellular rod-like crystals, which raised suspicion for masked glomerular Ig deposits. Therefore, paraffin IF showed IgG staining with kappa restriction along the glomerular capillary wall. Serum testing was positive for IgG cryoglobulin. The patient was ultimately diagnosed with type 1 cryoglobulinemic glomerulonephritis.

Conclusion: In cases of suspected C3GN, paraffin IF is important to ensure the absence of immune complex GN. Patients with paraproteinemia or EM findings of fibrillary or microtubular substructure warrant consideration for paraffin IF to avoid misdiagnosis.

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A Case of Groove Pancreatitis Presenting with Intermittent Gastric Outlet Obstruction

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Mentor: Shane Manatsathit

Program: Gastroenterology and Hepatology

Type: Case Report

Background: Groove pancreatitis is a rare form of chronic pancreatitis that notably involves inflammation of the groove in-between the head of the pancreas, duodenum, and common bile duct. Presentation can often be difficult to distinguish from duodenal, ampullary, or pancreatic malignancy.

Case: A 58-year-old male with a past medical history of alcohol abuse and a 30-pack-year smoking history presents with a chief complaint of worsening abdominal pain, nausea, and vomiting. The patient reports two and a half years of chronic abdominal pain worsened with increased alcohol intake. He endorses discomfort with oral intake, abdominal distention, early satiety, and intermittent emesis of previous undigested meals. A CT abdomen was obtained, showing mild proximal duodenal wall thickening with pancreatic groove and head fat stranding (Figure 1). Patient's chronic nausea and vomiting with obstructive-like symptoms were attributed to chronic groove pancreatitis. MRCP was obtained to rule out malignancy, and repeat MRI was recommended for surveillance in two years. Alcohol cessation was advised to minimize acute flares, and no surgical interventions were planned at this time, given the lack of underlying malignancy.

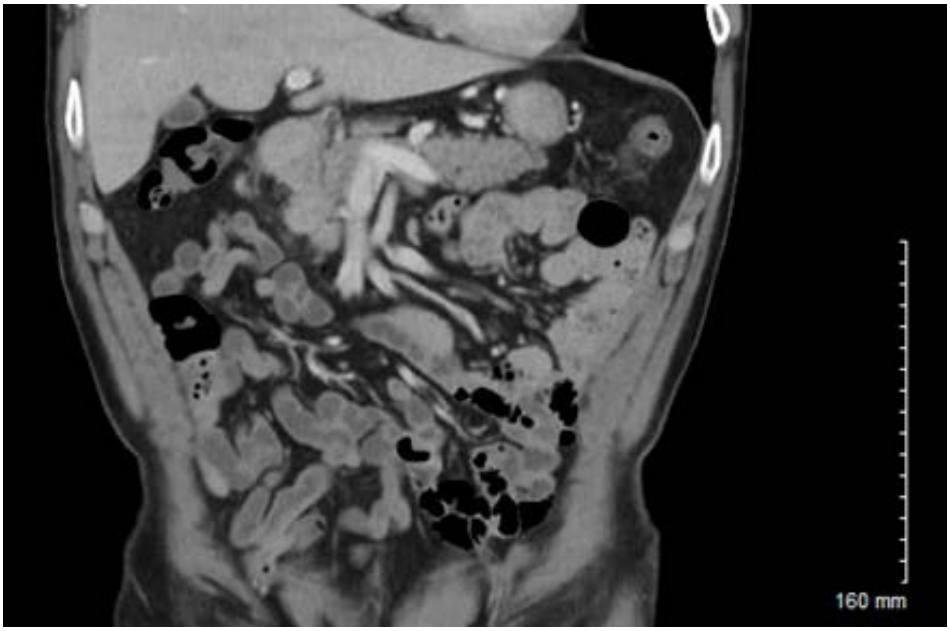

Figure 1. Coronal View of CT scan depicted with Duodenal, Pancreatic Head, and Groove Inflammation.

Conclusion: Groove pancreatitis symptoms often overlap with chronic pancreatitis, but chronic obstructive symptoms often are unique to the prior. Imaging findings showing inflammation of the pancreatic head, groove, and duodenum are imperative in diagnosis and merits further workup, including MRCP or ERCP with EUS to evaluate for malignant etiologies. These patients ultimately undergo pancreaticoduodenectomy for improved symptom control or when malignancy cannot be ruled out.

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