Abdominal Imaging Manifestations of Systemic Autoimmune Diseases

Kristen Olinger, MD¹, Maitraya Patel, MD², Cecilia Jude, MD², Shaden Mohammad, MD², Daniel Margolis, MD³, Anokh Pahwa, MD²

¹Department of Radiological Sciences, David Geffen School of Medicine at UCLA
²Department of Radiology, Olive View-UCLA Medical Center
³Department of Radiology, Weill-Cornell Medicine
Financial Disclosures

• None

Target Audience

• General and abdominal radiologists, residents and fellows

Overview

• Introduction

• Epidemiology, Pathophysiology and Abdominal Radiologic Features of:
  • Systemic Lupus Erythematosus (SLE)
  • Rheumatoid Arthritis
  • Systemic Vasculitis Syndromes (Polyarteritis nodosa, Takayasu arteritis)
  • Systemic Sclerosis Syndrome
  • Behcet’s Disease
  • Autoimmune Hepatitis
  • IgG4-related Disease

• Conclusion
Introduction

• Systemic autoimmune diseases are complex entities
• Abdominal involvement is seen in a large proportion of cases
• Radiologists should be familiar with clinical presentations of these disease processes and understand the abdominal radiologic findings that help guide clinical management
• After review of the presentation, participants will be able to:
  • Discuss the epidemiology and pathophysiology of abdominal manifestations of systemic autoimmune diseases
  • Identify CT, MRI, and fluoroscopic patterns associated with these disease entities
  • Substantiate an integrated radiological and clinical approach to managing systemic autoimmune diseases
Systemic Lupus Erythematosus

• Epidemiology:
  • Peak onset in 20-40 years old
  • Female to male predominance of 9-13:1 (however, lower female predominance in the juvenile/elderly)
  • Higher rates in African-American, African-Caribbean descent population

• Pathophysiology:
  • Autoimmune process characterized by inflammation, immune complex deposition, vasculitis and vasculopathy
  • Activation of the complement system leads to formation of immune complexes in tissues
  • Immune complexes recruit B lymphocytes, which lead to autoantibody creation
  • Dysfunction of the normal suppressive control of the immune system leads to an uncontrolled, widespread autoimmune response
  • Fibrinoid necrosis of the small vessels leads to end-organ ischemia, hemorrhage
  • Can also see increase in lymphoreticular malignancy, infection
  • Hypothesized environmental triggers include UV light, smoking, infection
  • Diagnosis made if 4 out of the 11 WHO clinical criteria are met
    • Malar rash
    • Discoid lesions
    • Photosensitivity
    • Oral ulcers
    • Nonerosive arthritis
    • Serositis
    • Renal involvement
    • Seizures/psychosis
    • Hematologic abnormalities
    • Immunologic abnormalities
    • Positive antinuclear antibody test
Systemic Lupus Erythematosus

• Radiologic Features:
  • Vascular findings:
    • Arterial and veno-occlusive disease, particularly when antiphospholipid syndrome is present
    • End-organ ischemia (e.g. ischemic enteritis, splenic infarction)
  • Gastrointestinal findings:
    • Reflux esophagitis (due to esophageal dysmotility)
    • Gastritis
    • Pancreatitis (from the autoimmune process or as a side effect of medications) – acute and chronic
    • Ischemic enteritis – particularly SMA territory
    • Budd-Chiari syndrome
    • Acalculous cholecystitis
  • Renal findings:
    • Chronic renal failure, including renal atrophy
    • Renal vein thrombosis, ischemic infarcts

A. Contrast enhanced axial CT image in a 48-year-old female with known lupus, abdominal pain and elevated lactate demonstrates small bowel wall thickening. B. On the follow-up CT with oral contrast 1 day later, there is progression of small bowel wall thickening. Findings likely represent ischemic bowel secondary to lupus, which affects smaller mesenteric arteries and veins, not well seen by CT.
A. Coronal reconstruction from contrast-enhanced CT in a 41-year-old male with lupus and abdominal pain. Findings including diffuse small bowel wall thickening likely representing ischemic enteritis and ascites.

B. Coronal reconstruction from contrast-enhanced CT in a 40-year-old male with lupus and epigastric pain. Peripheral wedge-shaped areas of hypo-enhancement are seen in the left kidney and spleen, consistent with infarcts of varying age.
A. Contrast-enhanced axial CT in a 34-year-old female with lupus demonstrates large filling defect extending through the left renal vein consistent with renal vein thrombosis. B/C. Axial T1 fat saturated post-contrast images in a 51-year-old female with history of lupus demonstrates patchy hepatic arterial enhancement with irregular renal contours, felt to be secondary to scarring from prior ischemia.
Rheumatoid Arthritis

• Epidemiology:
  • Peak incidence at 40-60 years
  • Female to male predominance of 2-3:1
  • Up to 70% of patients express HLA-DR4 (in particular the HLA-DR B1 allele)
  • Extra-articular manifestations occur in up to 40% of patients

• Pathophysiology:
  • Activation of CD4 T cells leads to a systemic inflammatory response
    • Antigens are presented by macrophages
    • Leads to production of T lymphocytes
    • Cytokine and antibody production occurs
    • Antibody production leading to immune complex deposition
    • Ultimately results in pannus formation
  • Exact cause is unknown
  • Hypothesized environmental triggers include infection (EBV), smoking
  • Per the American College of Rheumatology criteria, diagnosis is made based
    upon a combination of radiographic findings of location-specific arthritis
    (peripheral joints) and presence of rheumatoid factor
Rheumatoid Arthritis

• Radiologic Features:
  • Vascular findings:
    • Rheumatoid vasculitis
    • Rare and severe complication of longstanding rheumatoid arthritis
    • Primarily small to medium sized vessel involvement
  • Gastrointestinal findings:
    • Often iatrogenic and medication-induced
    • Intestinal ischemia
    • Splenomegaly (Felty syndrome: the triad of rheumatoid arthritis, splenomegaly and neutropenia)
  • Renal and genitourinary findings:
    • Mesangial glomerulonephritis
    • Interstitial Cystitis
    • Non specific imaging findings
  • Other:
    • Lymphadenopathy
    • Hematologic malignancies

Contrast-enhanced axial CT cystogram in a 66-year-old female with rheumatoid arthritis presenting with hematuria. Imaging demonstrates diffuse circumferential bladder wall thickening, which was biopsy-proved interstitial cystitis.
Systemic Vasculitis Syndromes

• Polyarteritis Nodosa (PAN):
  • Epidemiology:
    • Peak incidence in 40-60 years old
    • Female to male predominance of 1.6-2:1
    • Hepatitis B infection has been strongly associated with PAN
  
  • Pathophysiology:
    • Fibrinoid necrotizing vasculitis affecting the small to medium-sized arteries
    • Preferential involvement at the vascular bifurcations
    • Transmural inflammation of the vessel wall leads to fibrinoid necrosis, thereby weakening the vessel wall and resulting in microaneurysms and hemorrhage
    • Fibrous thickening leading to thrombosis and vessel occlusion can be seen in the chronic stage
    • Exact cause is unknown
Polyarteritis Nodosa

- Radiologic Features:
  - Vascular findings:
    - Microaneurysms, luminal irregularity, stenoses and arterial occlusion
  - Gastrointestinal findings:
    - Involvement in 50-70% of cases, with hepatic involvement in 50-60% and pancreatic involvement in 25-35%
    - Bowel ischemia, infarction, hemorrhage, perforation
  - Renal findings:
    - Most frequently involved organ (80-90%)
    - Arterial aneurysms, infarction

Coronal MIP reconstruction from contrast-enhanced CT angiography in a 63-year-old male with polyarteritis nodosa. Characteristic findings include beaded intrahepatic arteries, intraparenchymal microaneurysms and a resulting subcapsular hematoma. Similar findings in the pancreas are partially seen. Additional splenic and renal involvement was present (not included).
Systemic Vasculitis Syndromes

• Takayasu Arteritis:
  • Epidemiology:
    • Peak incidence in younger patients (<50 years old)
    • Female to male predominance of 8-9:1
    • Increased prevalence in Asian and Indian populations
  • Pathophysiology:
    • Granulomatous large vessel vasculitis leading to destruction of the arterial media
    • Adventitial mononuclear infiltrate with perivascular cuffing of the vasa vasorum early in the disease
    • Predominately affects the aorta and its major branches
    • Results in aneurysms, stenosis and occlusions
    • Exact cause is unknown
    • Clinical presentation includes classic “pulseless” disease in the late-phase
Takayasu Arteritis

• Radiologic Features:
  • Acute phase: wall thickening and wall enhancement of the aorta and/or branches
  • Chronic phase: stenosis, occlusion, aneurysmal dilation and pseudo-aneurysms of the aorta and/or branches
  • Type I-V classification system based upon location
    • I: aortic arch branches, classic type
    • IIa: ascending thoracic aorta, aortic arch and its branches
    • IIb: type IIa plus involvement of the descending thoracic aorta
    • III: thoracic descending aorta, abdominal aorta, renal arteries or a combination
    • IV: abdominal aorta and/or renal arteries
    • V: generalized involvement of all aortic segments and its branches

Time of flight MR Angiography of the renal arteries in a 26-year-old male with Takayasu arteritis who presents with refractory hypertension. Characteristic findings include aneurysmal dilation of the suprarenal abdominal aorta and multifocal large vessel stenoses involving the aorta, left main renal artery, and superior mesenteric artery (not included).
Systemic Sclerosis Syndrome

• Also known as scleroderma

• Epidemiology:
  • Peak incidence in 30-50 years old
  • Female predilection, with female to male predominance of 3:1 (up to 10:1 in reproductive years)

• Pathophysiology:
  • Collagen and extracellular matrix protein deposition disorder which results in abnormal immune response and tissue fibrosis
  • Microvascular disease
    • Early involvement of small vessels
    • Therefore organs with dense capillary networks are preferentially affected
  • Skin involvement can be limited (primarily hand and distal forearm involvement and associated with CREST syndrome: calcinosis, Reynaud’s phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia) or diffuse (involves upper arm, shoulder and trunk and associated with more visceral involvement)
  • Exact cause is unknown, hypothesized exposures include silica, solvents, radiation, viral (CMV, HHV5, parvovirus B19)
Systemic Sclerosis Syndrome

• Radiologic Features:
  • Vascular findings:
    • Small vessel stenoses
  • Gastrointestinal findings: seen in up to 90% of patients
    • Esophageal involvement (dilation, hypomobility, incompetency of the lower esophageal sphincter) in up to 90% of cases
    • Up to 50% of cases demonstrate small bowel involvement
    • Smooth muscle atrophy, hypomotility in small bowel leads to dilation, air-fluid level
    • “Hidebound” bowel sign: narrow separation of the valvulae conniventes despite small bowel dilation
  • Renal findings: in up to 25% of patients
    • Scleroderma renal crisis: abrupt onset hypertension, acute renal failure, spotted nephrogram due to focal ischemia in the setting of severe arteriolar narrowing

A. Coronal reconstruction from CT enterography in a patient with systemic sclerosis demonstrates narrowing of the spaces between the valvulae conniventes despite bowel dilation, resulting in a characteristic “hidebound bowel” appearance. Multiple cystic lesions in the pancreatic head are incidentally noted. B. Barium upper GI series demonstrates the “stack of coins” appearance in hidebound bowel.
A. Axial contrast-enhanced CT in a 60-year-old female with known systemic sclerosis and abdominal pain demonstrates diffuse small bowel dilation and the characteristic "hidebound bowel" appearance. Perforation was present (not well seen). B. Coronal reconstruction in contrast-enhanced CT in a 56-year-old female with mixed connective tissue disorder (SLE/scleroderma) demonstrates a partially obstructing fecalith in the descending colon. C. Coronal T2 MRI image from a 31-year-old female with history of systemic sclerosis and recurrent pseudo-obstruction demonstrates the "hidebound bowel" appearance.
Systemic Sclerosis Syndrome

A/B. Axial CT images with oral contrast in a 58-year-old female with history of scleroderma and unexplained weight loss demonstrates esophageal distension and dilation of the jejunum and proximal ileum with the characteristic “hidebound bowel” appearance of the small bowel. C. Non-contrast axial CT image in a 75-year-old female with history of scleroderma and abdominal pain demonstrates markedly distended loops of small bowel without discrete transition point.
Behcet’s Disease

• Epidemiology:
  • Peak incidence in 20-30 years old
  • Males more commonly affected
  • More prevalent along the Silk Road (Eastern Asia, Mediterranean and Middle East)
  • Increased risk associated with HLA-B51 allele

• Pathophysiology:
  • Abnormal autoimmune response and hyperfunctioning of neutrophils
  • Leads to vasculitis and perivascular inflammatory infiltrates
  • Chronic, recurring symptoms
  • Exact cause is unknown
  • Hypothesized triggers include viral infection, environmental factors

• Diagnostic criteria:
  • Minor or major apthous ulcers occurring at least 3 times in a 12-month period
  • Recurrent genital apthous ulcers
  • Eye lesions (uveitis, retinal vasculitis)
  • Skin lesions (erythema nodosum, pseudofolliculosis, acneform nodules)
  • Positive pathergy test
Behcet’s Disease

- Radiologic Features:
  - Vascular findings:
    - In up to 30% of cases
    - Mural thickening of the aorta/SVC
    - Vascular thrombosis
    - Aneurysmal dilatation
  - Gastrointestinal findings:
    - Separate from oral ulcerations
    - In up to 50-60% of cases
    - Most commonly due to small vessel vasculitis in the bowel wall
    - Bowel wall thickening
    - Localized versus diffuse intestinal ulcerations, particularly ileocecal region
    - Complications: bowel perforation, fistulas, hemorrhage
    - Pancreatitis

A-C. Axial and coronal reformats from time of flight MRA in a 39-year-old male with family history of Behcet’s and splenic artery aneurysm status post coiling. Numerous splenic collateral vessels and fusiform aneurysm of the celiac artery and left internal iliac artery are seen.
Autoimmune Hepatitis

• Epidemiology:
  • All ages can be affected, however most commonly 40-60 years old
  • Female to male predominance of 3.6:1

• Pathophysiology:
  • Hypothesis includes environmental agent triggering an inflammatory cascade directed at liver antigens
  • Results in necroinflammatory and fibrotic changes in the liver
  • Type 1: “classic”
    • Characterized by elevated circulating antinuclear antibodies (ANA), smooth muscle antibodies, antiactin antibodies, atypical perinuclear antineutrophilic cytoplasmic antibodies (pANCA) and autoantibodies against soluble liver antigen (SLA) and liver-pancreas antigen (LP)
  • Type 2: rare
    • Antibodies to liver-kidney microsomes (ALKM-1) and liver cytosol antigen (ALC-1)
Autoimmune Hepatitis

• Radiologic Features:
  • Widely variable, ranging from normal to manifestations of end-stage liver disease
  • Imaging is particularly useful to identify complications of cirrhosis and to evaluate for autoimmune involvement of additional abdominal organs
  • Hepatomegaly
  • Macronodular cirrhosis (more commonly seen in disease processes where hepatocellular regeneration plays a significant role)
    • Liver surface nodularity
    • Hypertrophy of the caudate lobe with atrophy of the right hepatic lobe
    • Confluent hepatic fibrosis from chronic liver injury (appears as wedge-shaped areas of hypoattenuation on CT, T2 hyperintensity on MR)
  • Sequelae of portal hypertension (varices, ascites, splenomegaly)
  • Periportal edema

A/B. Axial T1 fat saturated post contrast MRI images in a 48-year-old female with autoimmune hepatitis demonstrates a macronodular liver with confluent hepatic fibrosis.
Autoimmune Hepatitis

A. Contrast enhanced CT scan in a 47-year-old female with autoimmune hepatitis demonstrates geographic hypoattenuation and a macronodular pattern of cirrhosis.

B. Coronal reformat from a contrast enhanced CT scan in a 49-year-old female with autoimmune hepatitis demonstrates a macronodular pattern of cirrhosis.
IgG4-Related Disease:

- Epidemiology:
  - Peak incidence in middle-age/elderly (mean age 50-60s)
  - Male to female predominance of 3-7:1

- Pathophysiology:
  - Extensive infiltration of IgG4-positive plasma cells and T lymphocytes into organs
  - Leads to characteristic “storiform” (whorled) and obliterative fibrosis, tumefactive lesions
  - Pathogenesis is poorly understood

- Radiologic Features:
  - Pancreas is the most commonly involved organ
    - Sclerosing pancreatitis is a form of autoimmune pancreatitis
    - Diffuse versus less commonly focal enlargement of the pancreas (focal can mimic tumor)
    - Hypoechoic rim of pancreatic parenchyma
    - Less commonly associated with severe peripancreatic stranding, changes of chronic pancreatitis (such as calcifications, pseudocyst formation)
    - Diffuse or segmental narrowing of the main pancreatic duct
  - Hepatobiliary tract: seen in 60-80% of patients with autoimmune pancreatitis
    - Sclerosing cholangitis
    - Intrapancreatic common bile duct most commonly affected

A. Axial contrast-enhanced CT images in a 63-year-old male with epigastric pain demonstrates diffuse enlargement of the pancreas with a subtle hypointense rim of pancreatic parenchyma, consistent with autoimmune pancreatitis. B. Follow-up CT in same patient 6 months following initiation of steroid therapy demonstrates resolution of findings.
IgG4-Related Disease:

- **Radiologic Features:**
  - Renal: seen in up to 35% of patients with autoimmune pancreatitis
    - 5 patterns of involvement:
      - Bilateral cortical lesions (round or wedge-shaped peripheral lesions): most common
      - Diffuse patchy involvement
      - Soft tissue rim around the kidneys
      - Bilateral renal sinus nodules
      - Diffuse wall thickening of the renal pelvis
  - **Other:**
    - Lymphadenopathy
    - Retroperitoneal fibrosis: in 20% of patients with autoimmune pancreatitis, periaortic soft tissue mass that can surround or encase the ureters
    - Periaortitis
    - Sclerosing mesenteritis
    - Rare: gastritis/ulceration, prostatitis

A/B. Contrast enhanced CT scan in a 42-year-old male presenting with malabsorption and weight loss. Findings include diffuse pancreatic enlargement with a rim of hypoenhancing pancreatic parenchyma and peripheral wedge-shaped areas of hypoenhancement within the bilateral kidneys, consistent with autoimmune pancreatitis and IgG4-related renal disease.
A-C. Axial and coronal reformed contrast-enhanced CT in a 70-year-old male with history of autoimmune pancreatitis with acutely elevated alkaline phosphatase/bilirubin. Findings include a rim of soft tissue thickening surrounding the bilateral kidneys and insinuating into the left renal hilum. Of note, IgG4 levels were above the reportable range (above 300 mg/dl).
A. Coronal MRCP image from a 76-year-old male with history of biliary stricture demonstrates a smooth distal common bile duct stricture with proximal intrahepatic biliary dilatation. IgG4 levels were elevated at 117. B. Coronal MRCP image from a 46-year-old male with history of primary sclerosing cholangitis demonstrates mild intrahepatic biliary duct beading, including areas of stenoses and aneurysmal dilatation. IgG 4 levels were elevated at 227 and findings were consistent with IgG4 cholangiopathy.
A. Axial T1 fat saturated post contrast and B. Axial T2 fat saturated MR images through the liver in a 62-year old male demonstrate an amorphorous, mildly T2 hyperintense lesions with subtle rim enhancement in segment 6 of the liver (additional lesion in segment 6 not included on these images. Previous biopsy demonstrated lymphoplasmacytic infiltrates containing IgG4-positive plasma cells, consistent with IgG4 sclerosing disease in the liver.
A-C. Axial contrast-enhanced CT images in a 50-year-old male with history of mesenteric mass demonstrate an ill-defined mesenteric mass which encases the SMA and mesenteric branches, surrounds the pancreas and extends into the porta hepatis. Percutaneous biopsy demonstrated “dense storiform fibrosis with lymphoplasmacytic infiltrate” which in the setting of elevated IgG4 (285) most likely represented IgG4-related disease.
Summary

- Systemic autoimmune diseases can be complex
- Many cases demonstrate abdominal involvement
- Predilection for specific organs and vascular involvement can be helpful in narrowing the differential diagnosis
- An improved understanding of the epidemiology and pathophysiology, in addition to the radiologic presentation, can help guide diagnosis and management
References


Contact

• Kristen Olinger, MD  David Geffen School of Medicine at UCLA
  • klinger@mednet.ucla.edu