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Unusual Intestinal and Extra Intestinal Findings in Crohn's Disease Seen on Abdominal Computed Tomography and Magnetic Resonance Enterography

Pictorial Essay

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ABSTRACT

The magnetic resonance (MR) enterography technique has improved over the past few years to provide an excellent means of evaluating the gastrointestinal tract for suspected Crohn's disease. Although the prevalent intestinal manifestations of Crohn's disease have been extensively discussed in the radiology literature, some of its rare complications, especially extra intestinal, have received less attention. Uncommon findings that may be seen on MR enterography and abdominal CT examinations performed in patients with Crohn's disease include hepatic sinusoidal dilatation, primary sclerosing cholangitis, fistulas in unusual locations, hepatic and splenic abscesses, and spondylarthritis. Radiologists should be aware of these potentially rare manifestations. They should be kept in mind during clinical examinations and should be routinely searched for and reported if present.

Keywords:

Crohn's disease, extra intestinal manifestations, intestinal manifestations, extra enteric complications

BODY TEXT

INTRODUCTION

Computed tomography (CT) and magnetic resonance enterography (MRE) are currently routinely performed in patients with suspected or known Crohn's disease (CD). Imaging features of the intestinal manifestations and usual complications of CD have been extensively described throughout the literature (1). However, less frequent findings may be missed by the radiologist confronted with CT or MRE in a context of CD assessment. They include rare sites of involvement of the disease, unusual patterns of common complications, and extra intestinal findings. These manifestations have to be kept in mind and should be routinely searched for and reported if present.

To this aim, we review and illustrate the unusual findings that may be seen on abdominopelvic CT or MR enterography (MRE) performed for the evaluation of patients with CD. These include unusual locations of the disease, manifestations of the disease, complications, associated extra intestinal findings, and potential incidental findings.

UNUSUAL SITES OF INVOLVEMENT

Although the ileum is the most common site of involvement in CD, other less common sites have been described, such as the stomach (2), duodenum (Fig. 1), the proximal small bowel, Meckel's diverticulum, and the appendix. Of note, in a recent study involving 1329 patients, 16.7% showed involvement of the proximal small bowel (3).

The appendix is frequently involved with ileocolonic CD, with similar findings to those found in the small bowel. However, it rarely is the first presentation of CD. Appendiceal involvement may also be caused by contact inflammation in the setting of ileitis (Fig. 2). Interestingly, in a study of 76 patients with CD studied with CT enteroclysis (4), hyperenhancement of the appendiceal wall had a specificity of 100% for active CD versus inactive CD.

UNUSUAL TYPES OF COMPLICATIONS

1. ENTERIC COMPLICATIONS

1.1 Fistulas

Fistulas developing anywhere around the gastrointestinal tract may be diagnosed on CT or MR images. Some locations are particularly rare such as enterocutaneous, sigmoidovaginal and enterovesicular fistulas.

As stated in recent consensus recommendations for the utilization of CT and MRE in patients with CD, imaging of the entire anus should be obtained for every CT and MRE examination in order to evaluate the presence or absence of perianal disease. If perianal disease is present, or if clinically indicated, then a dedicated MR of the pelvis may be performed for more detail and precision by a dedicated MR pelvic examination.

Moreover, fistulas connecting bowel inflammatory segments to some part of the skeletal system may cause spondylodiscitis, osteomyelitis, and abscesses. Bone must be examined by bone windowing to find focal sclerosis along the femoral head.

These fistulas may be indistinct and difficult to detect. They most frequently involve the sacrum and the ilium because of the proximity of these structures to the ileum (Fig. 3, 4). Muscles may also be a site of involvement, more likely those of the anterior abdominal wall.

1.2 Cancer

Patients with longstanding CD have an increased risk of developing small bowel and anal adenocarcinoma (5). They present a diagnostic challenge, as the tumor is often indiscernible from the underlying inflammatory bowel disease (IBD). Loss of stratification of the bowel wall and asymmetric marked focal mural thickening are findings suggestive of malignancy in these patients. Small bowel adenocarcinomas most often occur in a specific region of chronic inflammation such as a fistula tract or in strictured segments (Fig. 5) (5,6).

Likewise, cancers may develop in longstanding anoperineal fistulas. They consist of either squamous cell carcinomas or mucinous adenocarcinomas. Longstanding fistulas thus have to be carefully assessed for any changes in size or shape. In cases of mucinous adenocarcinomas, the MRI findings are those of a hypersignal T2-weighted lobulated lesion with peripheral enhancement on gadolinium-enhanced fat suppressed T1-weighted MR images (6) (Fig. 6).

2. EXTRA ENTERIC COMPLICATIONS

2.1 Hepatobiliary

Most of the extra intestinal complications are hepatic, including drug-induced hepatitis, gallstones in part due to vitamin B12 deficiency, hepatic abscesses, and sepsis-related hepatic sinusoidal dilatation (Fig.7). Fatty liver is the most common hepatobiliary complication of CD (7), resulting from chronic malnutrition, protein loss, and corticosteroid therapy.

Liver abscess is a rare but serious complication of CD (Fig. 8). Several risk factors for liver abscess and related conditions have been reported, such as intra abdominal abscesses or fistulas, steroid or metronidazole therapy, and cholangitis. Abscesses are mostly of bacterial origin, *Streptococcus milleri* being the most frequent (8). However, they may rarely be aseptic with negative microbiologic investigations and failure of antibiotic therapy. It has been suggested that aseptic abscesses could result from an immunoinflammatory process associated with CD due to the aberrant homing of gut T memory/effector lymphocytes in the liver. This hypothesis is supported by the effectiveness of immunosuppressive therapy (9).

Hepatic sinusoidal dilatation may be observed in CD as in any other acute extrahepatic disease associated with a marked systemic inflammatory syndrome (Fig. 7). CT and MRI then show a reticulated enhancement pattern of the liver, reversible with the resolution of the initial disease. This pattern is usually visible at both arterial and portal phases and disappears during the delayed phase (10). The areas showing a fern-like pattern are hypoattenuated on unenhanced CT, hypointense on T1-weighted, and hyperintense on T2-weighted images. The associated

clinical findings may include right upper quadrant abdominal pain, hepatomegaly, and minimal elevation of liver function tests. The main pathological finding is enlargement of the sinusoid lumen by more than one hepatic plate in width.

Drug-induced hepatitis may result from iatrogenic hepatotoxic effects of thiopurines, methotrexate, sulfasalazine, cyclosporine, infliximab, adalimumab, and certolizumab used for treatment of CD. Generally, non-specific imaging features of hepatitis can be found, such as hepatomegaly, peri-portal edema, hepatic steatosis, and gallbladder wall thickening. The association of these findings with elevated results of liver function tests should raise concern in CD patients.

Iatrogenic complications such as nodular regenerative hyperplasia (NRH) have been described. Cases of NRH are mainly reported in patients receiving thiopurines for CD (11).

Cholangiocarcinoma has been described as a CD-related primary sclerosing cholangitis (PSC) complication with a poor prognosis. (12, 13).

Imaging findings of PSC and cholangiocarcinoma may overlap, usually leading to delayed diagnosis of cholangiocarcinoma at an inoperable stage. However, persisting or progressing bile duct stricture, large nodular defects, capsular retraction, portal vein invasion, and mass-forming lesions with delayed enhancement may raise concern about malignant transformation of PSC.

2.2 Musculoskeletal

Rare musculoskeletal complications include drug-related avascular necrosis of the femoral head and chronic non-bacterial osteomyelitis, which may partly be explained by potential CD-related mutations in CARD 15, encoding the NOD2 protein (14).

2.3 Urinary

The incidence of urinary complications in patients with Crohn's disease has been reported to be 4%–23%, ranging from the most common simple cystitis to rarer advanced urinary sepsis (15).

The most commonly encountered urinary disorders are urolithiasis and pyelonephritis.

Renal stone formation may be partly explained by hypocitraturia and hypomagnesiuria, influencing crystal nucleation (16). Urolithiasis and pyelonephritis incidence ranges from 4% to 23% with a risk 10-100 times greater than the risk for the general population (17).

Hydronephrosis may result from nephrolithiasis as a manifestation of CD, as the two disorders are associated in up to 12% of cases. The composition of kidney stones is usually based on calcium oxalate (resulting from hyperabsorption of oxalate) or uric acid (due to increased bicarbonate losses). It may also result from acalculous ureteral inflammatory entrapment, compression or fibrosis as a complication of penetrating CD, preferably in longstanding diseases (18) (Fig. 9). Classic Crohn's disease granulomas may also very rarely develop in the kidney, causing granulomatous interstitial nephritis and mimicking hypervascular renal tumors in imaging (19).

2.4 Genital

Genital involvement mainly results as a complication of penetrating CD, either from anoperineal fistulizing disease or from colonic or enteric involvement. For instance, tubo-ovarian abscesses may occur and may be depicted on CT.

To allow adequate analysis of genital complications, subsequent high-resolution perianal MRI with T2-weighted sequences and intravenous contrast is needed. (20).

2.5 Vascular

Patients with CD have an increased risk of thromboembolic events, particularly venous embolism. These thromboembolic complications may be explained by many factors, such as common histories of abdominal surgery, corticosteroid use, and increased concentration of

clotting factors in severe disease (21, 22). The portal vein and its branches are the veins which are most affected by thrombosis. However, the superior or inferior mesenteric veins and the inferior vena cava may also be involved and detected on abdominopelvic CT or MRE (Fig. 10). Pulmonary embolism, which is a major cause of mortality in these patients, also has to be suspected. Thrombi in the mesenteric veins generally resolve without anticoagulation, but peripheral mesenteric venous thrombi frequently evolve into chronic peripheral mesenteric venous occlusion seen on follow-up imaging, with development of collateral pathways or small bowel varices (23).

2.6 Peritoneal inclusion cysts

In patients with Crohn's disease, women, almost exclusively premenopausal, may present with peritoneal inclusion cysts. These cyst develop as a result of adhesions and/or dysfunction of the peritoneum related to prior episodes of inflammation of prior surgeries

The fluid thus accumulates in the locules formed by the potential adhesions inside the peritoneum. Loculated fluid in the pelvis surrounding normal ovaries will be observed both by CT and MRE and should not be mistaken for pelvic cystic lesions, as it conforms to the peritoneal space.

UNUSUAL FINDINGS AND ASSOCIATED DISEASES

1. Hepatobiliary

CD patients have an increased incidence of hepatobiliary findings, including PSC and its complications (25), granulomatous Crohn's hepatitis, and PSC–autoimmune hepatitis overlap syndrome.

PSC is the most common hepatobiliary Crohn's-associated disease, characterized by progressive inflammation, obliterative fibrosis, and destruction of the bile ducts.

PSC may be recognized on abdominopelvic CT or MRE when some segments of the biliary tree are dilated, but diagnosis is far easier when PSC is more advanced or even complicated with cirrhosis. PSC will be, of course, best evaluated using further complementary hepatic MRI and MR cholangiography which can show evidence of alternating stenoses and dilatations on the biliary intra or extrahepatic ducts. (Fig. 11).

In IBD patients, the use of MRI increases the detection of PSC 3-fold compared to detection based on symptoms alone (26). Indeed, only 10%–15% of patients exhibit symptoms at the time of diagnosis (27).

When CT or MRI show features of PSC and autoimmune hepatitis in the same patient, the diagnosis of autoimmune hepatitis overlap syndrome can be suspected. The definitive diagnosis is based on the International Autoimmune Hepatitis Group Criteria, which includes histologic, demographic and biomarkers (28).

Granulomatous Crohn's hepatitis is also a challenging unusual diagnosis in CD patients, often caused by medications (sulfasalazine), malignancies, infections, or CD metastasis (28).

2. Musculoskeletal

The prevalence of ankylosing spondylitis (AS) in CD (1%-6%) is higher than in the general population (0.25%-1%) (29). Axial manifestations of AS frequently precede the diagnosis of CD by several years.

Sacroileitis is the most obvious finding that may be depicted on CT or MRE, more often as an incidental finding showing long standing disease than acute inflammation (Fig. 12). CT features initially include joint space irregularity, followed by classic erosion, sclerosis, and eventually ankyloses. MRI allows early diagnosis of osteitis in acute sacroiliitis, seen as subchondral bone marrow edema on short tau inversion recovery (STIR)-weighted images. Subchondral sclerosis, periarticular erosions, synovitis, capsulitis, and enthesitis may also be described in CD-associated sacroiliitis. Some patients may present imaging features of sacroiliitis without AS criteria, called isolated sacroiliitis. Its reported prevalence is between 16% and 46% (25).

Spondylitis may also be seen on MRE, including Romanus lesions, bone marrow edema called shiny corners, and post inflammatory fatty bone marrow degeneration in a chronic phase.

Other musculoskeletal manifestations have been reported in the literature, such as inflammatory bowel disease-related arthropathy, osteoporosis, osteomalacia, hypertrophic osteoarthropathy, and osteonecrosis (25).

3. Pancreatitis

In CD patients, acute pancreatitis is usually idiopathic, with granulomatous inflammation of the pancreas being a hypothesis (30). CD-associated pancreatitis frequently remains clinically silent and hyperamylasemia or exocrine pancreatic insufficiency may be the only manifestation of the disease. CT and MR imaging features of acute pancreatitis are non specific.

In autoimmune pancreatitis, a “sausage-like” appearance of the pancreas and a low attenuation halo may be seen. The role of antibodies against exocrine pancreatic tissue (PABs) in the pathogenesis of autoimmune pancreatitis is still under discussion (5).

Three other main causes of pancreatitis in CD are duodenal involvement as well as biliary and iatrogenic etiologies such as the use of azathioprine. However, pancreatitis is often overdiagnosed in these patients because of non specific elevation of serum lipase and recurrent abdominal pain (31).

CD patients may also develop chronic pancreatitis. Intrapancreatic duct changes in patients with CD may partly explain the development of chronic pancreatitis, whose pathogenesis remains unclear (32). Classic signs of chronic pancreatitis may be seen on either CT or MRE images.

4. Miscellaneous disorders

Hidradenitis suppurativa

Hidradenitis suppurativa (HS) is a recurrent inflammatory disease of the pilosebaceous follicle consisting of inflamed lesions of apocrine glands, usually of the anogenital, axillary, and inguinal regions (Fig. 12). HS is an unusual Crohn’s-associated disease (33). HS-related anoperineal abnormalities may also be a differential diagnosis of CD-related anoperineal disorders. Indeed, when the disease is primarily perianal, the differential diagnosis can be challenging since the presentations may overlap. However, perianal disease in HS is characterized by the fact that the lesions are not predominant in the perianal area, unlike those observed in perineal involvement in CD. They are rather located in the anterior/inguinal and/or sacral/gluteal regions. HS-related anoperineal involvement is also characterized by bilaterality of the features. Moreover, the rectal wall is rarely thickened. (34).

INCIDENTAL FINDINGS NOT RELATED TO CD

The radiologist must not forget to look for incidental findings. However, the most common fortuitous findings discovered on MRE are simple liver or renal cysts (35). Jensen et al. reported a 20% incidence of incidental extra enteric findings on MRE images, but only 6% had substantial or incompletely characterized findings warranting additional examinations such as CT (36).

CONCLUSION

Radiologists should be aware of these potentially rare findings and complications that can be seen on MR enterography and pelvic MRI in order to provide referring clinicians with the means to make the appropriate diagnosis warranting additional imaging examinations.

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FIGURE LEGENDS

Figure 1

Coronal balanced fast field echo MRE (True FISP)–weighted MR image in a 39-year-old male with longstanding Crohn’s disease involving the ileum, jejunum, and duodenum and displaying a short fibrous stenosis of the third duodenum responsible for a marked dilatation of the upstream second duodenum and stomach (arrow). The patient was undergoing immunosuppressive and anti-tumor necrosis factor treatment. This stenosis was confirmed with an upper GI endoscopy and biopsy.

Figures 2 a and b

Coronal single shot fast spin echo (HASTE) T2–weighted (a) and axial gadolinium-enhanced fat-suppressed T1-weighted (b) MRE images showing an enlarged appendix with a thick markedly enhanced wall (arrows, a and b). The 25-year-old male patient had an acute flare up of Crohn’s colitis and underwent surgery. A histological analysis of the appendix confirmed its involvement.

Figures 3 a and b

Axial fat-suppressed T1-weighted gadolinium-enhanced MR images (a,b) showing an inflammatory mass and fistula (arrow,a) extending to the right sacral root (arrow, b) in a 38-year-old male with Crohn’s disease presenting with right sciatica.

Figure 4 a and b

Coronal HASTE T2 (a) and axial fat-suppressed gadolinium-enhanced T1-weighted (b) MRE images showing a sacral abscess (arrows,a and b) related to an entero-osseous fistula (arrowhead,b) in a 17-year-old male with active Crohn’s disease

Figure 5

Coronal single shot fast spin echo (HASTE) T2-weighted MRE image performed at follow-up of a 71-year-old female patient with longstanding ileal Crohn’s disease showing an irregular heterogeneous mass (arrows) developed at the ileocaecal junction. Note the distal ileum, which is involved in her Crohn’s disease (arrowhead). Surgery was performed and the pathological examination confirmed a mucinous adenocarcinoma developed at the ileocaecal junction over underlying CD.

Figures 6 a, b, and c

Axial contrast-enhanced abdominopelvic CT image (a) in a 50-year-old male with a longstanding complex anoperineal fistula showing a large hypodense lesion surrounding the anal canal (arrow,a). Pelvic MRI was performed and coronal single shot fast spin echo (HASTE) T2 (b) and sagittal gadolinium-enhanced fat-suppressed T1-weighted MR images (c) display a large lobulated heterogeneous lesion superimposed on the bed of the former fistula with peripheral enhancement, consistent with mucinous adenocarcinoma which was confirmed by pathological examination (arrows, b and c).

Figures 7 a, b, and c.

Coronal gadolinium-enhanced fat-suppressed T1-weighted image at the arterial phase (a) and portal phase (b). MRE images show fern-like abnormalities of the liver, predominantly in the arterial phase and at the periphery of the liver (arrows, a and b) consistent with sinusoidal dilatation. Coronal single shot fast spin echo (HASTE) T2-weighted MRE images (c) show discrete hypersignal intensity areas (arrow, c) at the periphery of the liver in this 29-year-old male presenting at our emergency department with anemia, considerable weight loss for the last year, asthenia, and psoriasis. A large abscess in the psoas was diagnosed (black arrow, c) related to a fistula from severe adjacent ileal Crohn’s disease. Findings were confirmed at surgery. Nine

months later, MRE showed complete resolution of the liver abnormalities and abscess (not shown).

Figure 8

Coronal abdominopelvic CT scanner image showing a hepatic (white arrow) and subhepatic abscess (black arrow), with a fistula to the right psoas (arrowhead) complicating active CD.

Figures 9 a, b, and c

Coronal single shot fast spin echo (HASTE) T2-weighted images (a) and axial gadolinium-enhanced fat-suppressed T1-weighted MR images (b) showing a right ureteral dilatation (arrow, a) upstream of an inflammatory mass (arrow b).

Coronal CT scanner image (c) performed one year after the acute episode of the fistula and inflammatory mass shows a dilated right ureter related to the fibrous sequelae of the fistula (arrowhead, c).

Figures 10 a, b, and c

Coronal fat-suppressed gadolinium-enhanced T1-weighted MRE image (a) showing a thrombus in the right iliac vein extending upwards to the inferior vena cava (arrow) in a 25-year-old patient with a flare up of colonic Crohn's disease. In the same patient, a coronal single shot fast spin echo (HASTE)T2-weighted MR image (b) and coronal abdominopelvic CT (c) shows irregularity along the articular margins of the sacroiliac joint with subchondral sclerosis and edema, consistent with ankylosing spondylitis (arrows).

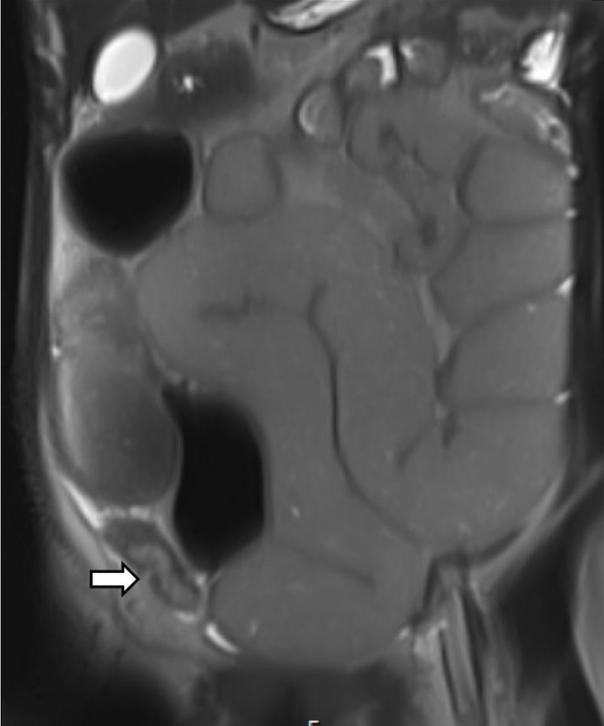
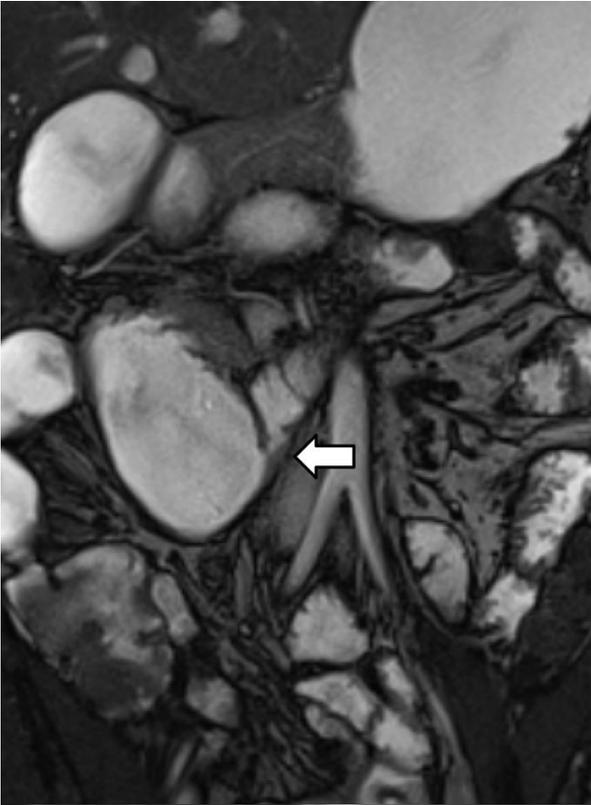
Figures 11 a and b

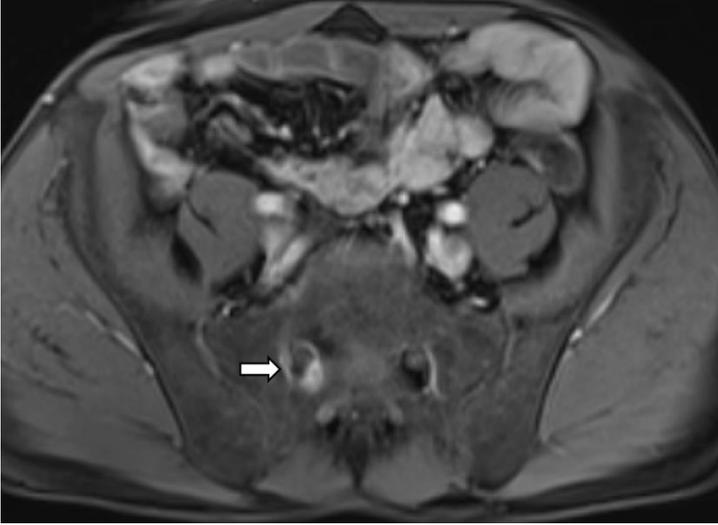
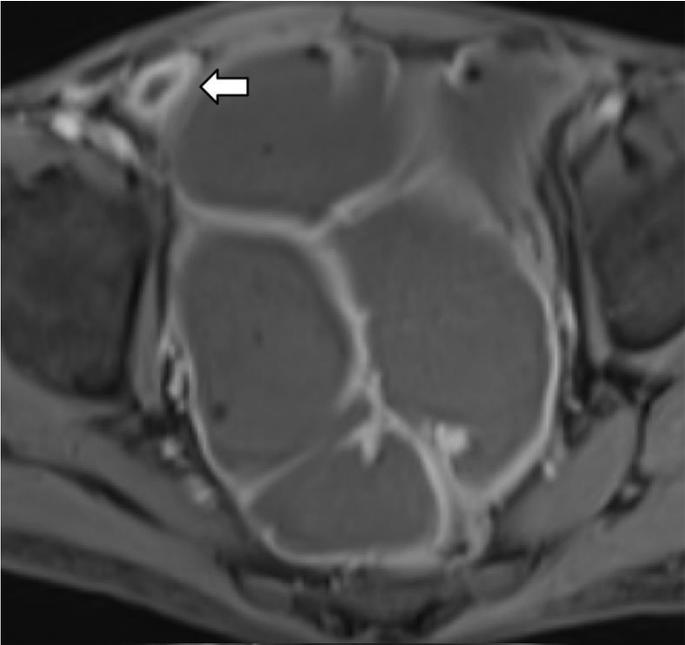
Axial single shot fast spin echo (HASTE) T2-weighted MRE image (a) showing a somewhat irregular discrete dilatation of the intrahepatic bile ducts in a 21-year-old male patient with Crohn's disease (arrow). Further cholangic MRI (b) depicts findings consistent with primary sclerosing cholangitis that was subsequently confirmed, including alternate small stenoses and dilatations of the intrahepatic bile duct (arrows, b) as well as a narrow benign stenosis of the common bile duct (arrowhead).

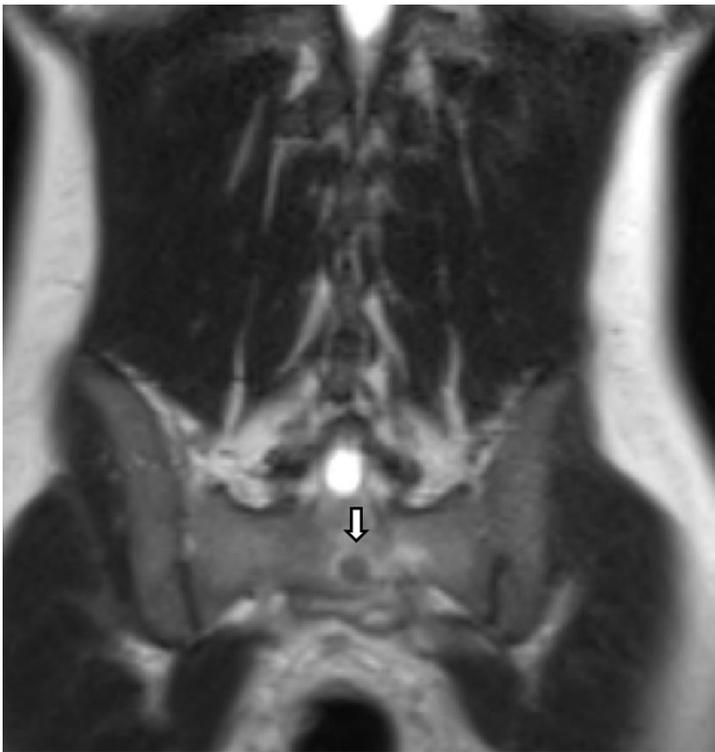
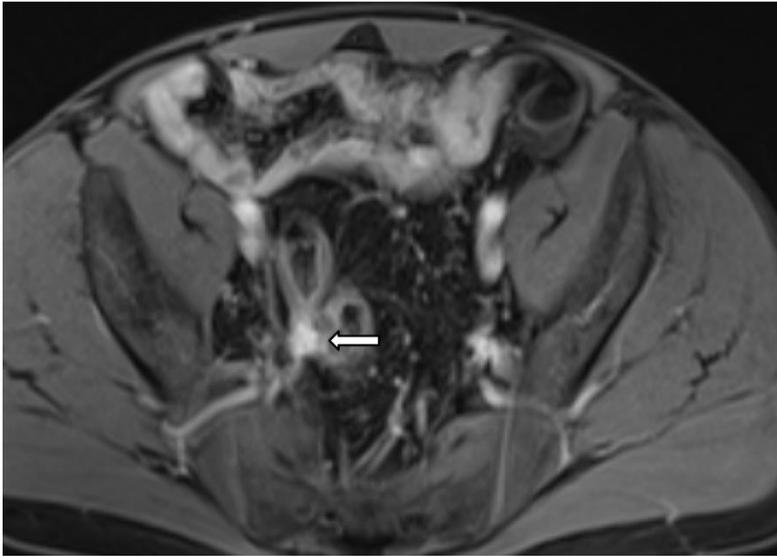
Figure 12

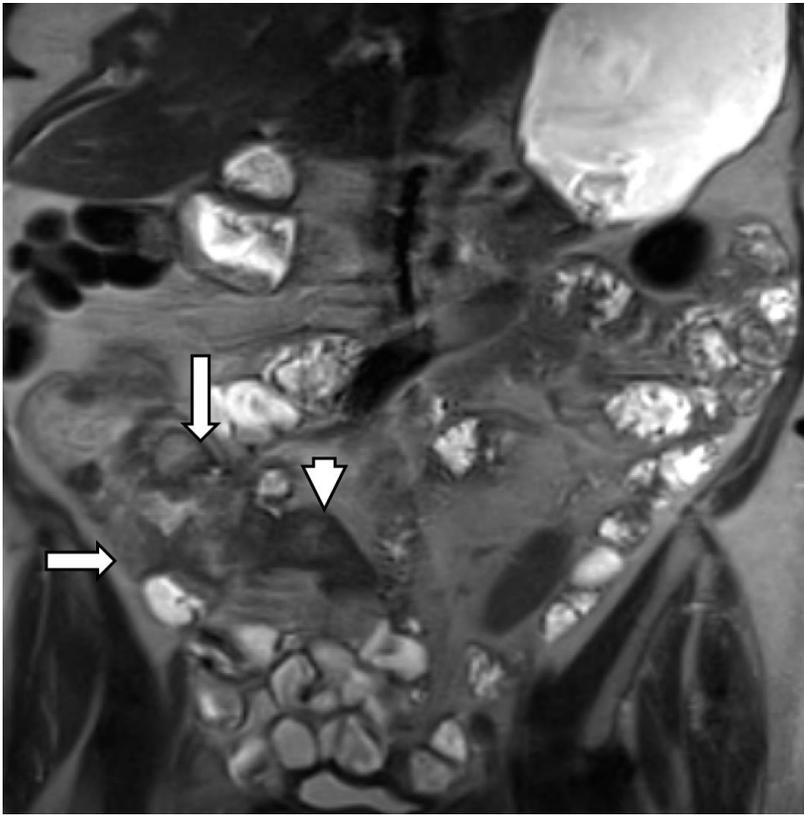
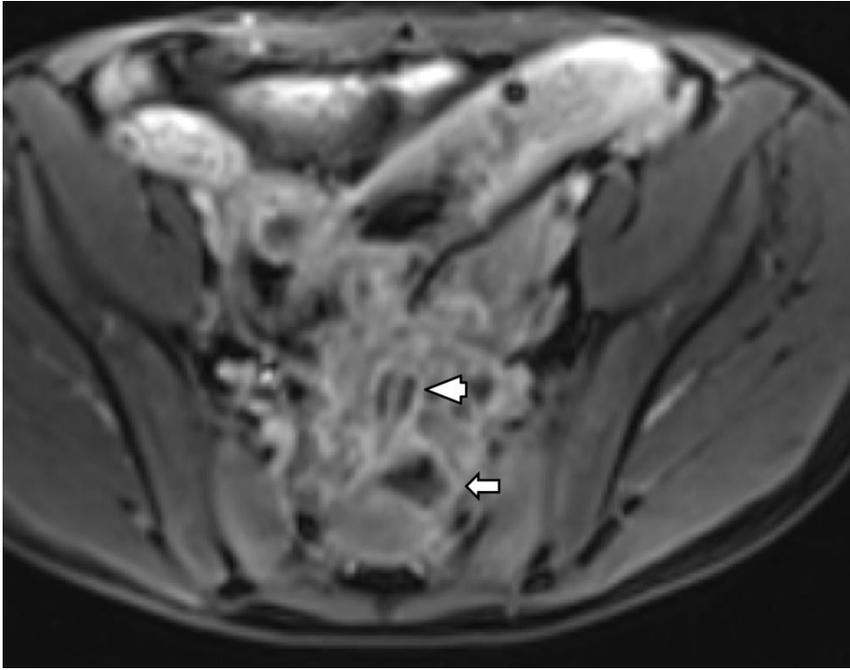
Axial fat-suppressed gadolinium-enhanced MR image showing multiple abscesses and marked granuloma enhancement in the setting of hidradenitis associated with Crohn's disease (arrow). The bilaterality of features and the anterior and posterior involvement of the inferior part of the perineum point to hidradenitis.

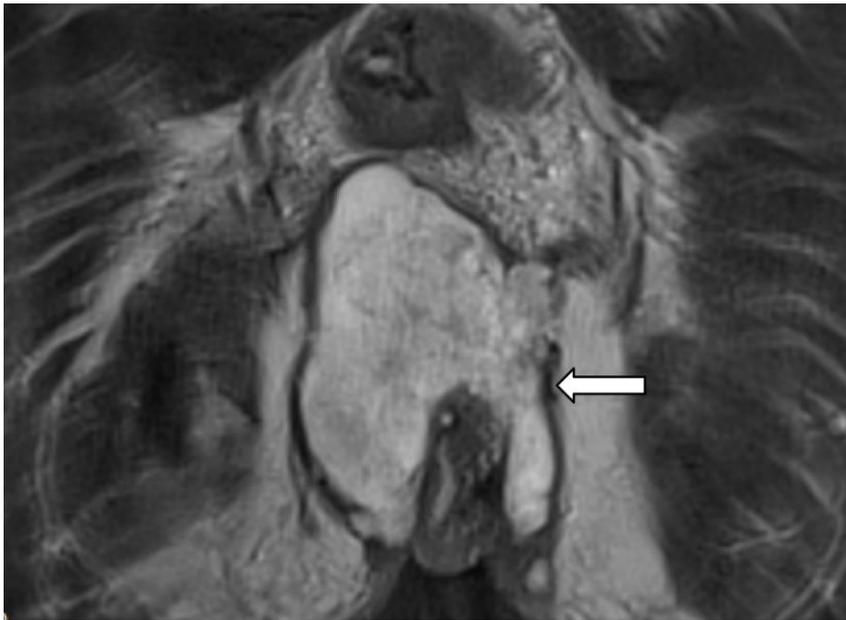
FIGURES

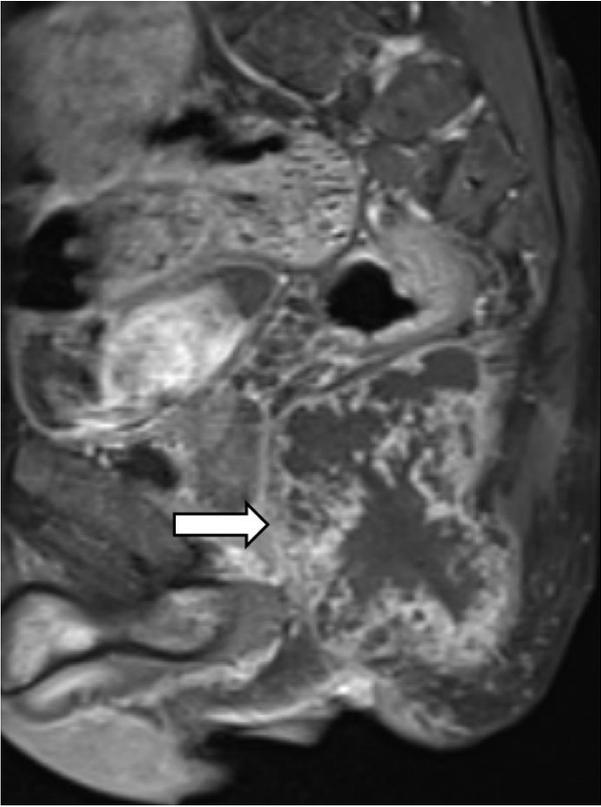


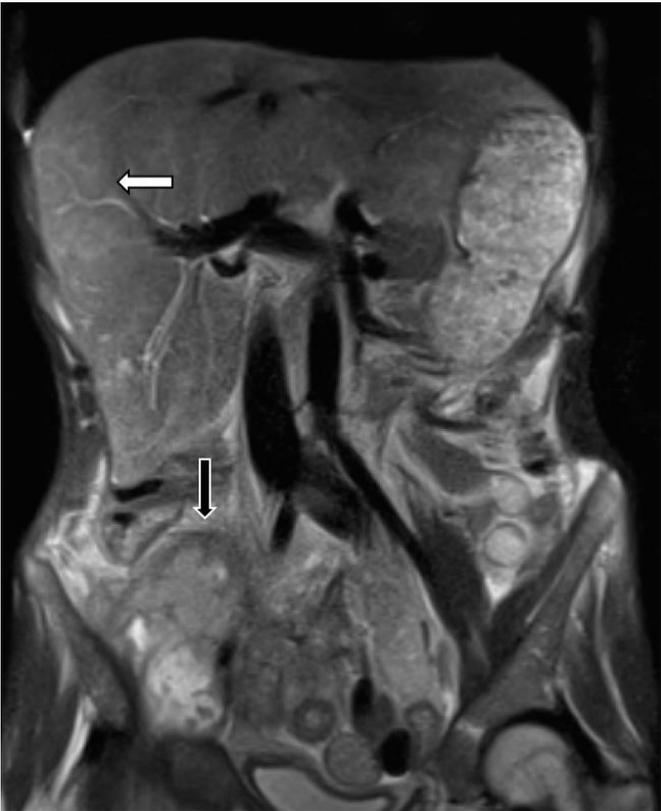


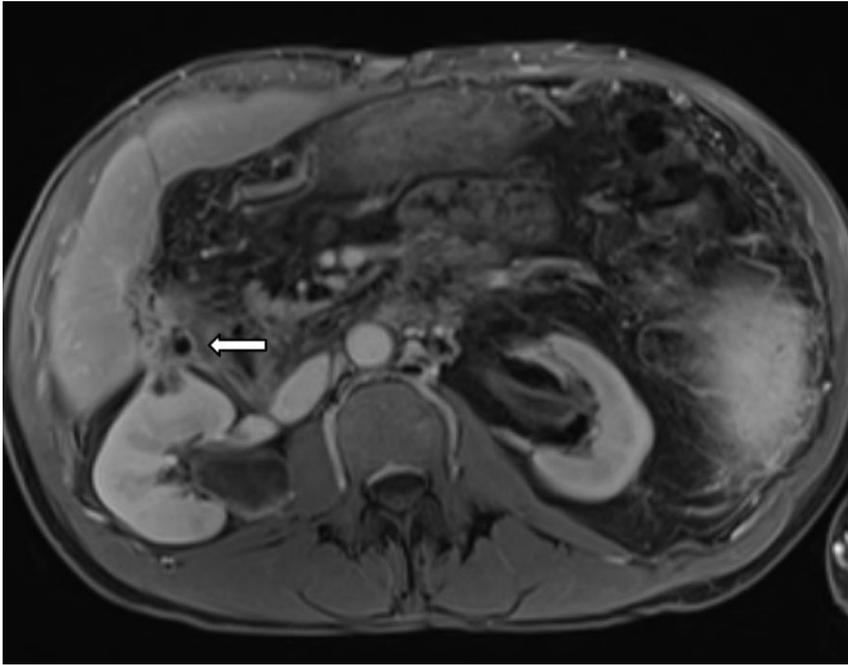


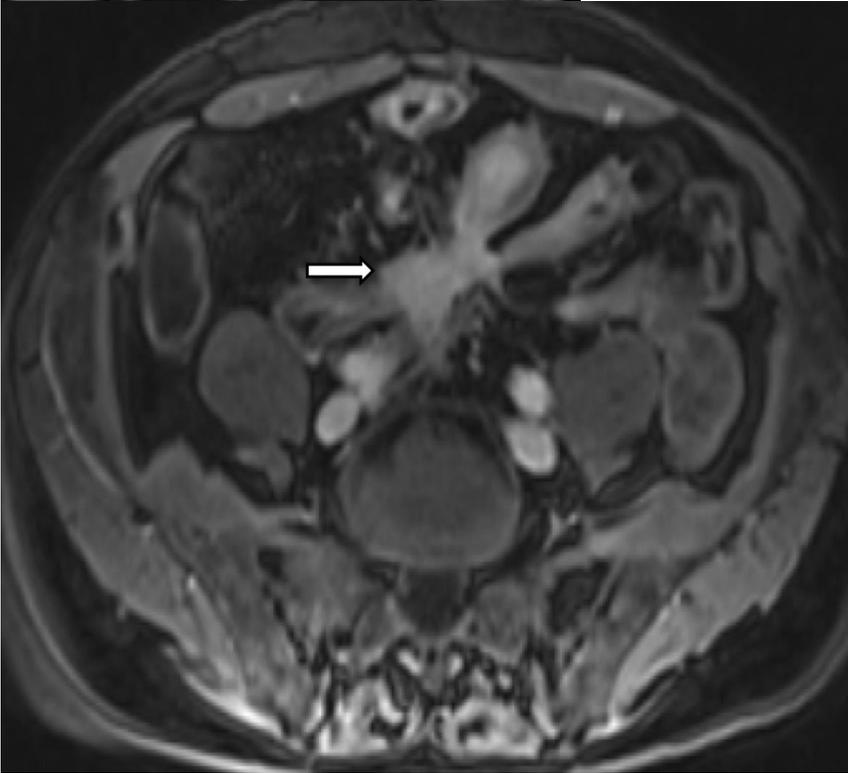
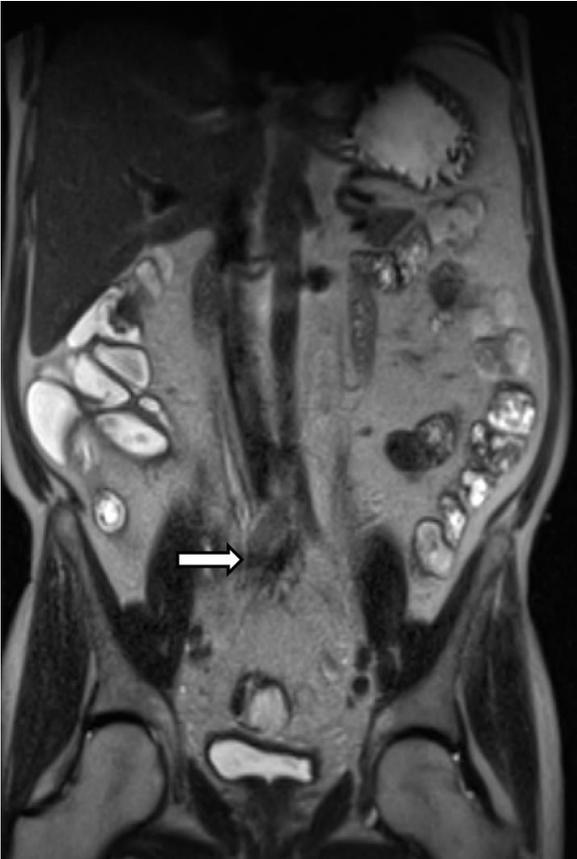






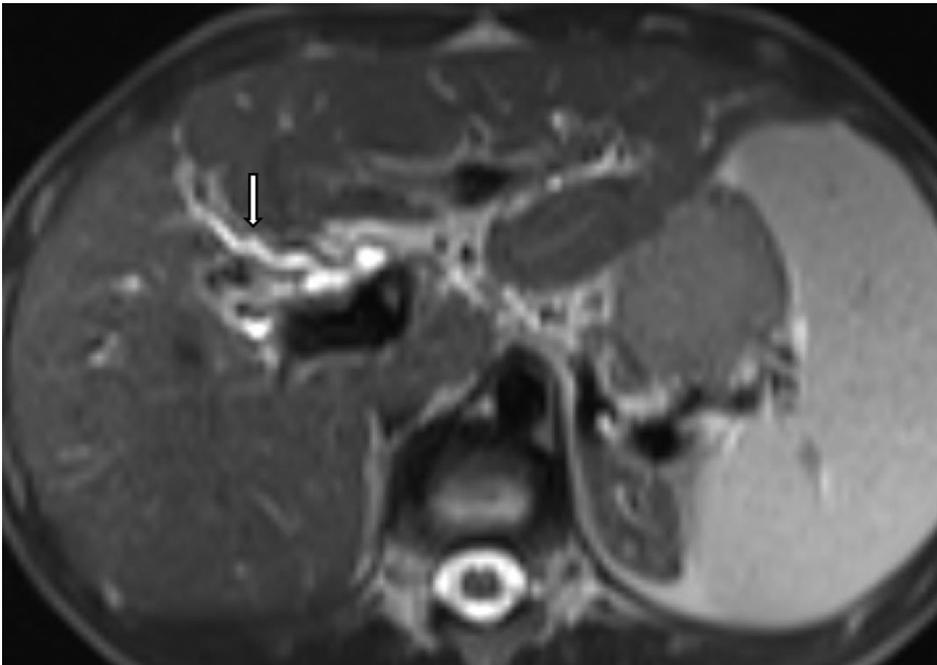


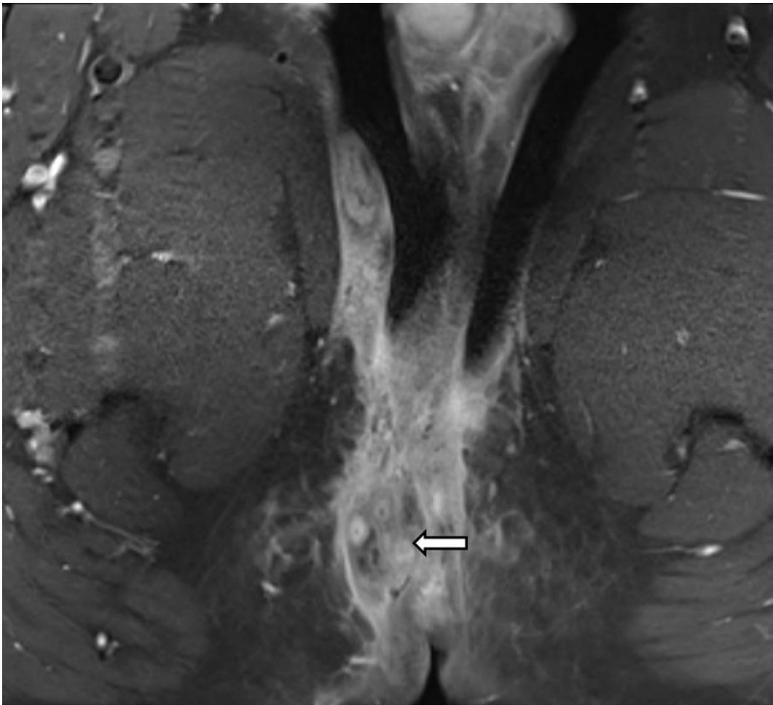












HIGHLIGHTS

- **Unusual sites of involvement**
 - Although the ileum is the most common site of involvement in CD, other less common sites have been described, such as the stomach, the duodenum, the proximal small bowel, Meckel's diverticulum, and the appendix.
- **Unusual types of complications**
 - Enteric
Rare fistulas may occur such as enterocutaneous, sigmoidovaginal and enterovesicular fistulas.
Patients with longstanding Crohn disease have an increased risk of developing small bowel and anal adenocarcinoma, including mucinous adenocarcinoma.
 - Extra enteric
Unusual extra enteric complications include sepsis-related hepatic sinusoidal dilatation, avascular necrosis of the femoral head, non-bacterial osteomyelitis, acalculous ureteral inflammatory entrapment, thromboembolic events, peritoneal inclusion cysts.
- **Unusual associated diseases**
 - Unusual associated disease include PSC and its complications, granulomatous Crohn's hepatitis, PSC–autoimmune hepatitis overlap syndrome, ankylosing spondylitis, osteomalacia, hypertrophic osteoarthropathy, pancreatitis, hidradenitis suppurativa
- **Incidental findings**

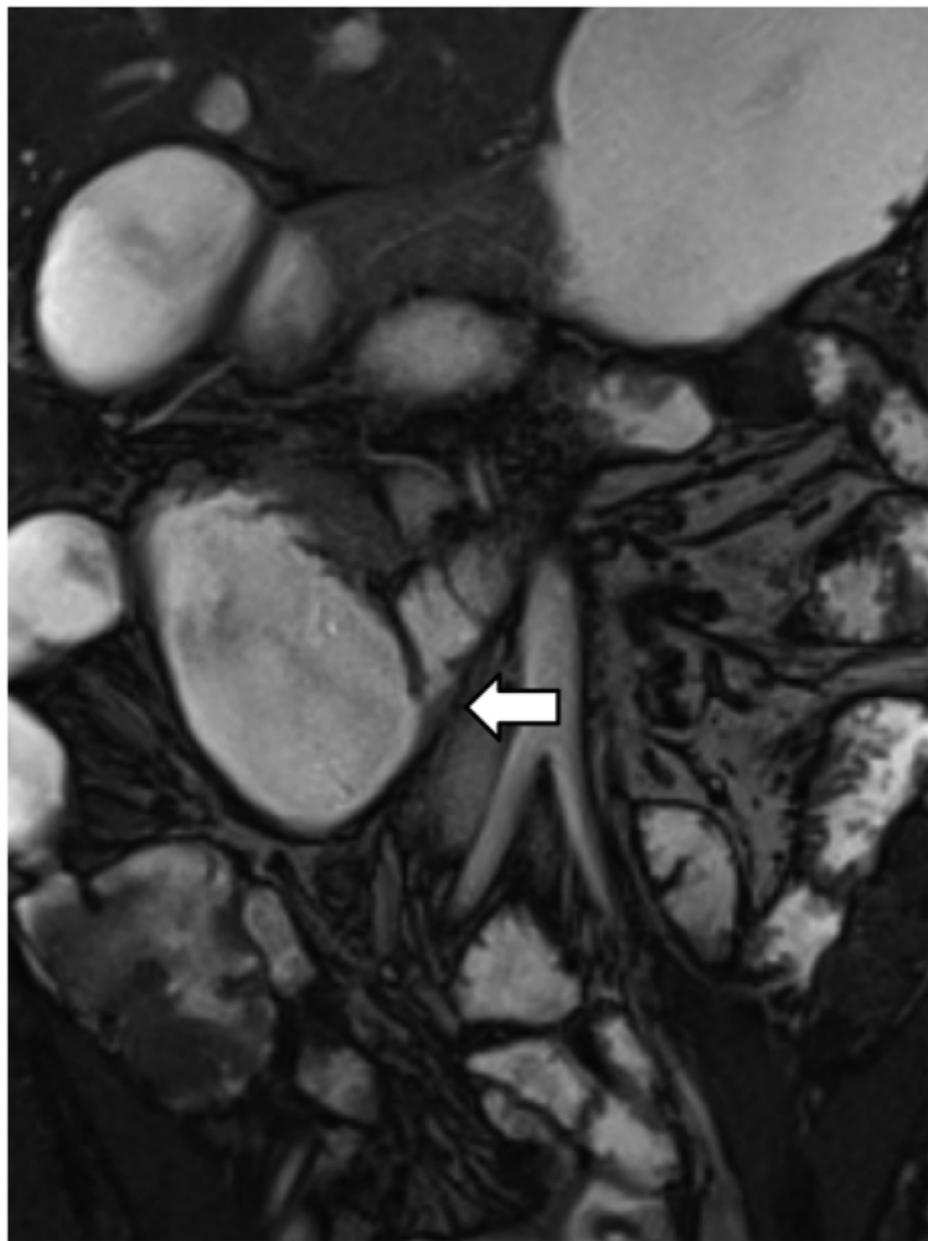
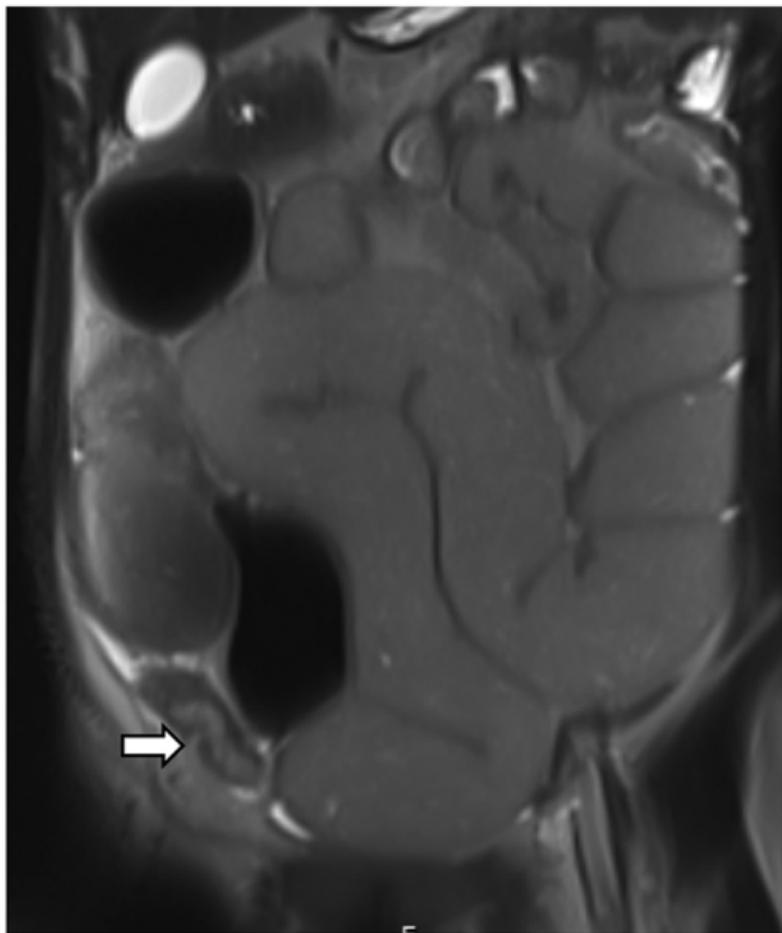


Figure 1

A



B

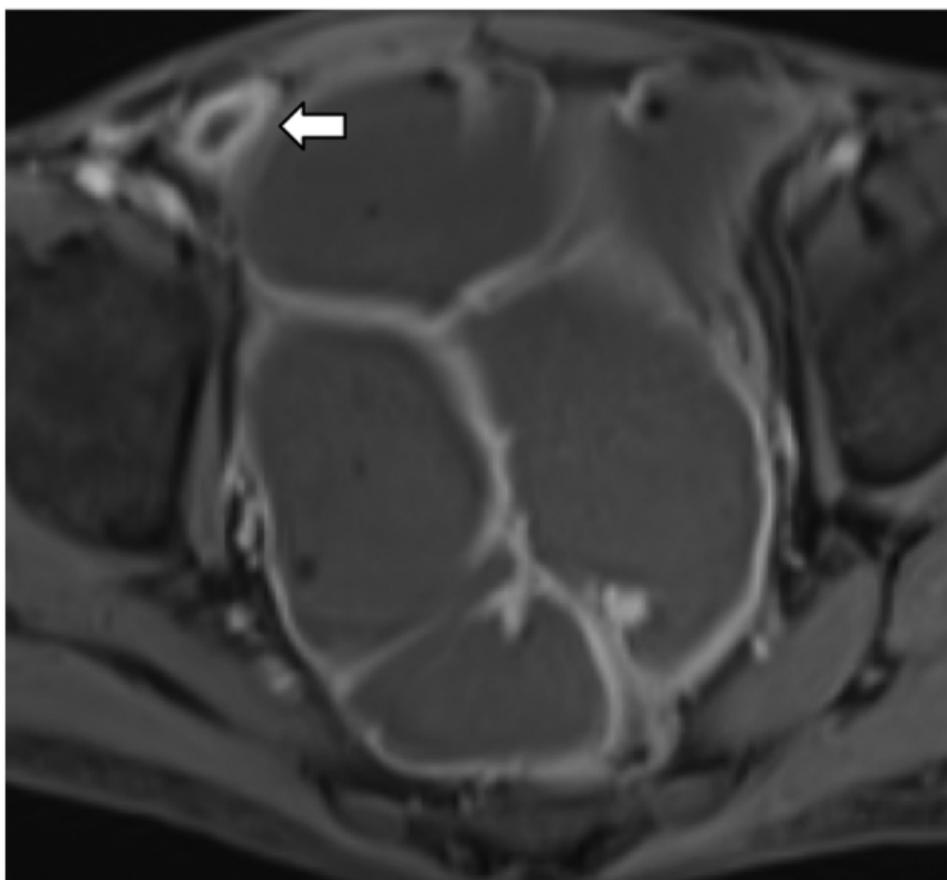
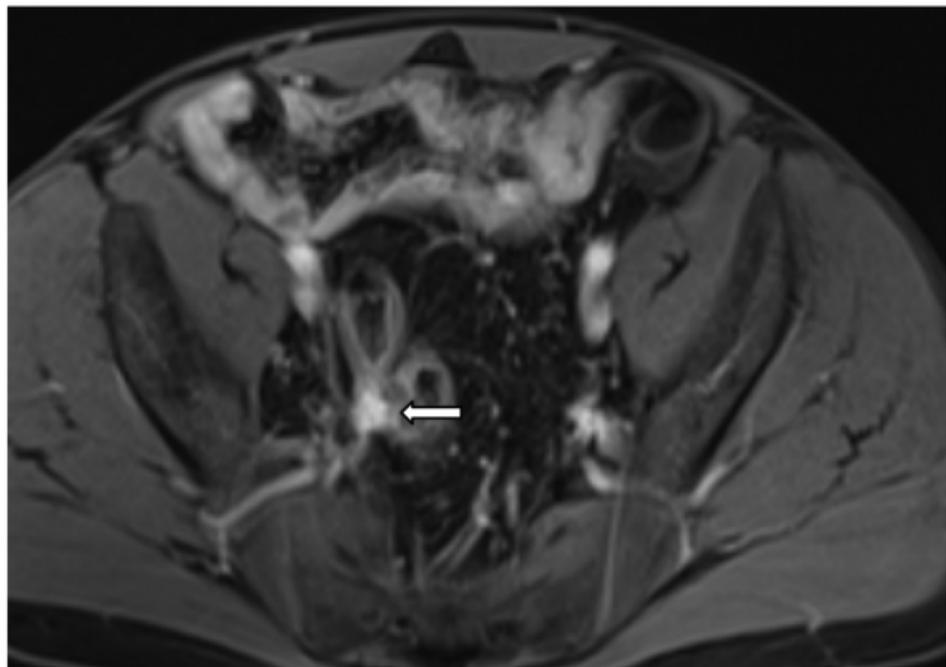


Figure 2

A



B

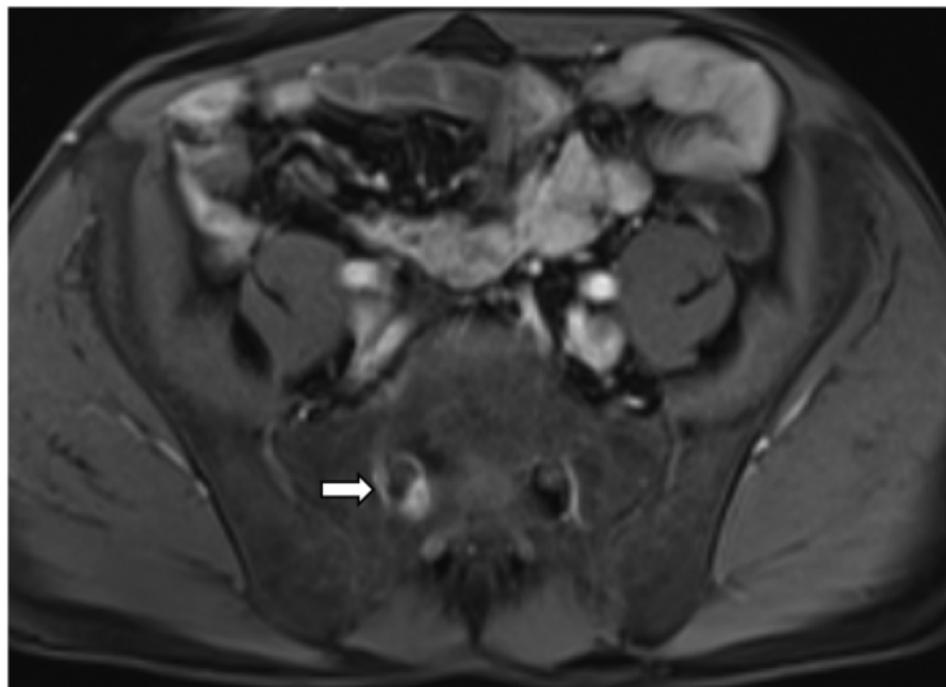
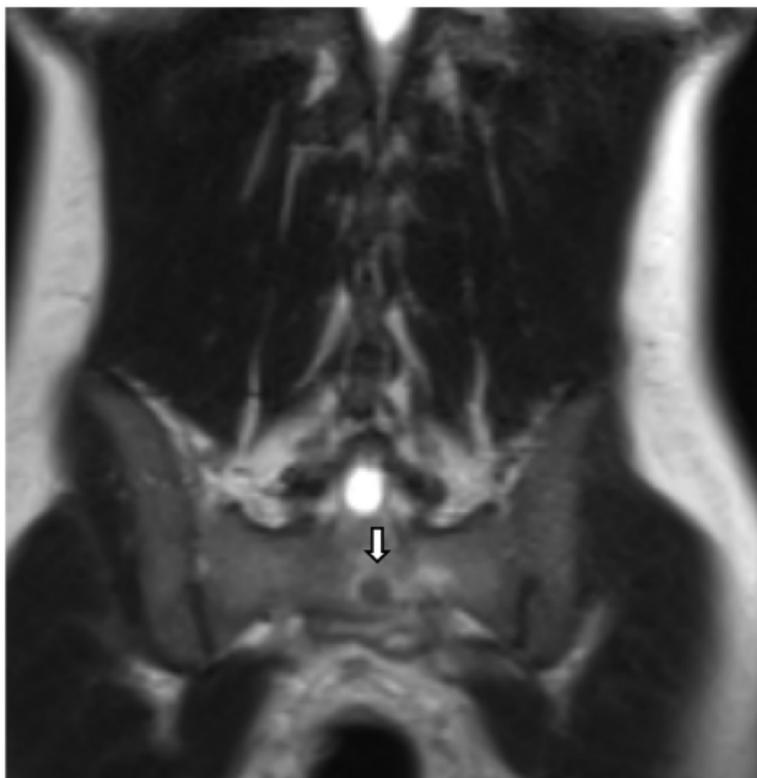


Figure 3

A



B

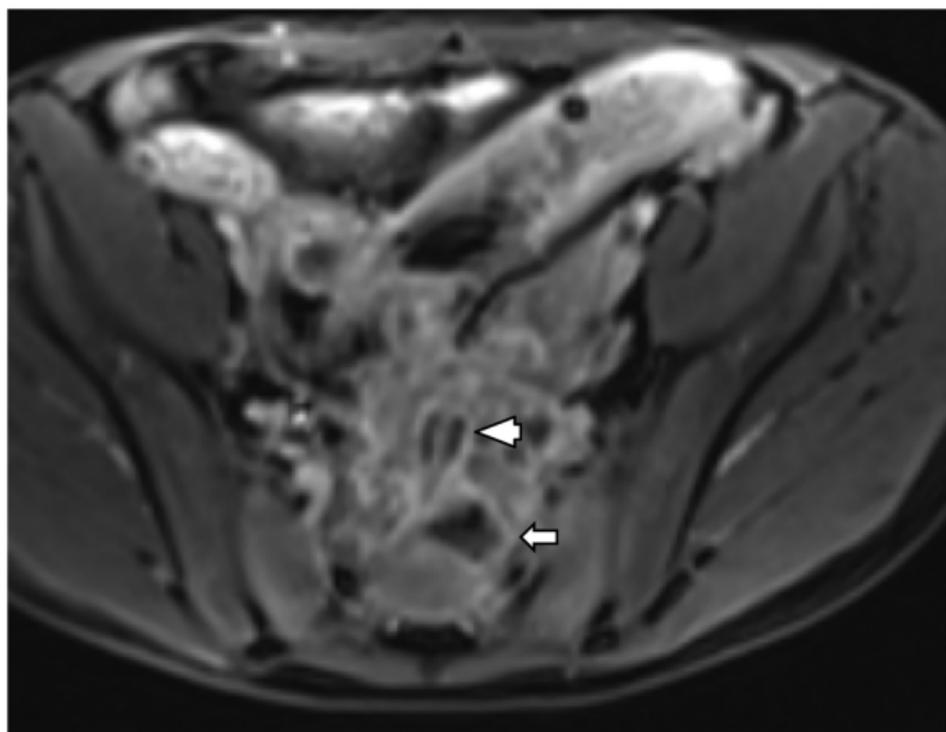


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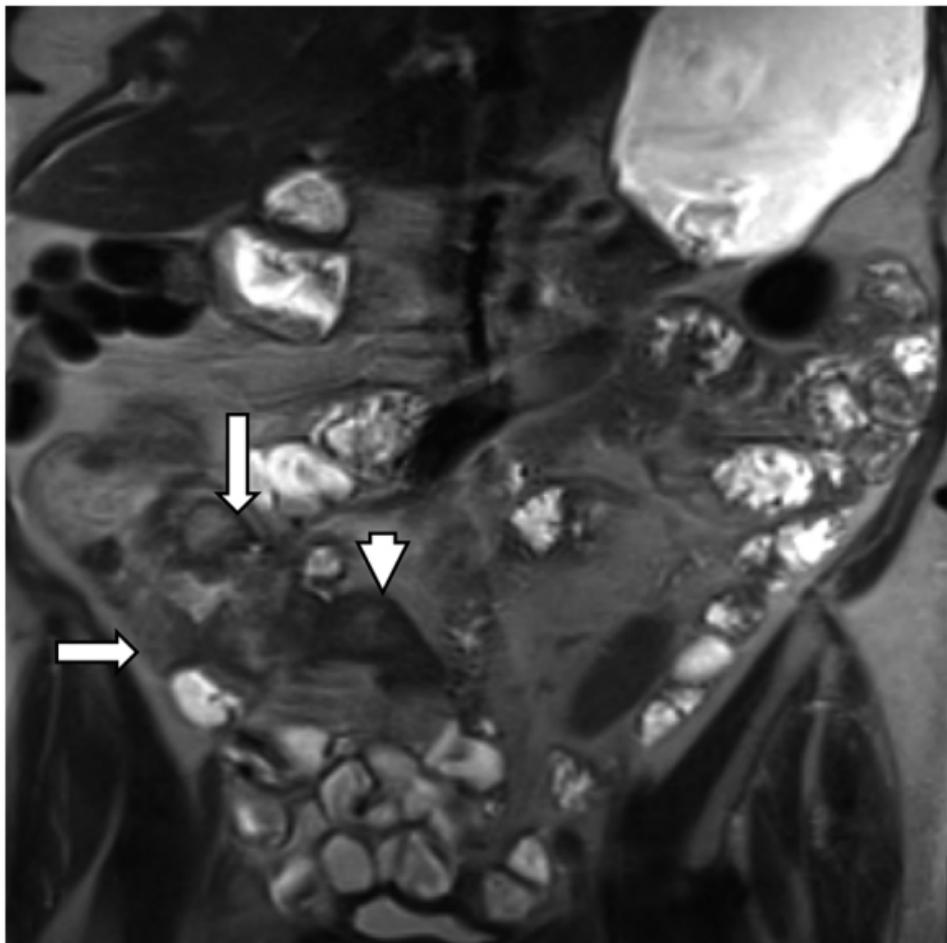
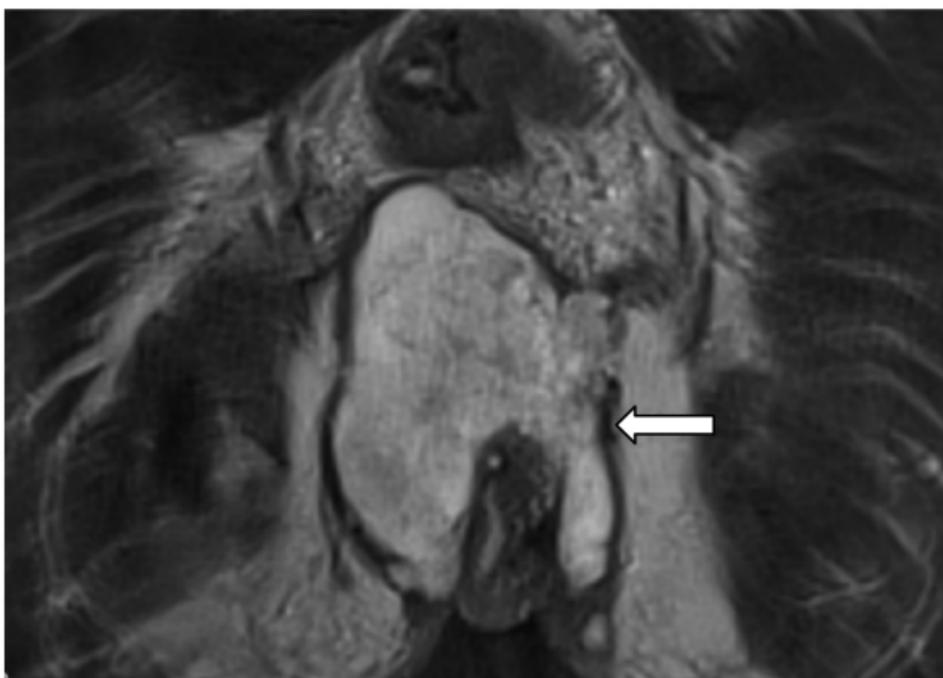


Figure 5

A



B



C

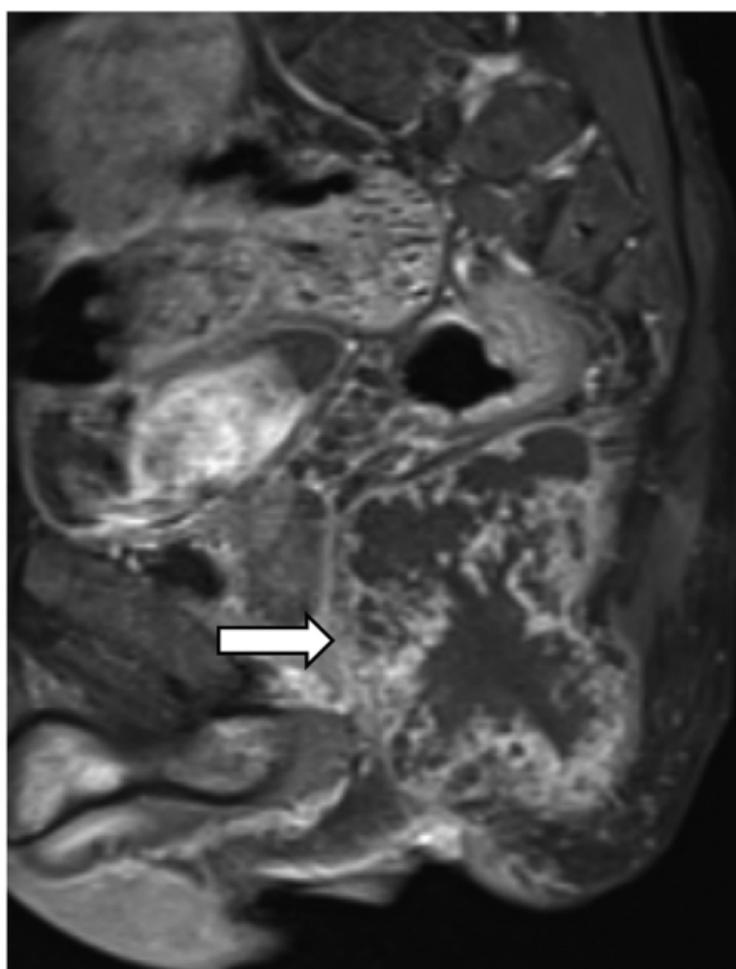


Figure 6

A



B



C

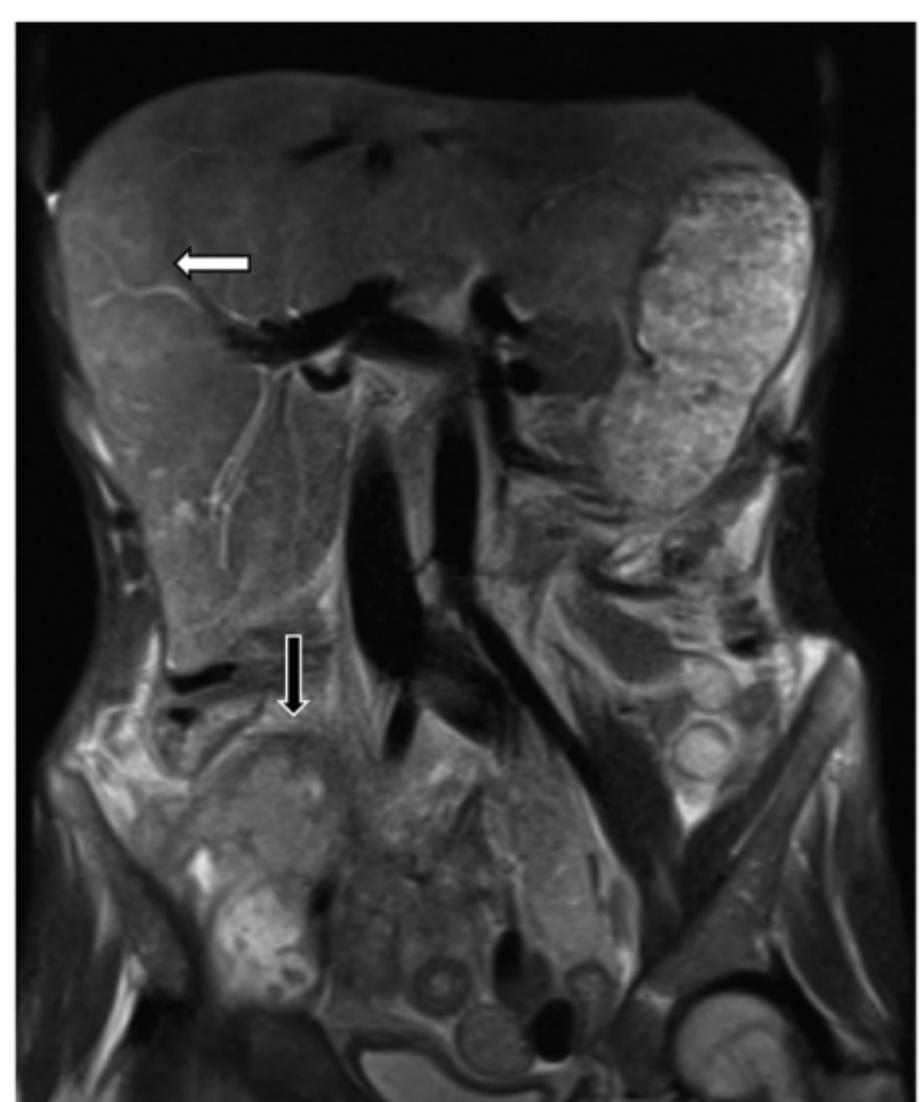
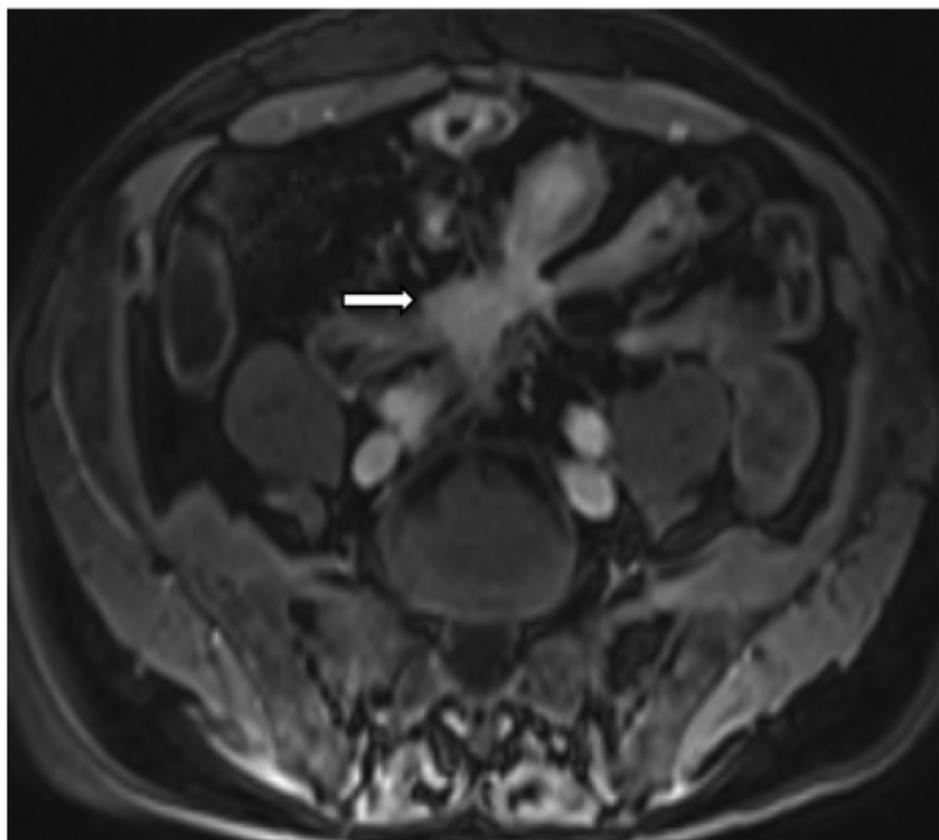


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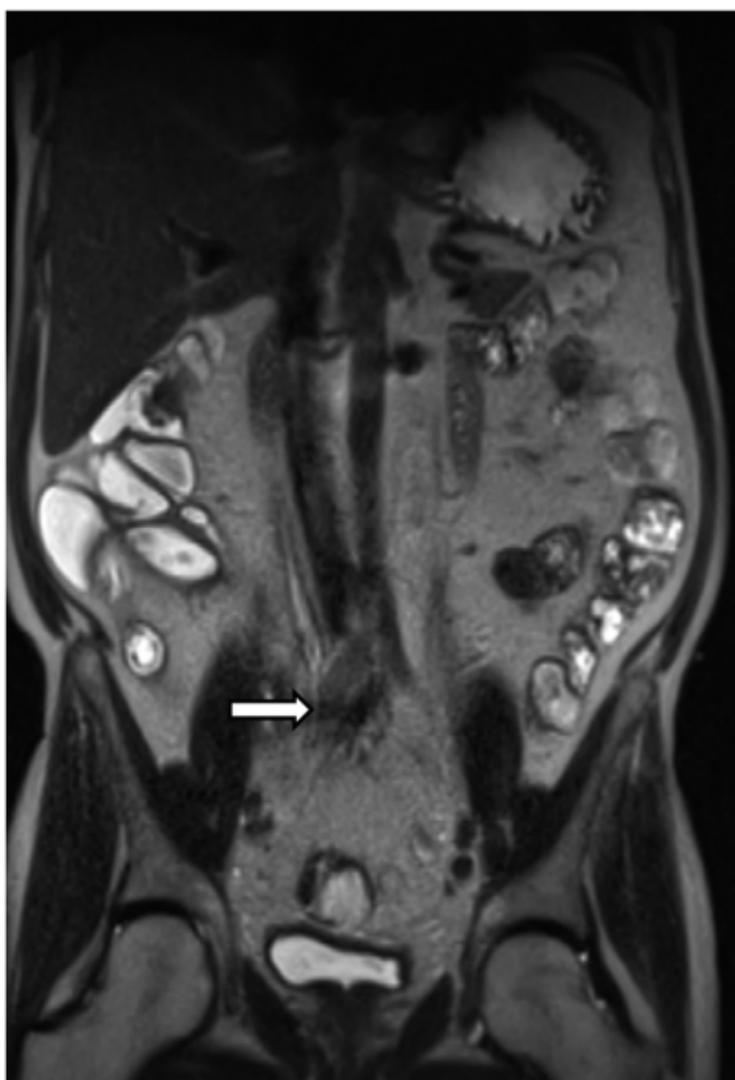


Figure 8

A



B



C

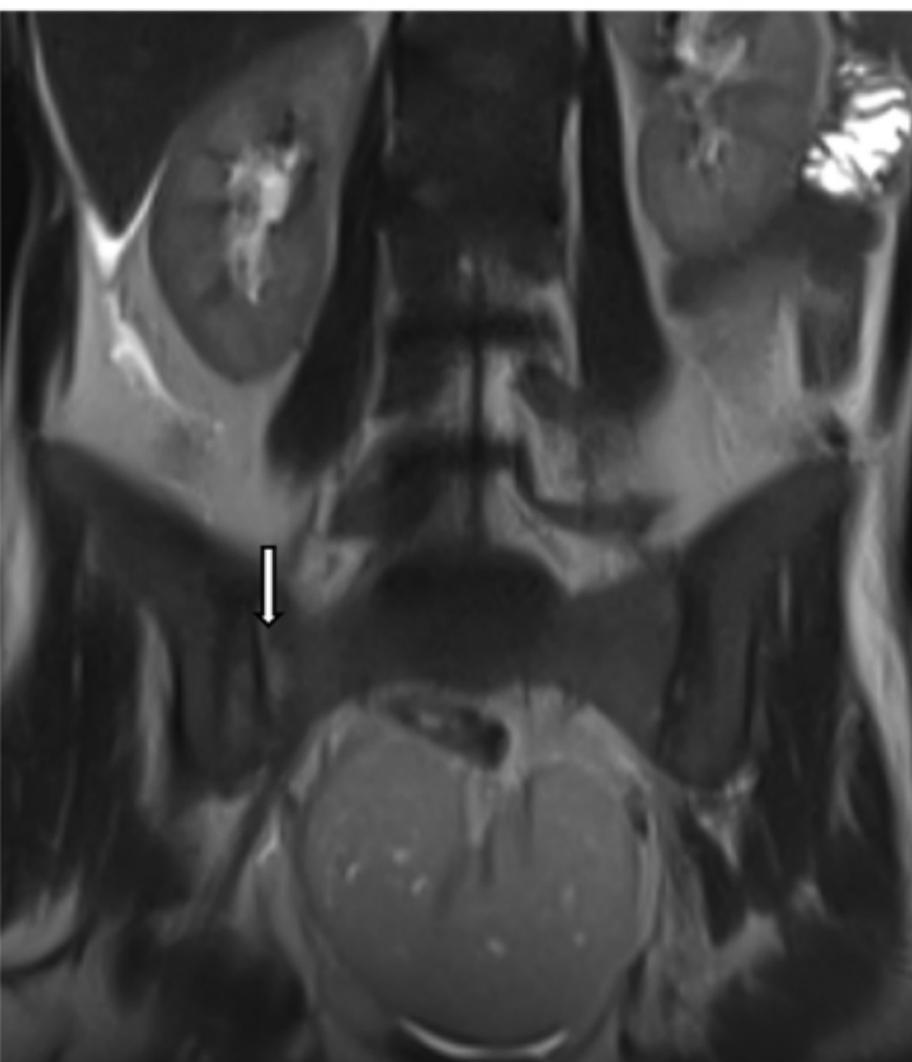


Figure 9

A



B

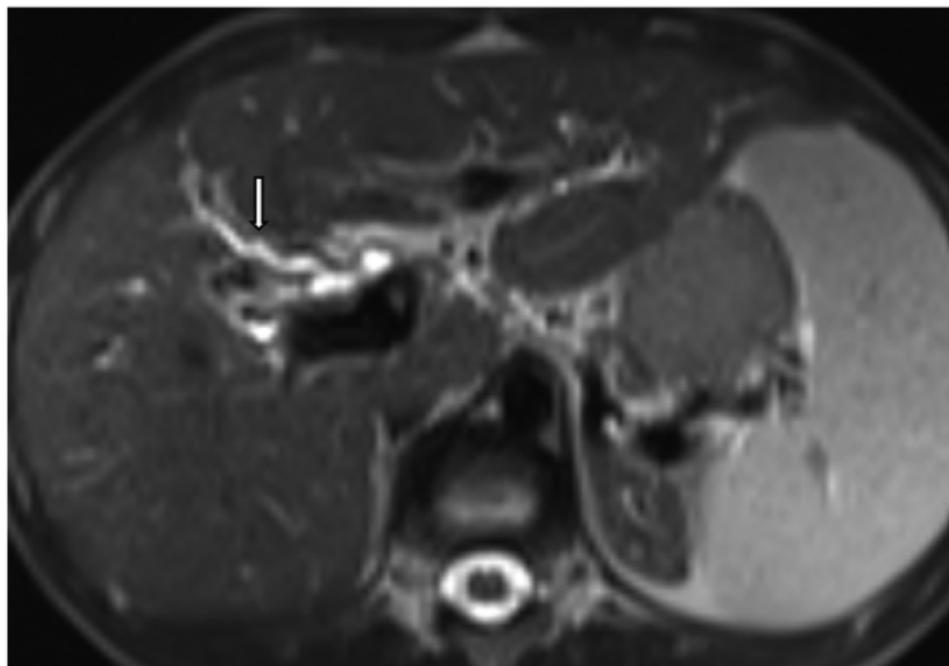


C



Figure 10

A



B

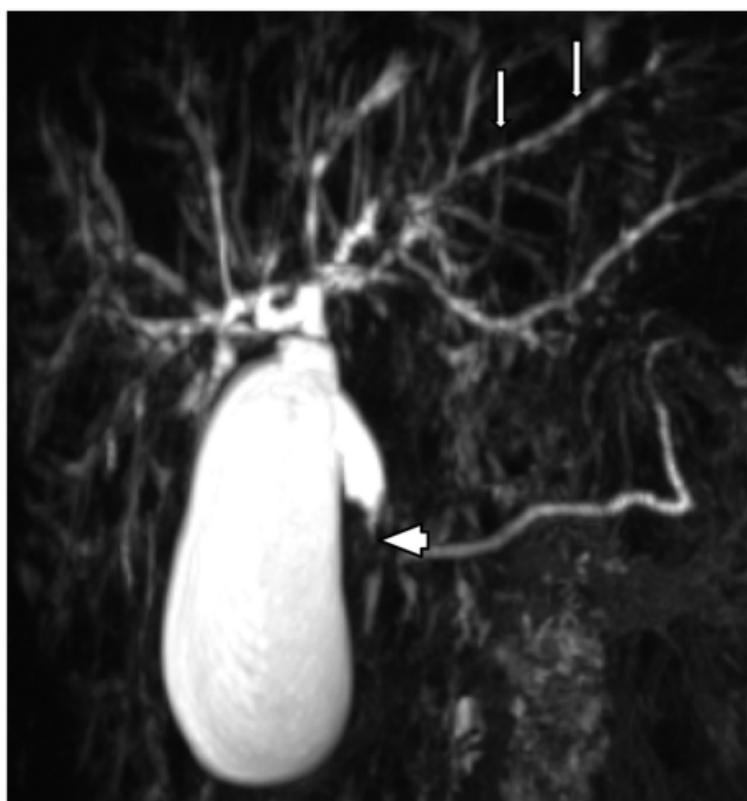


Figure 11

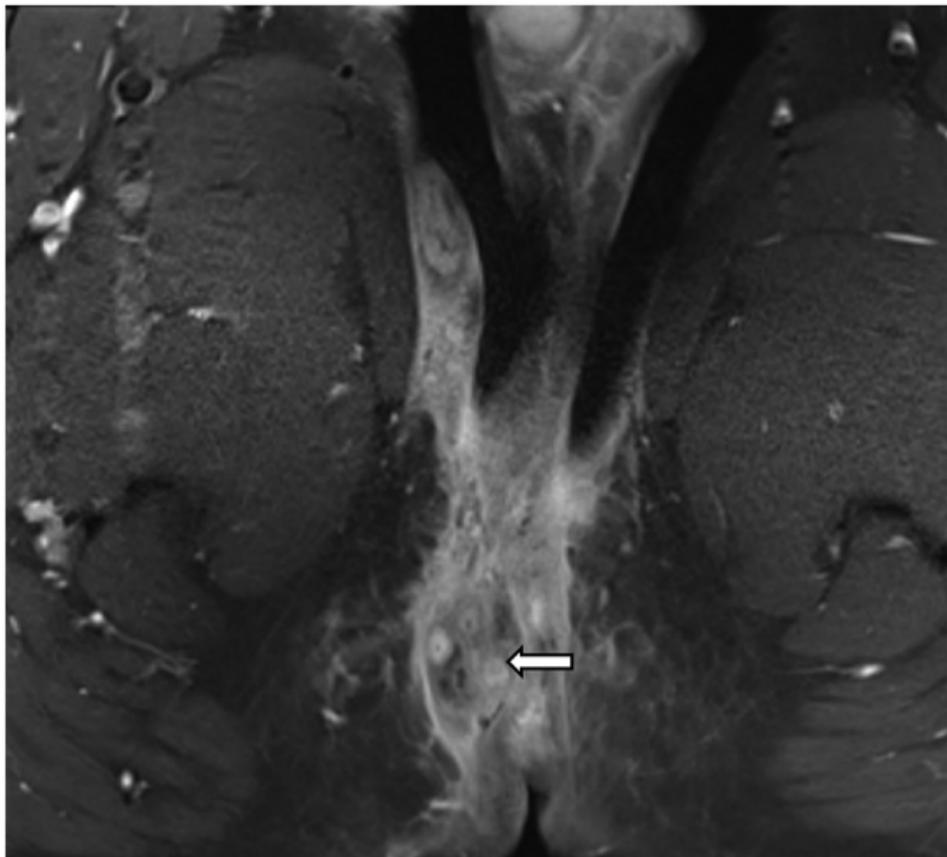


Figure 12