**Case report**

# A patient with systemic lupus erythematosus who developed massive small intestinal hemorrhaging during treatment for chronic lupus peritonitis

Shin-ya Kawashiri[1], Ayako Nishino[1], Eijun Sueyoshi[2], Akitomo Okada[1], Tomohiro Koga[1], Satoshi Yamasaki[1], Hideki Nakamura[1], Tomoki Origuchi[3], and Atsushi Kawakami[1]

[1]Unit of Translational Medicine, Department of Immunology and Rheumatology, Graduate School of Biomedical Sciences, Nagasaki University, 1-7-1 Sakamoto, Nagasaki 852-8501, Japan

[2]Department of Radiological Sciences, Nagasaki University Graduate School of Biomedical Sciences

[3]Nagasaki University School of Health Sciences

*Address for correspondence and reprint requests:*

Shin-ya Kawashiri, M.D., Ph.D.

Unit of Translational Medicine,

Department of Immunology and Rheumatology,

Graduate School of Biomedical Sciences, Nagasaki University,

1-7-1 Sakamoto, Nagasaki 852-8501, Japan

Phone: + 81-95-819-7266

Fax: 81-95-849-7270

E-mail: shin-ya@hotmail.co.jp

**Abstract**

A 50-year-old Japanese woman, a patient with systemic lupus erythematosus (SLE) complicated with chronic lupus peritonitis, developed massive small intestinal hemorrhaging. She was treated with intravenous pulse of methylprednisolone, intravenous pulse of cyclophosphamide (IVCY), and immunoabsorption, but the peritonitis was refractory to these treatments. Subsequently, she was treated with oral corticosteroid and tacrolimus, and received IVCY monthly, but she developed massive small intestinal hemorrhaging 1 year after. Abdominal angiography detected multiple bleeding sites from the jejunal and ileal arteries. After transarterial embolization treatment, the melena disappeared. The pathology of this case appeared to be lupus mesenteric vasculitis.

**Key words**

Systemic lupus erythematosus, Lupus peritonitis, Small intestinal hemorrhage, Lupus mesenteric vasculitis

## Introduction

Systemic lupus erythematosus (SLE) is an extraordinarily complex autoimmune disease that affects various organs. Ascites, which is found in about 10% of patients, is a common complication of SLE. However, chronic lupus peritonitis is a rare complication in patients with SLE and is reported to be difficult to control [1–4]. Patients with SLE sometimes develop small intestinal hemorrhaging as the result of a variety of causes, including enteritis, vasculitis, drug side effects, and infection. Lupus mesenteric vasculitis (LMV) is one of the most serious causes of such hemorrhaging [5]. We describe herein a patient with SLE complicated with chronic lupus peritonitis who developed massive small intestinal hemorrhaging that appeared to have been caused by LMV.

**Case report**

The patient was a 50-year-old Japanese woman. She had no history of abortion. In November 2008, she complained of an abdominal protuberance and dyspnea. Massive ascites and mild pleural effusion were detected. Laboratory data were: white cell count 6,000/mm3 (lymphocytes 14.7%), hemoglobin 9.2 g/dl, and platelet count 188,000/mm3. C-reactive protein (CRP) was elevated to 3.71 mg/dl. Antinuclear antibodies (ANAs) were positive (1:640, homogeneous and speckled pattern). The titers of anti-double stranded (ds) DNA antibodies, anti-single stranded (ss) DNA antibodies, and anti-Sm antibodies were elevated to >400 IU/ml (normal range [NR]<12), >200 AU/ml (NR <25), and 19.3 U/ml, respectively. C3, C4, and CH50 were decreased to 26 mg/dl (NR 86–60), 4 mg/dl (NR 17–45), and <12 U/ml (NR 25–48), respectively, and immune complex (anti-C1q) was elevated to 19.3μg /ml (NR<3). Findings for proteinuria and urinary occult blood were positive. In urinary sediment, there were 51–100 red blood cells per high-power field (HPF), and 1–2 granular casts per HPF. Peritoneal and pleural effusions were exudative, and cytological diagnosis was negative. In the peritoneal effusion, ANA was positive (1:640, homogeneous pattern), and the levels of C3, C4, and anti-ds DNA antibodies were 5.9 mg/dl, <1.4 mg/dl, and >400 IU/ml, respectively.

The patient was diagnosed with SLE based on serositis, renal disorder, and positivity for anti-ds DNA antibodies, anti-Sm antibodies, and ANA. The SLE disease activity index (SLEDAI) [6] was 22. Additionally, she was diagnosed with secondary anti-phospholipid antibody syndrome (APS) based on positivity for anti-cardiolipin-β2 glycoprotein I complex antibodies (12.1 U/ml) and lupus anticoagulant (1.66), and multiple small infarction lesions on brain magnetic resonance imaging (MRI). Figure 1 shows the clinical course. In May 2009, SLEDAI decreased to 4 following treatment with intravenous pulse of methylprednisolone (mPSL; 1,000 mg/day, 3 days), intravenous pulse of cyclophosphamide (IVCY; 1,000 mg per body), and immunoabsorption. However, the ascites was refractory. The titers of anti-ds DNA antibodies in the serum and peritoneal effusion remained slightly higher than baseline levels after this treatment. Treatment with oral corticosteroid (prednisolone [PSL]) and tacrolimus (TAC) was then instituted, and IVCY was continued monthly, and the ascites was drained once a month.

In November 2009, the patient experienced discomfort in the upper abdomen. On 10 December 2009, she was urgently admitted to our hospital because of massive melena and hemorrhagic shock. Laboratory data showed that hemoglobin had decreased to 6.2 g/dl. Anti-ds DNA antibodies and immune complex were negative. Cytomegalovirus antigen (pp65, antigenemia method) was negative. The visible gastrointestinal mucosa on upper and lower gastrointestinal endoscopy was normal. Enhanced abdominal computed tomography (CT) detected hypertrophy of the small intestinal wall with contrast enhancement and leakage of contrast agents into the intestine (Fig. 2). Abdominal angiography (Fig. 3) detected multiple extravasations from pseudo-microaneurysms of the jejunal and ileal arteries. After treatment with transarterial embolization (TAE), the melena disappeared. Massive blood transfusion and intravenous mPSL pulse were administered at once. The patient was subsequently treated with IVCY

monthly. PSL and TAC were resumed as maintenance therapy. During follow-up in the past 15 months, the patient has had no further recurrence of SLE disease activity (SLEDAI: 0) and the ascites has disappeared.

**Discussion**

Lupus peritonitis is classified into acute type and chronic type. Acute lupus peritonitis occurs with gastrointestinal symptoms such as abdominal pain, vomiting, and diarrhea, and treatment with corticosteroids often produces rapid improvement [7, 8]. On the other hand, chronic lupus peritonitis is painless and responds poorly to corticosteroid therapy [1–4]. In previous reports [1–4], treatment of chronic lupus peritonitis involved a moderate or high dose of corticosteroids and concomitant use of an immunosuppressant such as cyclophosphamide or azathioprine. In the present patient, peritoneal effusion was persistent, regardless of aggressive treatment with intravenous pulses of mPSL and IVCY, and immunoabsorption. Her peritonitis was very difficult to control compared to that in previous cases [1–4], and there was no previous report of severe gastrointestinal manifestations developing in a patient with chronic lupus peritonitis. In our patient, anti-ds DNA antibodies and ANA were detected in the peritoneal effusion, and, interestingly, the levels were higher than those in serum. Moreover, the titers of anti-ds DNA antibodies in the peritoneal effusion were remarkably elevated, and they had decreased after treatment. Anti-DNA antibodies and ANA have been reported to be detected in peritoneal effusions, and they may be related to immunological activity in the peritoneum [1, 3]. However, no previous study investigated immunological findings in both serum and peritoneal effusion in patients with chronic lupus peritonitis receiving long-term treatment of. Pathology findings have shown immunoglobulin and complement in vessel walls in the peritoneum [9, 10]. Therefore, it is suggested that the immunological findings in peritoneal effusions reflect peritoneal vasculitis activity.

LMV was the main reported cause of acute abdomen in patients with SLE, in whom LMV develops insidiously [5]. Severe LMV can result in life-threatening complications, such as extensive gastrointestinal hemorrhaging, bowel perforation, and bowel infarction. The main pathologic lesions in LMV occur in small vessels in the bowel wall. Variable symptoms are caused by ischemia that involves four different layers of the bowel wall, as follows: serosa— ascites; muscular—pseudo-obstruction, dilatation, fluid accumulation; submucosa—submucosal edema, pseudotumors; mucosa—hemorrhaging, ulceration, diarrhea [5]. It is suggested from our patient’s angiography findingsthat she had bleeding from multiple pseudo-microaneurysms that may have developed because of weakness of the vessel wall caused by vasculitis [11]. Additionally, extensive mucosal damage caused by lupus enteritis may have exacerbated the massive small intestinal hemorrhaging. APS might be associated with mesenteric ischemia; the microvasculopathy in LMV results in worsening cascades of vasculitis and thrombosis, which are associated with circulating antiphospholipid antibodies [5]. Immediate and aggressive anti-inflammatory immunosuppressive therapy for LMV must include intravenous pulses of mPSL and IVCY [5, 12]. However, in the present patient, the vasculitis might gradually progress despite the aggressive therapy with intravenous pulses of mPSL and IVCY, because this treatment is insufficient to halt such progress.

In summary, we have reported a rare case of massive small intestinal hemorrhaging developing during

treatment of refractory chronic lupus peritonitis in a patient with SLE. The pathology of this hemorrhaging appeared to be LMV.

**References**

[1] Ito H, Nanamiya W, Kuroda N, Inoue M, Sasaoka A, Chijiwa T, Nishiya K, Hashimoto K, Nakagawa O. Chronic lupus peritonitis with massive ascites at elderly onset: case report and review of the literature. Intern Med. 2002;41:1056–61.

[2] Corbella X, Mitjavila F, Campoy E, Saez A, Moga I, Vidaller A. Chronic ascites in late onset systemic lupus erythematosus with antiphospholipid antibodies. J Rheumatol. 1994;2:1141–3.

[3] Kaklamanis P, Vayopoulos G, Stamatelos G, Dadinas G, Tsokos GC. Chronic lupus peritonitis with ascites. Ann Rheum Dis. 1991;50:176–7.

[4] Mier A, Weir W. Ascites in systemic lupus erythematosus. Ann Rheum Dis. 1985;44:778–9.

[5] Ju JH, Min JK, Jung CK, Oh SN, Kwok SK, Kang KY, Park KS, Ko HJ, Yoon CH, Park SH, Cho CS, Kim HY. Lupus mesenteric vasculitis can cause acute abdominal pain in patients with SLE. Nat Rev Rheumatol. 2009;5:273–81.

[6] Bombardier C, Gladman DD, Urowitz MB, Caron D, Chang CH. Derivationof the SLEDAI. A disease activity index for lupus patients. The Committee on Prognosis Studies in SLE. Arthritis Rheum. 1992;35:630–40.

[7] Uzu T, Chikamori Y, Yamato M, Iwatani H, Kakihara M, Yamauchi A. Acute lupus peritonitis during treatment of lupus nephritis: successful treatment with methylprednisolone pulse therapy. Nephron. 2000;86:511–2.

[8] Weinstein PJ, Noyer CM. Rapid onset of massive ascites as the initial presentation of systemic lupus erythematosus. Am J Gastroenterol. 2000;95:302–3.

[9] Bitran J, McShane D, Ellman MH. Arthritis rounds: ascites as the major manifestation of systemic lupus erythematosus. Arthritis Rheum. 1976;19:782–5.

[10] Schocket AL, Lain D, Kohler PF, Steigerwald J. Immune complex vasculitis as a cause of ascites and pleural effusions in systemic lupus erythematosus. J Rheumatol. 1978;5:33–8.

[11] Ko SF, Hsien MJ, Ng SH, Wong HF, Lee TY, Lee CM. Superior mesenteric artery aneurysm in systemic lupus erythematosus. Clin Imaging. 1997;21:13–6.

[12] Grimbacher B, HuberM, von Kempis J,Kalden P, UhlM, Köhler G, Blum HE, Peter HH. Successful treatment of gastrointestinal vasculitis due to systemic lupus erythematosus with intravenous pulse cyclophosphamide: a clinical case report and review of the literature. Br J Rheumatol. 1998;37:1023–8.

**List of Abbreviations used**

Anti-ds DNA antibodies: Anti-double-stranded DNA antibodies

Anti-ss DNA antibodies: Anti-single-stranded DNA antibodies

ANA: Anti-nuclear antibody

APS: Anti-phospholipid antibody syndrome

CRP: C-reactive protein

CT: Computer tomography

IVCY: Intravenous pulse of cyclophosphamide

mPSL: Methylprednisolone

LMV: Lupus mesenteric vasculitis

MRI: Magnetic resonance imaging

PSL: Prednisolone

SLE: Systemic lupus erythematosus

SLEDAI: SLE disease activity index

TAC: Tacrolimus

TAE: Transarterial embolization

## Figure Legends

**Figure 1**

Clinical course of the present patient. Anti-ds DNA antibodies anti-double-stranded DNA antibodies, DEX dexamethasone, FFP fresh frozen plasma, IVCY intravenous pulse of cyclophosphamide, mPSL methylprednisolone, PSL prednisolone, RCC red cell concentrate, TAE transarterial embolization

**Figure 2**

Enhanced abdominal computed tomography (CT) showing small intestinal wall hypertrophy with contrast enhancement and leakage of contrast agents into the intestine

**Figure 3**

Abdominal angiography showing multiple extravasations (arrows) from pseudo-microaneurysms of the jejunal and ileal arteries

Figure 1

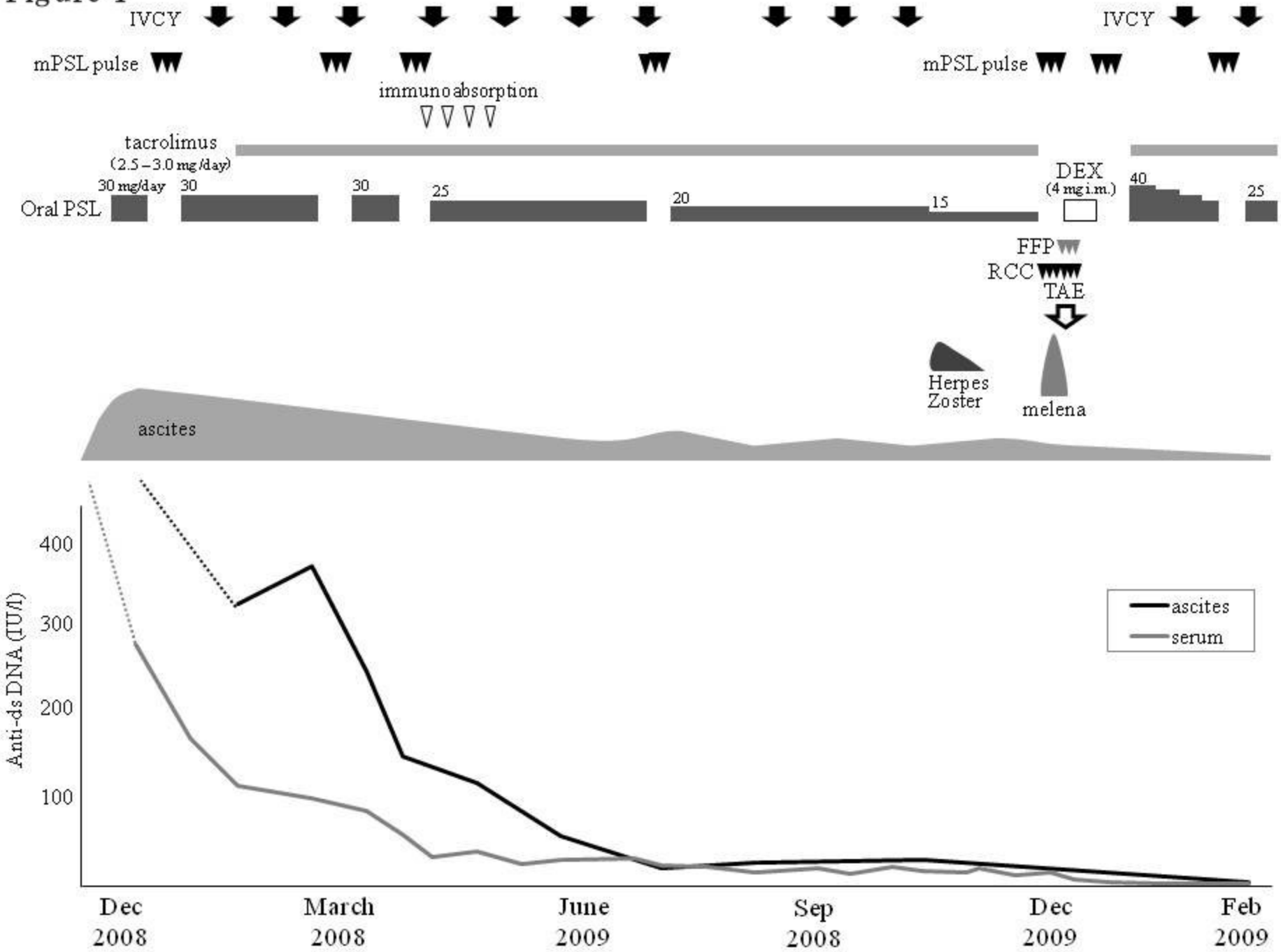
IVCY
mPSL pulse
immunoabsorption
IVCY
mPSL pulse
tacrolimus
(2.5 – 3.0 mg/day)
Oral PSL
30 mg/day
30
30
25
20
15
DEX
(4 mg i.m.)
40
25
FFP
RCC
TAE
Herpes
Zoster
melena
ascites
Anti-ds DNA (IU/l)
400
300
200
100
ascites
serum
Dec
2008
March
2008
June
2009
Sep
2008
Dec
2009
Feb
2009

Figure 2

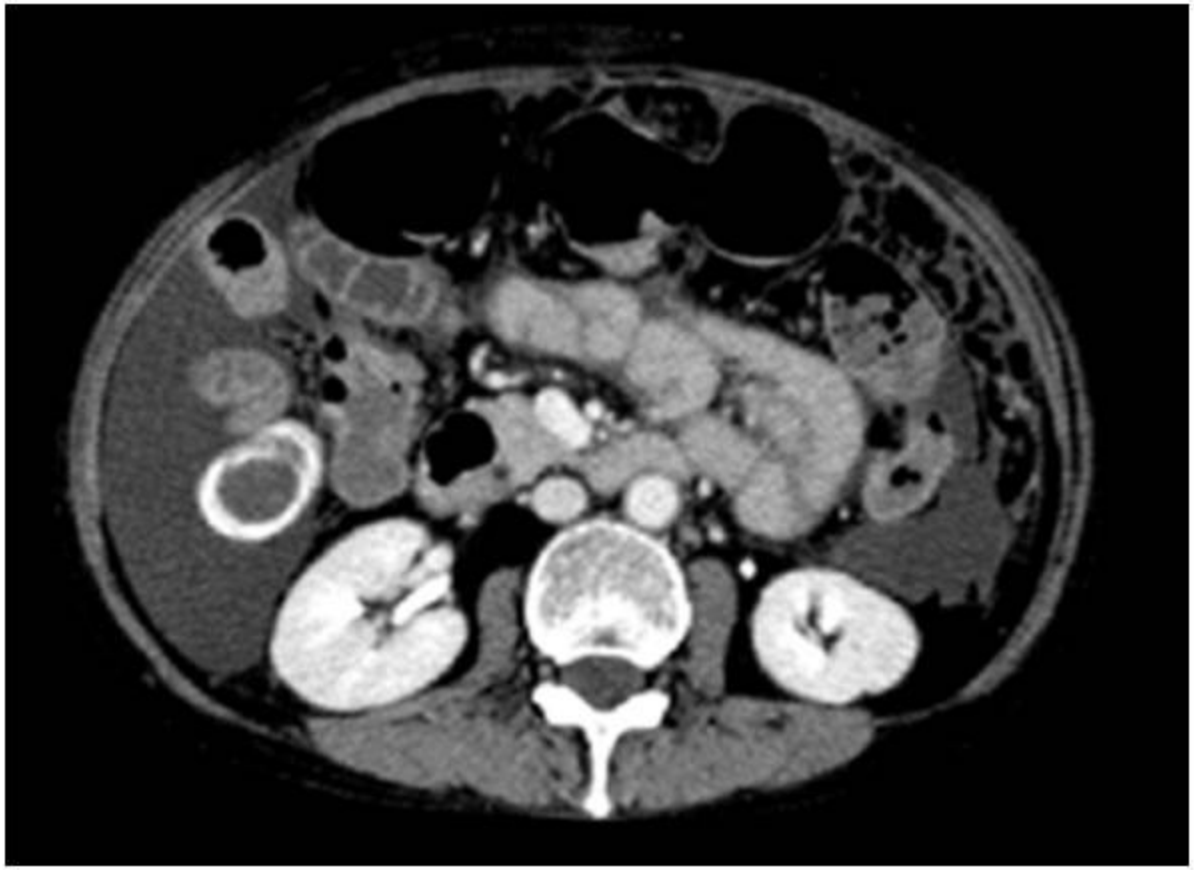

Figure 3