Seminars in Arthritis and Rheumatism 43 (2014) 759–766

Contents lists available at ScienceDirect

Seminars in Arthritis and Rheumatism

journal homepage: www.elsevier.com/locate/semarthrit

Lupus mesenteric vasculitis: Clinical features and associated factors for the recurrence and prognosis of disease

Shiwen Yuan, MD, Yujin Ye, MD*, Dongying Chen, MD, Qian Qiu, MD, Zhongping Zhan, MD, Fan Lian, MD, Hao Li, MD, Liuqin Liang, MD, Hanshi Xu, MD, PhD, Xiuyan Yang, MD*

Department of Rheumatology & Clinical Immunology, the First Affiliated Hospital of Sun Yat-sen University, No. 58, Zhongshan 2nd Rd, Guangzhou 510080, China

ARTICLE INFO

Keywords:
Lupus erythematosus
Systemic
Mesenteric vasculitis
Prognosis
Recurrence

ABSTRACT

Objective: To evaluate the clinical characteristics of lupus mesenteric vasculitis (LMV) and identify the potential factors and appropriate treatments that are associated with disease relapse and prognosis in LMV.

Methods: A retrospective cohort study was performed among patients admitted to the First Affiliated Hospital of Sun Yet-sen University between 2002 and 2011. Demographic information, clinical symptoms, laboratory findings, imaging characteristics like abdominal CT scan, ultrasonography, medications including corticosteroid, cyclophosphamide, and other immunosuppressive agents, and outcomes were documented. The endpoints of the study were defined as occurrence of severe complications that needed surgical intervention, disease recurrence, or death.

Results: Out of 3823 systemic lupus erythematosus (SLE) patients, 97 were diagnosed with mesenteric vasculitis with the overall prevalence of 2.5%. Among these 97 LMV patients, 13 died because of serious complications (13/97, 13.4%) and 2 presented intestinal perforation during the induction therapy stage. The logistic regression multivariate analysis indicated that leukopenia [peripheral WBC, odds ratio (OR) = 0.640, 95% confidence interval (CI): 0.456–0.896, $P = 0.009$], hypoalbuminemia (serum albumin, OR = 0.891, 95% CI: 0.798–0.994, $P = 0.039$) and elevated serum amylase (OR = 7.719, 95% CI: 1.795–33.185, $P = 0.006$) were positively associated with the occurrence of serious complications, while intravenous cyclophosphamide (CYC) therapy inhibited the occurrence of serious complications (OR = 0.220, 95% CI: 0.053–0.903, $P = 0.036$). A total of 79 patients who achieved remission were followed-up for 2–96 months and 18 cases experienced disease relapse (18/79, 22.8%). The statistical analysis adjusted by Cox proportional hazards models indicated that high-dose CYC therapy (≥ 1.0 g/m^2/month) was a protective factor for disease relapse and led to better outcomes [hazard ratio (HR) = 0.209, 95% CI: 0.049–0.887, $P = 0.034$], while the severe thickness of the bowel wall (> 8 mm) was a risk factor (HR = 7.308, 95% CI: 1.740–30.696, $P = 0.007$). LMV and lupus cystitis occurred concurrently in 22 (22/97, 22.7%) patients, and the symptoms of urinary tract resolved after treatment with corticosteroid and immunosupressants.

Conclusion: LMV is one of the serious complications of SLE with high mortality. The current study demonstrated that leukopenia, hypoalbuminemia, and elevated serum amylase were associated with severe adverse events, while CYC therapy led to better outcomes during remission-induction stage. Severe thickness of the bowel was a risk factor while high-dose CYC therapy was a protective factor for disease relapse in intensification therapy stage. It is necessary to evaluate the urinary tract involvement once LMV is diagnosed due to the frequent coexistence of these 2 diseases.

Lupus mesenteric vasculitis (LMV) is one of the most serious gastrointestinal complications in systemic lupus erythematosus (SLE) patients presenting acute abdominal pain [1–3]. Other terms, such as mesenteric arteritis, lupus arteritis, lupus enteritis, gastrointestinal vasculitis, intra-abdominal vasculitis, and acute gastrointestinal syndrome have been used to describe LMV [4]. Severe bowel ischemia caused by LMV may lead to life-threatening complications—intestinal hemorrhage, infarction, and perforation,

This work was supported by the Guangdong Provincial Science and Technology Foundations, China (2009B030801098, 2011B050300009, 2008B080703015, 2005B30701001, and 2007B031500007); Guangdong Natural Science Foundation (S2012010009075); and National Natural Science Foundations of China (81102270 and 81102270).

* Corresponding authors.
E-mail addresses: graceyeyj@hotmail.com (Y. Ye), yang_xiu_yan@hotmail.com (X. Yang).

0049-0172/$ - see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.semarthrit.2013.11.005

resulting in a poor outcome and a high mortality of up to 50% [1,3]. Some previous studies suggest early surgical interventions for severe LMV [3], but more and more recent reports demonstrate that it has a benign clinical course [2,4–6]. High-dose pulsed intravenous corticosteroid has been proven to be an effective treatment for serious LMV [2,4–6]. However, disease relapses are not rare events, even in those who had shown a good response to adequate corticosteroid therapy. Meanwhile, some patients present with corticosteroid-resistant or refractory LMV. In such cases, the reasons or predictive factors for disease recurrence and the appropriate treatments in addition to corticosteroid have not been well established.

In the current retrospective study, clinical and laboratory features of patients with LMV were reviewed to access the potential clinical predictors that may be associated with the prognosis and recurrence of LMV. Medications were also investigated to further determine the appropriate therapy for the relapse of LMV.

Materials and methods

Patients

A retrospective review of the medical records between January 2002 and December 2011 was performed at the First Affiliated Hospital of Sun Yat-sen University. All together, 3823 patients were classified as having SLE who fulfilled at least 4 of the 1997 American College of Rheumatology (ACR) revised classification criteria for SLE [7]. Among these SLE patients, 97 had a dual simultaneous diagnosis of LMV according to the following inclusion criteria [8,9]: (1) clinical evidence of multi-focal bowel (ie, segmental involvement of small and large bowel loops with intervening normal bowel segments like skip lesions [10,11]) or multiple vascular territories involvement (ie, affecting multiple anatomic regions and not confining to a single vascular supplying territory [10,11]), duodenal ischemic changes (ie, the following ischemic changes detected by CT or segmental edema and discrete ulcers detected by endoscopies [12]), and bowel wall thickening, which resolved on the treatment with intravenous steroid or immunosuppressant [13] and (2) satisfaction of at least 3 of the following signs that were identified by abdominal computed tomography (CT)—bowel wall thickening, target sign, dilatation of intestinal segments, engorgement of mesenteric vessels, and increased attenuation of mesenteric fat. Bowel wall thickening was defined if the intestinal wall was at least 3-mm thick in an area that was distended maximally and 5 mm for gastric wall [10]. Bowel dilation was defined if the diameter of intestinal segment exceeded 2.5 cm for the small bowel and 8.0 cm for the large bowel [11].

Study variables

Clinical and demographic information was collected from admission and outpatient clinic records, including gender, age, duration of SLE, duration of abdominal pain, serological examinations, other organ involvement, complications, lupus disease activity, image characteristics, and therapeutic medications.

The laboratory data included antinuclear antibody, antibody to double-stranded DNA (ds-DNA), anti-Sm antibody, anti-ribonucleoprotein (RNP) antibody, anti-Ro antibody, anti-La antibody, anti-cardiolipin antibody (aCL), anti-β_2-glycoprotein 1 (β_2-GP1) antibody, the white blood cell (WBC) count, hemoglobin, platelet (PLT), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), compliment 3, immunoglobulin G (IgG), serum creatinine (SCr), serum albumin (ALB), serum amylase, and urinalysis. Antinuclear antibody and anti-ds-DNA antibody were detected by enzyme-linked immunosorbent assay (ELISA) (Captia™ ANA/dsDNA screen test kit, Trinity Biotech, NY). Anti-Sm antibody, anti-RNP antibody, anti-Ro antibody, and anti-La antibody were all detected by blot techniques (EUROASSAY test kit, EUROIMMUN Medizinische Labordiagnostika AG, Hangzhou, China). Anti-cardiolipin antibody was detected by cardiolipin IgG/IgM ELISA test kit (Zeus Scientific Inc., NJ). Anti-β_2-GP1 antibody was detected by β_2-Glyco-GM ELISA test kit (AESKU.Diagnostics, Wendelsheim, Germany).

Other organs involved included skin, joints, serosae, ureter/renal, pancreas, and the cardiovascular, pulmonary, and central nervous systems. Lupus nephritis (LN) was defined if clinical and laboratory manifestations met the ACR criteria [14]. After ruling out other non-SLE-related causes such as urinary calculus, infection, neuropathy, malignancy, and side effects of medication, we considered lupus urinary tract involvement when pathology obtained from cystoscopy/surgical biopsy indicated interstitial cystitis or the following signs were identified by abdominal CT/ultrasonography: bladder wall thickening, stenosis/dilatation of the ureters, and hydroureteronephrosis [15,16]. Serum amylase was detected by biochemical tests. Cardiovascular involvement included structural abnormalities detected by echocardiography, congestive heart failure, and arrhythmia. Central nervous system involvement consisted of 12 manifestations of neuropsychiatry syndromes that were defined by the ACR [17].

The most severe complications included intestinal obstruction, intestinal perforation, and alimentary tract hemorrhage. The first 2 were identified by plain abdominal radiograph and the last 1 was diagnosed by clinical manifestation, positivity of occult blood test, and endoscopy.

The disease activity was evaluated by calculating the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score [18,19] and European Consensus Lupus Activity Measurement (ECLAM) score [20,21] at the time of admission.

Abdominal CT scans were performed at the time of admission and after relief of abdominal pain. The radiographic changes in the affected organs (stomach, small intestine, colon, and rectum), bowel wall thickness (slight, 4–5 mm; moderate, 6–8 mm; and severe, >8 mm [13]), mesentery, lymph nodes, urinary tract, and ascites were recorded. Radiographic films were read by 2 radiologists who were both blinded to the outcomes. If disagreement existed about the diagnosis, discussion was needed to achieve consensus.

Medications including corticosteroids and additional immunosuppressive agents were also recorded. The dosage of corticosteroid was defined as high dose (>30 mg but ≤ 100 mg prednisone or equivalent per day) and very high dose (>100 mg prednisone or equivalent per day) [22]. Intravenous (IV) cyclophosphamide (CYC) was administered only if 3-day adequate corticosteroid therapy could not alleviate the abdominal pain or LMV was accompanied with other severe visceral organ injury, such as LN or neuropsychiatric lupus. The dose intensity and interval of CYC therapy were quite different because of the disease severity and the doctor's personal experience. In the current study, CYC dose intensity was divided into 3 grades: none, low dose (average dose <1.0 g/m^2 body surface area per month), and high dose (average dose ≥ 1.0 g/m^2 body surface area per month).

Other immunosuppressive agents administered to patients with LMV were also documented, including mycophenolate mofetil and hydroxychloroquine.

Study outcomes

Short-term outcomes included death or severe adverse event like intestinal perforation that needed surgical intervention during hospitalization [1,3,23].