

## Case Report

# A case report of serum sickness-like syndrome as the first manifestation of inflammatory bowel disease IBD

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**Abstract:** This is a case of Inflammatory Bowel Disease IBD presentation that resembles Serum Sickness Syndrome. This would shed more light on IBD autoimmune nature. Establishing autoantibodies and immune complexes causality will help in diagnosis and treatment of IBD. 34-year-old female presents with constellation of symptoms including fevers, chills, diarrhea, recent hematochezia, diffuse arthralgia and anasarca. Erythematous skin lesions on arms and legs. Progressive edema in her extremities. The patient was admitted for further evaluation of possible serum sickness disease and systemic connective tissues disease. Gastroenterology and Rheumatology services were consulted. She was started on oral steroids. The patient started to improve symptomatically. Serum sickness disease was the probable diagnosis with rheumatology work-up suggesting immune complex pathology. Colonoscopy was planned given her diarrhea, hematochezia and anemia. Biopsies were consistent with Crohn's disease. Management plan was to continue as outpatient on steroid taper. This case represents a unique systemic process. One explanation of such phenomenon would be serum sickness disorder with deposits of Immune complexes IC in various tissues causing symptoms. Rheumatologist work-up goes with picture of immune complexes although antigens are not clear yet. Searching for source of stimuli for immune complex formation; the eventual diagnosis of IBD suggested causality. Patient's symptoms improved dramatically on high dose prednisone. This would work on serum sickness like disease process but also can manage the flare-up related to her IBD. This case report raises questions about the pathogenesis of IBD. Further understanding of this can help the future of IBD diagnosis, management and treatment.

**Keywords:** Inflammatory bowel disease, serum sickness syndrome, immune complexes

### Introduction

Inflammatory Bowel Disease (IBD) occurs with different manifestations. Some are common while some are unique, which adds to the complexity of the pathogenesis and disease progression. This case presents an interesting presentation that resembles Serum Sickness Syndrome and can shed more light on the nature of IBD, especially the autoimmune pathology. Establishing autoantibodies and immune complexes' causality will help in the diagnosis and treatment of IBD.

### Case summary

Our patient is a 34-year-old Caucasian female with past medical history of hemorrhoids and recent laparoscopic cholecystectomy. She was transferred to our hospital with a constellation

of symptoms including fevers, chills, diffuse arthralgia and anasarca.

She reported undergoing a laparoscopic cholecystectomy for symptomatic gallstones approximately 1 month prior to her presentation. She presented a few days after her surgery with hematochezia, which she attributed to her hemorrhoids. Her hemoglobin at that presentation was 6.5 g/dl, so she was transfused 2 units of packed red blood cells RBCs and was observed overnight. She was discharged after subjective improvement. No endoscopic evaluation was done and she was scheduled to follow-up with the gastroenterology clinic.

Shortly afterwards, she started to experience progressive arthralgia that started at her ankles, and then later involved several joints bilaterally. It was associated with watery diar-

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fever (as high as 103°F) and chills. Erythematous skin lesions on the extensor surfaces of her arms and legs were documented on examination. There was also progressive bilateral edema in her lower and upper extremities. She was admitted to an outside hospital with these complaints and underwent an extensive evaluation for infectious causes. This included urinalysis, urine and blood cultures. Chest radiograph, along with CT scan of the abdomen and pelvis were also conducted. They showed evidence of urinary tract infection and colitis. She was given a course of Metronidazole and Levofloxacin for 1 week with no benefit, and was then referred to our hospital.

On clinical evaluation, she was in distress. Her vital signs showed a temperature of 98°F, blood pressure 117/68 mmHg, and pulse 123. Further physical examination was significant for +2/+3 pitting edema in the bilateral upper and lower extremities. Bilateral swelling with evidence of mild synovitis, tenderness to palpation and restricted range of motion in the wrists and elbows was noted. The cardiopulmonary and abdominal examination was unrevealing. The initial laboratory work-up showed WBCs 11.8\*1000/cmm; hemoglobin 8.2 g/dl; platelet count 427\*1000/cmm; Na 139 meq/L; K 3.3 meq/L; creatinine 0.8 mg/dl; serum albumin 2.1 g/dl; AST 11 units/l; ALT 20 units/l; total bilirubin 0.7 mg/dl; ESR 55; C-reactive protein 178.6; and INR 1.2. Urinalysis was negative for proteinuria or hematuria.

The patient was admitted for further evaluation of inflammatory arthritis, possible serum sickness disease and systemic connective tissue disease. The gastroenterology and rheumatology services were consulted. Stool analysis showed positive for fecal lactoferrin, and negative for gastrointestinal stool antigen panel by PCR including *clostridium difficile*. She was started on oral Prednisone 60 mg daily as the rheumatologist was concerned about serum sickness disease. Further work-up showed low C3 level; normal C4; normal angiotensin converting enzyme (ACE) level; negative hepatitis B surface antigen; negative Hepatitis C virus HCV antibodies; and absent cryoglobulins. Additional tests included negative titers for autoantibodies including antinuclear antibodies (ANA), rheumatoid factor (RF), anti-cyclic citrullinated peptide, and anti-neutrophil cytoplasmic antibody. The Cytomegalovirus CMV titers were

low and blood cultures remained negative. Repeated review of her CT scan of the abdomen and pelvis showed nonspecific findings of persistent colitis.

The patient started to improve symptomatically with steroids on hospital day 3. Serum sickness disease was the probable diagnosis. However, a decision was made to proceed with a colonoscopy given her diarrhea and abdominal imaging findings, as well as her history of hematochezia and anemia.

Diffuse continuous abnormal vascularity, congestion and erythema were noted in the entire colon, consistent with severe pan-colitis. Terminal ileitis was noted as well. Biopsies were obtained from the terminal ileum and colon. Pathology showed chronic mild to moderate focally active ileitis and chronic active colitis with focal granulomatous inflammation. All of these were consistent with IBD, and specifically Crohn's disease.

The patient was started on Mesalamine and discharged on a steroid taper. She is following-up with the IBD clinic and her symptoms are under control.

### Discussion

This case represents an unusual presentation of IBD. Classically, IBD presents in multiple common presentations depending on the site and nature of the disease. While ulcerative colitis commonly presents with typical diarrhea, abdominal pain and rectal bleeding; Crohn's has a slightly more variable presentation. Fibrostenotic Crohn's presents with abdominal pain, weight loss and change in bowel habits. Fistulous Crohn's presents with inflammatory fistulas to internal organs or the external skin [7]. Interestingly, our patient presented with myalgia, fever of unknown cause, anasarca with progressive arthralgia and skin rash, all suggesting a systemic process. The rheumatologist's work-up showed decreased levels of C3 with normal C4, negative ANA, RF, elevated CRP and ESR. This supports the picture of immune complexes, although with the antigens not yet clear. One explanation of such a phenomenon would be serum sickness disorder with deposits of immune complexes IC in various tissues, causing symptoms. While most cases of serum sickness in the literature relat-

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ed to external antigens, this patient presented with no clear evidence of external antigen exposure throughout the course of the disease or prior to it. In searching for the source of stimuli for immune complex formation, the eventual diagnosis of IBD suggests it might have played a role. Antigens, or immune complexes, may arise from the disease process in the intestines as self-antigens get exposed, or by the loss of intestinal integrity due to inflammation with food proteins freely passing to the blood. This will cause immune complex formation with manifestations such as arthralgia, skin rash (probably Leukocytoclastic vasculitis), nephrotic syndrome and anasarca, as this patient presented. A previous study that included 86 IBD patients showed significantly higher levels of immune complexes than the controls ( $P < 0.001$ ) [1]. Interestingly, the IBD patients when compared with patients with other diseases that might cause loss of intestinal integrity (e.g. Clostridium difficile colitis) also showed significantly higher levels of IC. Hence, immune complexes might be part of the IBD pathogenesis, distinct from merely the simple leakage of antigens through a compromised intestinal-blood barrier. Later studies on IBD patients repeatedly found antibodies to self-antigens in this population. This may point to causality with further understanding of the pathogenesis. IBD could have caused the antibodies or vice versa. For example, a study showed that autoantibodies can be utilized in the diagnosis of Crohn's and differentiating Ulcerative Colitis (UC) from Crohn's disease CD. Anti-Saccharomyces cerevisiae antibodies are associated with Crohn's disease, while Perinuclear anti-neutrophil cytoplasmic antibodies are associated with UC [2]. Other studies showed increased prevalence of antiphospholipid antibodies [3], and more recent ones showed prevalence of pancreatic autoantibodies of anti-CU2D2, anti-GP2 with possible utilization in the diagnosis and differentiation between CD and UC [4].

Extra intestinal symptoms and signs were repeatedly reported in IBD, with approximately 6.2% of IBD patients developing at least one of the following extra-intestinal manifestations: Iritis/uveitis, Primary sclerosing cholangitis, Ankylosing spondylitis, Erythema nodosum, Pyoderma gangrenosum [5]. In another study, 16.9% of European patients developed at least one extra-intestinal manifestation in a cohort study of 10 years' duration [6]. Extra-intestinal

manifestations preceded the diagnosis of IBD in one-third of the patients studied, with these manifestations also more common in younger patients [6]. Theories explaining such manifestations include autoimmunity with genetic susceptibility and autoantibodies formed as part of the disease process. These might have occurred in similar ways as our patient's manifestations did. Our patient developed arthralgia in the right 2-3 PIP, left wrist, left elbow, both knees and right ankle. Such asymmetric distribution might suggest enteropathy arthritis, or be part of the overall serum-sickness-like picture. Both can be managed with steroids on which the patient was started. History of skin rash with the description of non-tender flat erythematous lesion on legs and arms symmetrically does not reflect classical Erythema nodosum or Pyoderma gangrenosum. More likely is that an autoimmune process was causing this rash. Unfortunately, no biopsy was possible since the rash disappeared in our patient on presentation. The patient denied experiencing any eye problems, while the liver function test was within normal limits, except for the albumin level that was explained by proteinuria. Interestingly, the patient's symptoms improved dramatically on high dose Prednisone of 60 mg daily with a taper down. This will work on arthralgia caused by serum-sickness-like diseases, but also can manage the flare-up attack related to her IBD.

The symptoms related to the gastrointestinal system that this patient presented with could be explained by the eventual diagnosis of IBD on biopsy. She reported a history of hematochezia that required 3 units of blood prior to admission. Anemia of likely iron deficiency developed naturally, and her hemoglobin level stabilized with iron supplements. History of menorrhagia also might be confusing, but she related the episodes to her OCP intake, with the progesterone component being the likely culprit.

Reflecting on the general population, this case raises questions about how pathogenesis can be better looked into while studying the interaction of autoimmune diseases, and importantly, how to approach diagnosis and treatment. Coincidence might certainly play a role. More case reports and case series are needed to help establish the relationship with greater certainty.

**Disclosure of conflict of interest**

None.

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