Received: 25 July 2020 | Revised: 24 September 2020 | Accepted: 19 October 2020

DOI: 10.1002/ccr3.3488

CASE REPORT

Clinical Case Reports Open Access WILEY

A woman with adult-onset Still's disease and acute intestinal pseudo-obstruction

Hiroshi Hori[1] | **Hiroki Yabe**[2] | **Takahiko Fukuchi**[1] | **Hitoshi Sugawara**[1]

[1]Division of General Medicine, Department of Comprehensive Medicine 1, Saitama Medical Center, Jichi Medical University, Saitama, Japan

[2]Division of Rheumatology, Department of Comprehensive Medicine 1, Saitama Medical Center, Jichi Medical University, Saitama, Japan

Correspondence
Hiroshi Hori, Division of General Medicine, Department of Comprehensive Medicine 1, Saitama Medical Center, Jichi Medical University, 1-847 Amanuma-cho, Omiya-ku Saitama City, Saitama 330-8503, Japan.
Email: ubm5134@mbr.nifty.com

Abstract

Adult-onset Still's disease may cause intestinal pseudo-obstruction via a cytokine storm. Early diagnosis and treatment are the key for patient survival before the development of serious complications such as macrophage activation syndrome.

KEYWORDS

acute intestinal pseudo-obstruction, adult-onset Still's disease, fever of unknown origin, hypercytokinemia, macrophage activation syndrome

1 | INTRODUCTION

A 47-year-old woman with a fever of 39°C exhibited abdominal distension with decreased peristaltic activity, and radiological examinations revealed a dilated intestine. She was diagnosed with acute intestinal pseudo-obstruction. Subsequently, she developed rashes and arthritis and was diagnosed with adult-onset Still's disease. Her symptoms improved after steroid administration.

The major symptoms of adult-onset Still's disease (AOSD) include remittent fever of ≥39°C, evanescent rash, and multiple arthritic joints. Moreover, this disease is an important causal disease of fever of unknown origin in adults.[1] Various cytokines, including interleukin (IL)-18, IL-1, IL-6, interferon (IFN)α, and IFN-γ, are involved in AOSD.[2] IL-18 is particularly high in patients with AOSD.[3] Serious complications of AOSD develop in 15% of patients and include macrophage activation syndrome, hemophagocytic syndrome, and disseminated intravascular coagulation (DIC).[2,4]

Acute intestinal pseudo-obstruction is a functional obstruction of the intestine in the absence of a mechanical cause. It is relatively rare and develops in only 100 of 100 000 hospitalized patients.[5] In Japan, 82.3% of the patients with acute intestinal pseudo-obstruction have an underlying disease,[6] and many are serious acute diseases.[6-8] Acute intestinal pseudo-obstruction can develop as a complication of diseases, such as cardiovascular disease, electrolyte abnormalities (especially hypokalemia), neurological diseases (such as myasthenia gravis), sepsis, inflammatory diseases (such as acute pancreatitis and cholecystitis), and endocrinopathies (such as hypothyroidism).[9,10] The mortality rate is 30%, and it increases to 45% in 10%-20% of the patients who develop ischemia and perforation of the colon.[5] Therefore, diagnosing the disease and providing prompt treatment during the early phase are important.

We describe a case of a woman with AOSD manifesting an acute intestinal pseudo-obstruction.

2 | CASE REPORT

A healthy 47-year-old woman developed fever of 39°C at night along with fatigue and sore throat 10 days before hospital admission. Eight days before hospital admission, she experienced severe fatigue and visited a clinic where she was treated with azithromycin. The drug was changed to garenoxacin mesylate due to lack of symptom improvements. However, she presented with muscle pain and edema in the lower extremities, and she was referred to our hospital and admitted.

Upon hospital admission, she exhibited a fever of 39.7°C, sinus tachycardia of 135 bpm, oxygen saturation at 91% (1-L cannula), respiratory rate at 26 respirations/min, and mild respiratory failure. Abdominal examination revealed abdominal distension, noticeable tympanic sounds on percussion, and an almost complete absence of bowel sounds on auscultation. Wheezing was confirmed by auscultation. Swelling and tenderness were confirmed in both proximal interphalangeal (PIP) joints and both ankle joints, with edema in the lower extremities. She did not present with rashes upon admission. After hospital admission, remittent fever of >39°C lasted after the administration of sulbactam/ampicillin.

Abdominal X-ray images revealed a large volume of gas in the colon and an elevated diaphragm (Figure 1). Contrast-enhanced computed tomography (CT) revealed enlarged lymph nodes in the mediastinum, enlarged colon, and the formation of a liquid surface, but no clear mechanical obstruction was evident. Hepatomegaly, spleen enlargement, and pericardial effusion were also confirmed (Figure 2). Subsequent colon endoscopy revealed no mechanical obstruction. We diagnosed the patient with intestinal pseudo-obstruction on Day 5 after hospitalization. We inserted a nasogastric tube and initiated metoclopramide administration but observed no abdominal finding of improvements. We suspected a *Clostridium difficile* infection, based on the megacolon syndrome-like findings. However, glucose dehydrogenase (GDH) antigen and *C difficile* (CD) toxin tests were negative, and the response to metronidazole was poor.

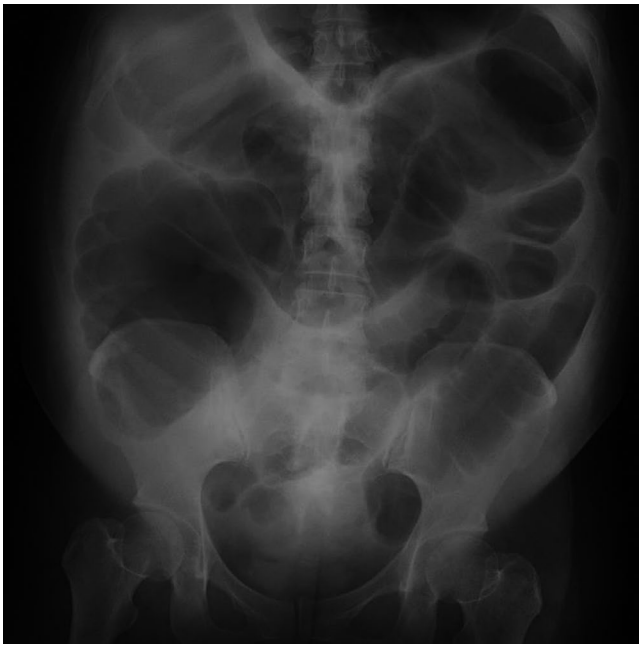

FIGURE 1 Abdominal X-ray image. Enlarged large intestine. An enlarged colon with gas can be observed

Since the patient's respiratory conditions had worsened, we admitted her to the intensive care unit on Day 6 for artificial ventilator management. We suspected that the patient had developed acute adult respiratory distress syndrome (ARDS) because the PaO_2/FiO_2 ratio had dropped to 177, and the permeability of the bilateral lung fields was reduced on chest X-ray radiography. We confirmed the presence of a salmon-pink edematous erythema on her skin and on the dorsal side and proximal parts of the extremities (Figure 3). We suspected a drug-related eruption and discontinued the administration of all suspected drugs, but her rash did not improve.

2.1 | Investigations

Blood tests upon admission revealed a white blood cell count at 18 560 cells/μL (89% neutrophils) and elevated liver enzymes (aspartate aminotransferase, 36 U/L; alanine aminotransferase, 45 U/L; and lactate dehydrogenase, 430 U/L). Antinuclear antibody titers were negative (<1:40), and rheumatoid factor was positive (29 IU/mL). Ferritin was high at 3551.4 ng/mL. Inflammatory markers were elevated (C-reactive protein of 27.6 mg/dL, erythrocyte sedimentation rate of 134 mm/h), procalcitonin was 0.4 ng/mL, and C3 and C4 were 113 and 29 mg/dL, respectively. Repeated blood cultures were negative, and antibody tests for Epstein-Barr and hepatitis virus acute infections were negative.

Colonoscopy, contrast CT revealed no evidence of malignant tumors, and we excluded inflammatory bowel disease and amyloidosis after random endoscopic biopsy pathological examinations of the colon. Bone marrow biopsy and random skin biopsy results suggested the absence intravascular lymphoma. A positron emission tomography-computed tomography (PET-CT) test revealed no accumulations, suggesting tumors; however, fluorodeoxyglucose accumulated in several joints, a wide region of the spine, and the spleen (Figure 4). These sites are consistent with those seen in previously reported cases of AOSD.[11]

2.2 | Differential diagnosis

We suspected AOSD on the basis of the remittent fever; swelling and tenderness in the PIP, ankle, and shoulder

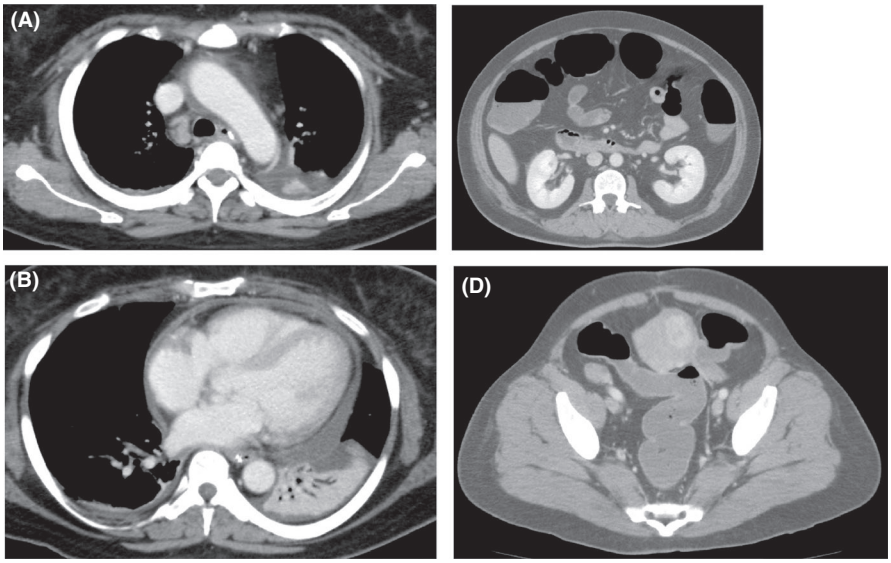

FIGURE 2 Computed tomography (CT) scan images. A, An enlarged mediastinal lymph node can be observed around the trachea. B, The image confirms the presence of pericardial effusion. C and D, Abdominal CT showed enlargement of the large intestine, but no mechanical obstruction was evident

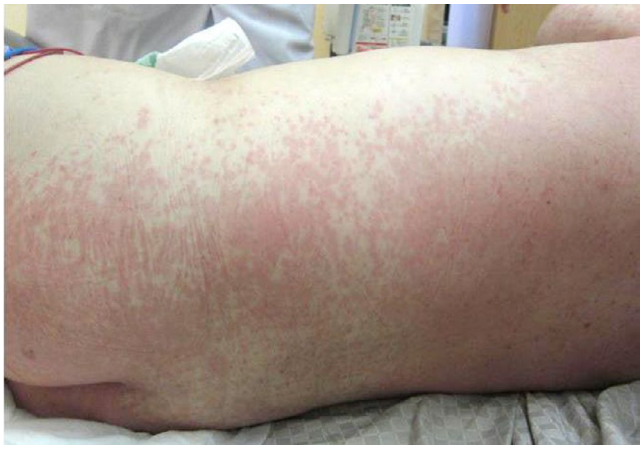

FIGURE 3 Photograph of the patient's skin. Rice-grain-sized to thumb-sized edematous erythema is observed in many sites of the extremities and trunk

joints; salmon-pink erythema; enlarged spleen; and hepatic dysfunction.

We ruled out bacterial infections after seeing no response to the administration of antibiotics and based on the results of various culture tests, and ruled out viral infection from results of serum antibody tests. Malignant tumors and lymphomas were ruled out based on the results of PET-CT, endoscopy, and random skin biopsy.

Based on these findings, we diagnosed the patient with AOSD, according to the Yamaguchi diagnostic criteria[12] (three large categories and three small categories).

2.3 | Treatment, outcome, and follow-up

We initiated administration of 40 mg prednisolone (PSL). Her fever was reduced to normal, joint pain improved, and

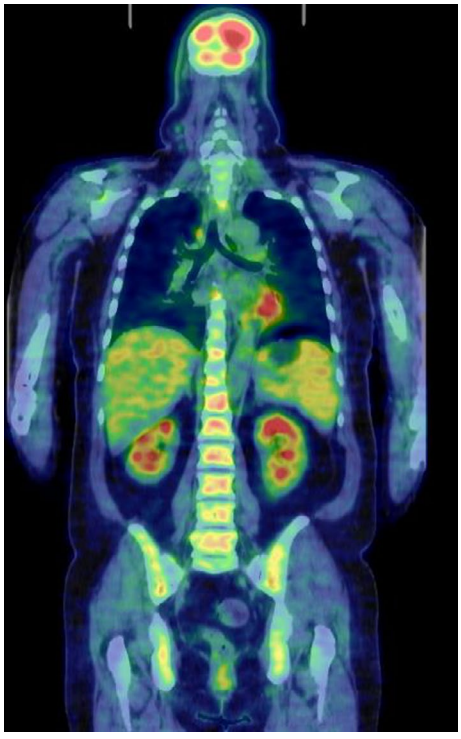

FIGURE 4 Positron emission tomography (PET) images. Diffuse fluorodeoxyglucose (FDG) accumulation can be observed in the bone marrow. The patient exhibited an enlarged spleen with increased FDG accumulation compared with that in the liver

respiratory condition improved. Her bowel movement improved, she defecated, and her abdominal distention disappeared. Then, we added 200 mg cyclosporine to PSL and noticed maintained improvements. We have decreased the dose of PSL since then, and the patient has remained symptom-free for 6 months after commencement of the treatment.

3 | DISCUSSION

We encountered a woman with a rare case of AOSD and an acute intestinal pseudo-obstruction. In the acute phase, AOSD may be complicated with very serious conditions, such as ARDS, hemophagocytic syndrome, and disseminated intravascular coagulation; therefore, prompt diagnosis and treatment are essential.

In this report, we focused on intestinal pseudo-obstruction, which may not be a characteristic serious complication of AOSD but was the most prominent symptom of the patient at the time of admission. We addressed the following three clinical questions regarding the relationship between the characteristics of intestinal pseudo-obstruction and AOSD:

1. When acute intestinal pseudo-obstruction is suspected, how should the diagnosis and management be performed?
2. Could patients with AOSD develop intestinal pseudo-obstruction as a complication?
3. Which mechanisms may lead to the development of acute intestinal pseudo-obstruction as a complication of AOSD?

3.1 | When acute intestinal pseudo-obstruction is suspected, how should the diagnosis and management be performed?

Pseudo-obstruction develops as a complication of various diseases, especially acute ones.[5] After excluding mechanical obstruction, assessing the presence of ischemia and perforation, which require surgical treatments, is important.[13] In our patient, the blood pressure was stable, and contrast CT and colon endoscopy examinations disproved any blood flow disturbances or mechanical obstructions in the intestinal tract. Thus, we selected a conservative treatment with infusion, fasting, and intestinal tract decompression. At the same time, we should discontinue drugs that could be causal and promote the treatment for underlying diseases.[13] Erythromycin has been reported to exert an excitomotor effect[14] and would be effective for intestinal pseudo-obstructions.[15]

3.2 | Could patients with AOSD develop intestinal pseudo-obstruction as a complication?

Pseudo-obstruction develops secondarily to various acute diseases, and it can also develop in patients with immunological diseases. Intestinal pseudo-obstruction can occur in patients with systemic lupus erythematosus, scleroderma, and chronic inflammation from autoimmune diseases.[16] On the other hand, intestinal pseudo-obstruction in patients with AOSD is extremely rare, and to our knowledge, only three cases like this have been reported.[17-19] Amyloidosis should also be excluded in cases of intestinal pseudo-obstruction in patients with AOSD.[19,20] AOSD may cause intestinal pseudo-obstruction in patients with acute onset and chronic stages complicated with amyloidosis.

3.3 | Which mechanisms may lead to the development of acute intestinal pseudo-obstruction as a complication of AOSD?

Various pathogenic mechanisms, such as interstitial cells of Cajal, enteric nervous system dysfunction, and autonomic imbalances, may cause acute intestinal pseudo-obstruction.[5] Ogilvie syndrome was reported in 1948 by William Heneage Ogilvie as an acute intestinal pseudo-obstruction disorder. Sympathetic/parasympathetic nerve imbalances may contribute to disease manifestations and help solve the question.[21] The intestinal tract is controlled by sympathetic (nerve ganglions of the inferior thoracic spinal cord and the lumbar spinal cord) and parasympathetic nerves (vagal nerve controls from the right hemi-colon region to the splenic flexure, and the remaining areas are controlled by the nerve from the sacral spine). This means that mechanical intestinal pseudo-obstruction may develop when the tone of the parasympathetic nerves is lowered or the tone of the sympathetic nerves on the left side is increased.[22]

Cytokines affect the nervous control of the sympathetic and parasympathetic nerves, and hypercytokinemia in patients with acute diseases may lead to intestinal pseudo-obstruction through autonomic nerve responses.[23] Shock and severe sepsis in critically ill patients and postoperative conditions may lead to increased risks of intestinal pseudo-obstruction, and this may be caused by cytokines.[5,8] Patients with AOSD may develop severe disease conditions with cytokine syndromes through IL-18 and IFNγ.[4]

In addition, intestinal pseudo-obstruction in patients with AOSD may be caused by complications, such as aseptic peritonitis, gastrointestinal stromal inflammation, and amyloidosis, as well as by autonomic disorders mediated by cytokines.[24] Our patient developed severe respiratory symptoms (ARDS) while presenting with intestinal pseudo-obstruction, and this suggests the involvement of cytokines. There is a report on a patient with AOSD and intestinal pseudo-obstruction who also developed ARDS and DIC.[19]

4 | CONCLUSION

In the case of intestinal pseudo-obstruction, differentiation of background diseases that cause cytokine storms is essential. AOSD may cause intestinal pseudo-obstruction via

a cytokine storm. Background diseases should be promptly treated before serious complications can occur.

ACKNOWLEDGMENTS

The authors would like to thank ENAGO (https://www.enago.jp/) for the English language review.

CONFLICT OF INTEREST

None declared.

AUTHORS' CONTRIBUTIONS

HH: wrote the manuscript; HY: helped in writing the manuscript; TF: helped in writing the manuscript; HS: helped in writing the manuscript and contributed to the helpful discussion of relevant literature.

ETHICAL APPROVAL

We obtained written consent from the patient for publication of this report.

INFORMED CONSENT

We obtained written consent from the patient for publication of this report.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author**,** [Hiroshi Hori], upon reasonable request.

ORCID

Hiroshi Hori https://orcid.org/0000-0001-9466-2125
Hitoshi Sugawara https://orcid.org/0000-0002-5060-9020

REFERENCES

1. Giacomelli R, Ruscitti P, Shoenfeld Y. A comprehensive review on adult onset Still's disease. *J Autoimmun*. 2018;93:24-36.
2. Asanuma YF, Mimura T, Tsuboi H, et al. Nationwide epidemiological survey of 169 patients with adult Still's disease in Japan. *Mod Rheumatol*. 2015;25:393-400.
3. Jamilloux Y, Gerfaud-Valentin M, Martinon F, Belot A, Henry T, Sève P. Pathogenesis of adult-onset Still's disease: new insights from the juvenile counterpart. *Immunol Res*. 2015;61:53-62.
4. Behrens EM, Koretzky GA. Cytokine storm syndrome: Looking toward the precision medicine era. *Arthritis Rheumatol*. 2017;69:1135-1143.
5. Wells CI, O'Grady G, Bissett IP. Acute colonic pseudo-obstruction: A systematic review of aetiology and mechanisms. *World J Gastroenterol*. 2017;23:5634.
6. Takagi Y, Abe T, Mochizuki R, Kanematsu M. A case report of Ogilvie syndrome. *J Ther*. 1992;74:1177-1180.
7. Vanek VW, Al-Salti M. Acute pseudo-obstruction of the colon (Ogilvie's syndrome). *Dis Colon Rectum*. 1986;29:203-210.
8. Vazquez-Sandoval A, Ghamande S, Surani S. Critically ill patients and gut motility: are we addressing it? *World J Gastrointest Pharmacol Ther*. 2017;8:174.
9. De Giorgio R, Knowles CH. Acute colonic pseudo-obstruction. *Br J Surg*. 2009;96:229-239.
10. Viallard JF, Vincent A, Moreau JF, Parrens M, Pellegrin JL, Ellie E. Thymoma-associated neuromyotonia with antibodies against voltage-gated potassium channels presenting as chronic intestinal pseudo-obstruction. *Eur Neurol*. 2005;53:60-63.
11. Yamashita H, Kubota K, Takahashi Y, et al. Clinical value of 18F-fluoro-dexoxyglucose positron emission tomography/computed tomography in patients with adult-onset Still's disease: a seven-case series and review of the literature. *Mod Rheumatol*. 2014;24:645-650.
12. Yamaguchi M, Ohta A, Tsunematsu T, et al. Preliminary criteria for classification of adult Still's disease. *J Rheumatol*. 1992;19:424-430.
13. Robinson AJ, Quigley JP, Banks A, Farmer M. Ogilvie's syndrome treated with an emergency laparotomy, right hemicolectomy and end ileostomy. *Case Rep*. 2017;2017:bcr-2017.
14. Smith AJ, Nissan A, Lanouette NM, et al. Prokinetic effect of erythromycin after colorectal surgery. *Dis Colon Rectum*. 2000;43:333-337.
15. Jiang D, Zhang Y, Jiang Z, Li ZZ. Intravenous low-dose erythromycin could be an efficacious treatment for acute colonic pseudo-obstrcution (ACPO)/Ogilvie's syndrome in children. *Med Hypotheses*. 2008;70:706.
16. Takahashi H, Ohara M, Imai K. Gastrointestinal manifestation. *Jpn J Clin Immunol*. 2004;27:1145-1155.
17. Reginato AJ, Schumacher HR Jr, Baker DG, O'Connor CR, Ferreiros J. Adult onset Still's disease: experience in 23 patients and literature review with emphasis on organ failure. *Semin Arthritis Rheum*. 1987;17:39-57.
18. El Younsi S, Perlemuter G, Clerc D, Buffet C, Pelletier G. Still's disease and intestinal pseudo-obstruction. *Gastroenterol Clin Biol*. 2014;28:309-310.
19. Shinohara T, Hidaka T, Matsuki Y, Suzuki K, Ohsuzu F. Calcinosis cutis and intestinal pseudoobstruction in a patient with adult onset Still's disease associated with recurrent relapses of disordered coagulopathy. *Intern Med*. 1999;38:516-520.
20. Harrington TM, Moran JJ, Davis DE. Amyloidosis in adult onset Still's disease. *J Rheumatol*. 1981;8:833-836.
21. Ogilvie H. Large-intestine colic due to sympathetic deprivation. *Br Med J*. 1948;2:671.
22. Durai R. Colonic pseudo–obstruction. *Singapore Med J*. 2009;50:237.
23. Kenney MJ, Ganta CK. Autonomic nervous system and immune system interactions. *Compr Physiol*. 2014;4:1177-1200.
24. Zhao DB, Dai SM, Liu XP, Xu H. Interstitial inflammation in visceral organs is a pathologic feature of adult-onset Still's disease. *Rheumatol Int*. 2011;31:923-927.

How to cite this article: Hori H, Yabe H, Fukuchi T, Sugawara H. A woman with adult-onset Still's disease and acute intestinal pseudo-obstruction. *Clin Case Rep*. 2021;9:153–157. https://doi.org/10.1002/ccr3.3488