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CASE REPORT

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Long-term maintenance of the mucosal healing induced by azacitidine therapy in a patient with intestinal Behçet's-like disease accompanied with myelodysplastic syndrome involving trisomy 8

Nahoko Tanaka[a], Hirotake Sakuraba[a], Hiroto Hiraga[a,b], Ko Mayama[a], Hidezumi Kikuchi[a], Dai Kishida[c], Yui Akemoto[a,d], Keisuke Hasui[a], Shinji Ota[a], Rina Watanabe[a], Yasuhisa Murai[a], Takato Maeda[a], Kosuke Kamata[a], Tetsuya Tatsuta[a], Manabu Sawaya[a], Daisuke Chinda[a,e], Tatsuya Mikami[a,f], Kazufumi Yamagata[a], Yoh Ishiguro[g], Masanori Tanaka[h] and Shinsaku Fukuda[a,f,g]

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ABSTRACT

Myelodysplastic syndromes (MDSs) are a group of myeloid neoplasms characterized by blood cell deformation and dysfunction, and MDS with trisomy 8 is closely linked with intestinal Behçet's-like diseases. Intestinal Behçet's-like disease is refractory to conventional therapies, including prednisolone, immunomodulators, and anti-tumor necrosis factor α agents. Here, we describe a 56-year-old woman with intestinal Behçet's-like disease ascribed to MDS with trisomy 8 who had multiple intractable intestinal ulcers. She presented with periodic fever and abdominal pain. The genetic analysis showed a heterozygous E148Q mutation in the Mediterranean fever gene. The patient did not tolerate treatment with colchicine because of diarrhea; therefore, azacitidine therapy was initiated. One cycle of azacitidine therapy improved the multiple intestinal ulcers, and the periodic fever and abdominal pain gradually disappeared. After eight cycles of azacitidine therapy, ileocolonoscopy, histological assessment and capsule endoscopy revealed mucosal healing. Azacitidine therapy was continued, and mucosal healing was maintained for more than 2 years. This case suggests that azacitidine therapy which has immunoregulatory effects and epigenetic modulations, might control intestinal Behçet's-like disease associated with MDS involving trisomy 8.

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Myelodysplastic syndrome; trisomy 8; Behçet's disease; azacitidine; mucosal healing

1. Introduction

Myelodysplastic syndromes (MDSs) are a group of myeloid neoplasms characterized by blood cell deformation and dysfunction. Systemic immunological disorders occur in 10–15% of patients with MDS [1], and MDS with trisomy 8 is closely linked with intestinal Behçet's-like diseases [2]. However, the mechanism by which intestinal Behçet's-like disease more frequently occurs in MDS patients with trisomy 8 is still obscure. Recent clinical studies revealed that anti-tumor necrosis factor α (TNFα) therapy dramatically improved intractable disease in patients with common Behçet's disease, such as intestinal, eye, and neural lesions [3]. However, intestinal Behçet's-like disease ascribed to MDS involving trisomy 8 is refractory to conventional therapies, including prednisolone, immunomodulators, and anti-TNFα agents [4–7]. There is no favorable treatment for intestinal Behçet's-like disease in patients with MDS with trisomy 8. Here, we describe a case of intestinal Behçet's-like disease ascribed to MDS in a patient with trisomy 8 who achieved successful endoscopic remission and sustained the remission with azacitidine (AZA) treatment over 2 years.

2. Case report

A 56-year-old woman had a simple oral ulcer, lower abdominal pain, and recurrent high-grade fever since April 2016. She visited another hospital with the chief complaint of the same symptoms and was

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admitted in February 2017. Although she had been diagnosed as having aplastic anemia at 15 years of age, her result of bone marrow aspiration could not be reevaluated in detail. she did not require any treatment. On admission, computed tomography revealed wall thickness of the ascending, transverse, and sigmoid colon and inflammation around these lesions. The ileocolonoscopic findings revealed multiple oval ulcers in the colon and terminal ileum. Because she had a medical history of aplastic anemia, bone marrow aspiration was performed. Her result of bone marrow aspiration indicated the increase of dysplastic hematopoietic cells. And then a clinical diagnosis of MDS was made (Figure 1(A,B)). Chromosomal analysis (Giemsa banding technique) of the bone marrow cells revealed 47, XX, +8 in 12 of 20 dividing cells (Figure 1(C)). Fluorescence in situ hybridization analysis showed the existence of a positive signal of trisomy 8 in 791 of 1000 cells (Figure 1(D)). She was treated with multiple antibiotic drugs, and her simple oral ulcer improved immediately. However, the fever and abdominal pain recurred.

She was transferred to our hospital for assessment of these symptoms in April 2017. We examined her gastrointestinal tract again. Ileocolonoscopic findings revealed multiple oval ulcers in various sites of the colon and terminal ileum. The ulcers were in the active and healing stages (Figure 2(A,B)). Capsule endoscopy revealed multiple small oval ulcers in the duodenum and jejunum (Figure 3(A)). Histological analysis of the biopsy samples of the inflamed lesions showed mild non-specific chronic inflammation and mild fibrosis (Figure 4(A)). Results of the laboratory data were as follows (Table 1): white blood cell count, 1490/μL; hemoglobin level, 9.1 g/dL; platelet count, 268 000/μL; mean corpuscular volume, 95.0 fL; C-reactive protein level, 2.163 mg/dL; and procalcitonin level, 0.25 ng/mL. No pathogens were found in the fecal culture, and the cytomegalovirus pp65 antigen was not detected. Mediterranean fever (MEFV) genetic testing revealed the exon 2 E148Q heterozygote. The human leukocyte antigen (HLA) analysis revealed A2, A24, and B61. Besides, as evidence of Behcet's sign, a needle hyper-reaction was observed. According to the 2003 Behçet's Disease Research Committee of Japan criteria, she became the diagnosis of suspected Behcet's disease. In addition, she became the diagnosis of atypical Familial Mediterranean fever (FMF) according to the criteria provided by the investigation and Research committee 2015 for FMF organized by the Japanese Ministry of Health, Labour and Welfare of Japan.

Those findings led to the diagnosis of MDS with trisomy 8 accompanied by intestinal Behçet's-like disease. Treatment with colchicine (1.0 mg per day) was started. However, this treatment failed because the patient could not tolerate the diarrhea and nausea. The following bone marrow aspiration indicated the increase of dysplastic megakaryocytes. Thus, the treatment which directly regulated the pathogenic factors of MDS was selected. Next, treatment with AZA (90 mg per day) was administered intravenously for 7 days of a 4-week cycle. After one cycle,

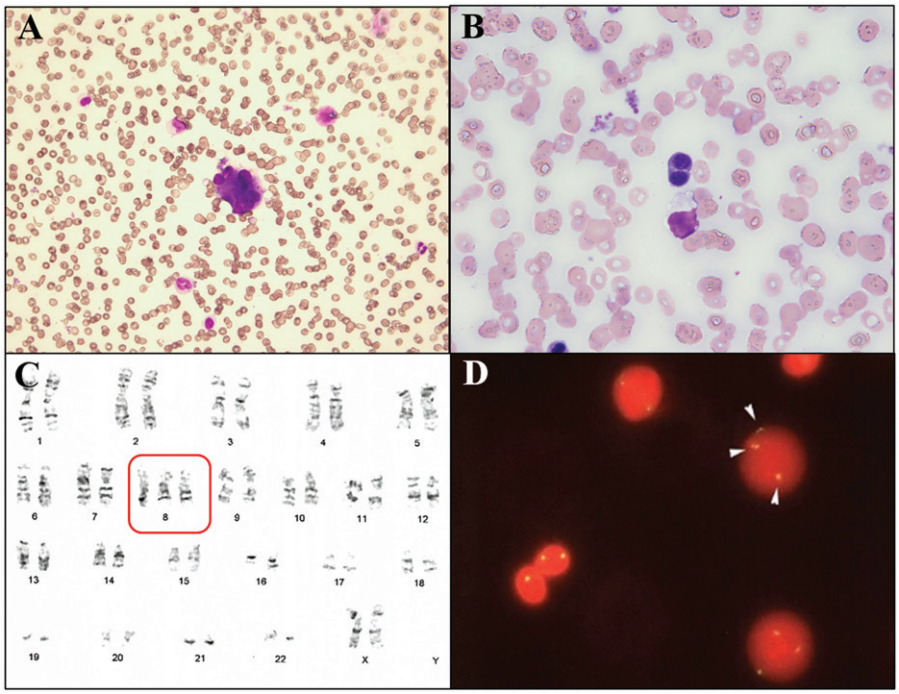

Figure 1. Histological and chromosomal findings of bone marrow. (A) Increased multinucleation in megakaryocytes was observed. (B) Erythroblastic multinuclearity was found. (C) Chromosomal analysis (Giemsa banding technique) and (D) Fluorescence in situ hybridization analysis of the bone marrow cells revealed 47, XX, +8.

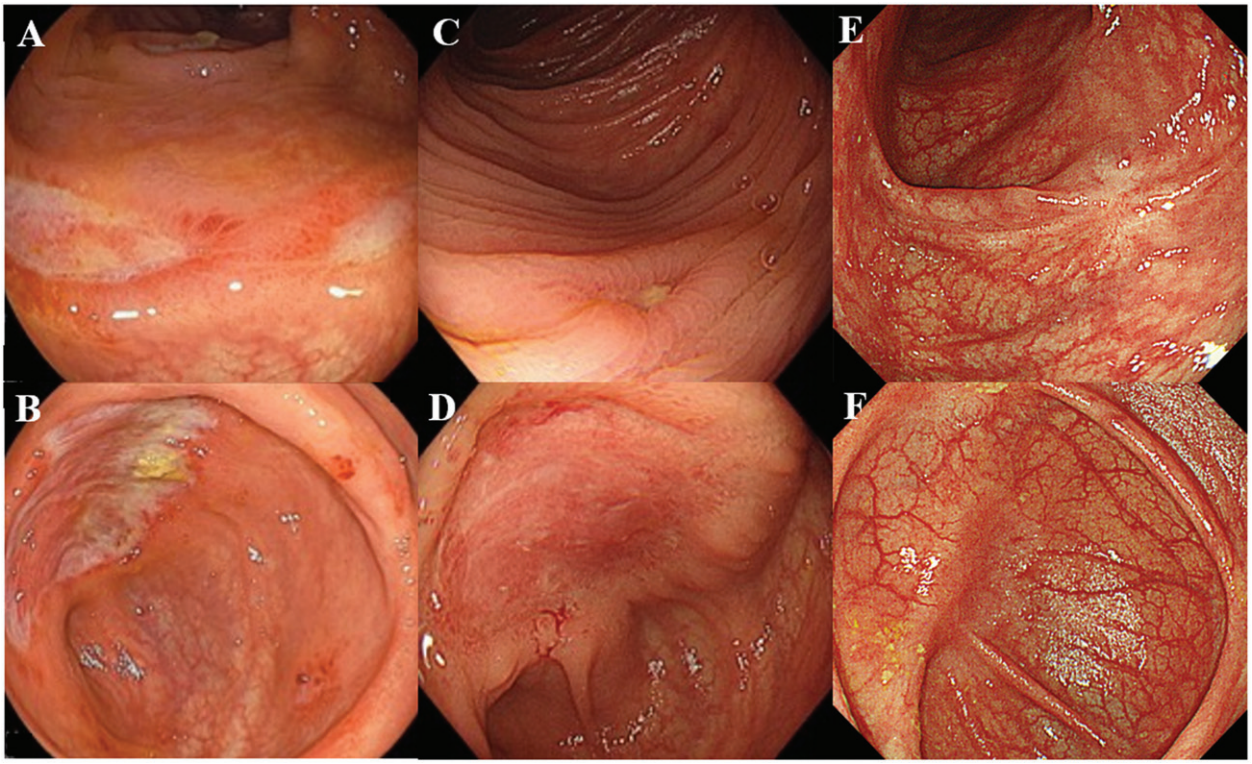

Figure 2. Endoscopic findings before and after treatment with AZA. (A and B) Endoscopic findings before AZA treatment revealing a geographic ulcer in the cecum and oval ulcers in the ascending colon. (C and D) Endoscopic findings after the first cycle of AZA treatment revealing improvement of the ulcers in the cecum and ascending colon. (E and F) Endoscopic findings after eight cycles of AZA treatment showing complete endoscopic remission.

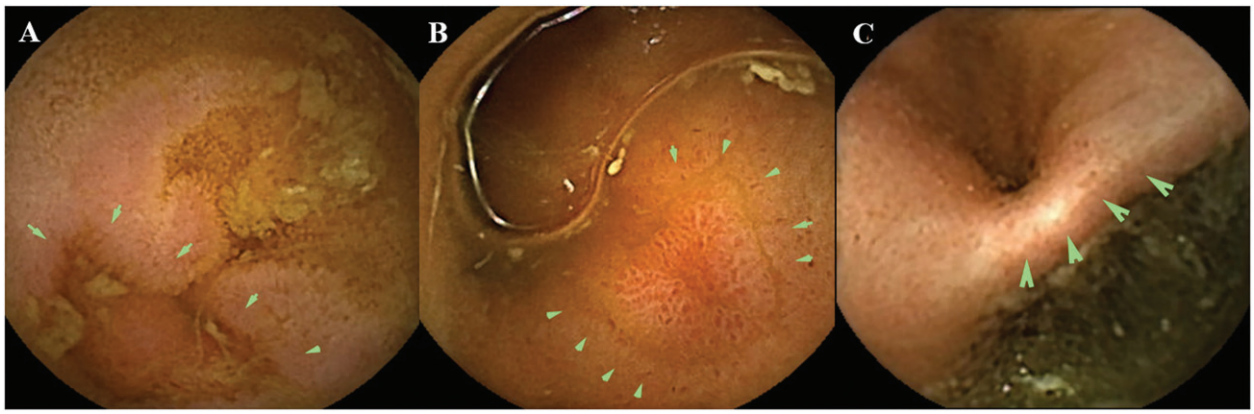

Figure 3. Capsule endoscopic findings before and after 8, 20 cycles of AZA therapy. (A) Capsule endoscopic findings before AZA treatment revealing the oval ulcers in the ileum. (B) Capsule endoscopic findings after 8 cycles or (C) 20 cycles of AZA therapy showing endoscopic remission.

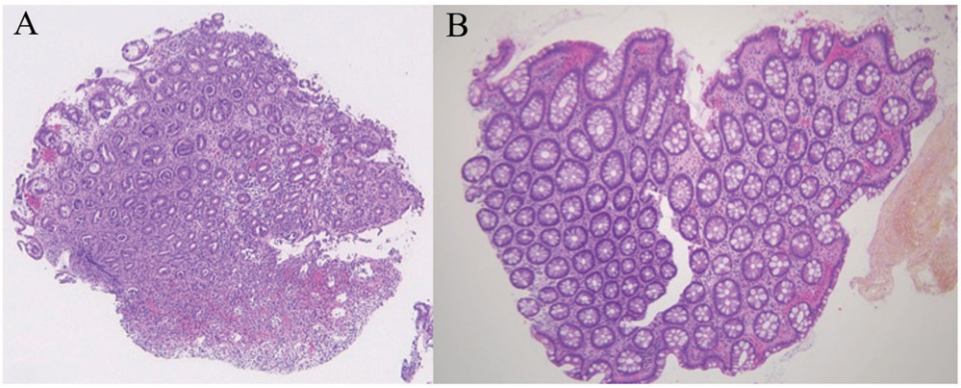

Figure 4. Histological findings of colonic biopsy samples stained with hematoxylin and eosin before and after 8 cycles of AZA therapy (A and B).

Table 1. Primary laboratory data on the initial visit.

WBC	1490	/μL	BUN	13	mg/dL
stab	44	%	Cre	0.58	mg/dL
seg	12	%	CRP	2.163	mg/dL
mono	30	%	PCT	0.25	ng/mL
baso	0	%	β-D glucan	<6.0	pg/mL
eosino	0	%	Ferittin	1238	ng/mL
blast	0	%	T-spot	negative	
RBC	282	10^3 /μL	CMV antigenemia	0/0	
Hb	9.1	g/dL	Fecal culture	negative	
Plt	26.8	10^4/μL	ANA	<40	
TP	6.5	g/dL			
Alb	2.9	g/dL	MEFV gene	Exon 2 E148Q heterozygote	
AST	40	U/L	HLA	A2, A24, B61, DRB1	
ALT	34	U/L		allele 04:05:01,09:01:02	
ALP	206	U/L	Chromosomal analysis	47, XX, +8 12cells/20cells	
LDH	352	U/L	FISH indicating trisomy 8		
γ-GTP	36	U/L	Signal number	2017.3	2018.1
Na	136	mmol/L	0-2	26%	35.1%
K	4.3	mmol/L	3	73%	64.6%
Cl	103	mmol/L	4	0%	0.3%

PCT: procalcitonin; MEFV: Mediterranean fever; FISH: fluorescence in situ hybridization.

follow-up ileocolonoscopy and capsule endoscopy revealed improvement of both small intestinal lesions and colonic lesions (Figure 2(C,D)). Although she developed a moderate grade of thrombocytopenia as an adverse event associated with the first course of AZA therapy, she recovered immediately. She was discharged from our hospital in May 2017. We continued to treat the patient with AZA (45 mg per day) for 5 days of a 4-week cycle.

Before the fourth cycle, she was admitted to our hospital again because of abdominal pain and high-grade fever of more than 39 °C. We started treatment with multiple antibiotic therapy, γ-globulin (5 g per day) for 2 days, hydrocortisone (200 mg per day) for 2 days, and prednisolone (20 mg) for 2 weeks. We reduced the dose of prednisolone by 5 mg for 2 weeks. The high-grade fever disappeared, and abdominal pain gradually diminished. She was discharged from our hospital in October 2017. We continued AZA therapy with a combination of prednisolone in the cycle every 4 weeks.

After the eighth cycle of AZA therapy, we performed follow-up examination of her gastrointestinal tract. Ileocolonoscopy revealed that all ulcer lesions reached endoscopic remission (Figure 2(E,F)). Capsule endoscopy revealed ulcer scar and ileum erosion (Figure 3(B)). She achieved endoscopic remission with histological improvement and did not experience abdominal pain and fever again. The 23 cycles of AZA therapy were continued and the endoscopic remission was sustained over 2 years (Figure 3(C)). Patient provided informed consent to analyze MEFV gene and agreed to publish her clinical characteristics and accompanying images.

3. Discussion

This is the first report of a case in which AZA treatment induced and maintained clinical and endoscopic remission of multiple intestinal ulcers ascribed to MDS involving trisomy 8 over 2 years. This result indicated that treatment for the pathway of MDS itself is one of most effective agents for inflammatory disorders due to MDS.

Immunological disorders are observed in 10–15% patients with MDS [2,8]. Especially, MDS patients with intestinal Behçet's disease-like disease tend to have a high prevalence of trisomy 8. We searched published literature worldwide about intestinal Behçet's-like disease ascribed to MDS accompanied with trisomy 8 using Pubmed, and we summarized the clinical features of 28 patients' reports in Table 2. The main subtype of MDS according to the World Health Organization classifications was the low-risk group including 12 patients with refractory anemia and 8 with refractory cytopenia with multilineage dysplasia. Patients' median age was 54 (range 4–81) years. Twenty of 24 patients (83.3%) had symptoms of Behçet's disease that preceded MDS. HLA-B51 positivity was found in 5 patients (19.2%). Compared with patients with common Behçet's disease, those with MDS involving trisomy 8 had more frequent gastrointestinal lesions, less frequent eye lesions, and a lower prevalence of HLA-B51 [2]. However, the association between chromosomal abnormality of trisomy 8 and intestinal Behçet's-like disease remains unclear. Chen et al. [9] recently reported that upregulated gene expressions of inflammatory cytokines were detected in purified CD34-positive hematopoietic progenitor cells derived from MDS patients with trisomy 8. Therefore, a high prevalence of intestinal Behçet's-like disease in patients with MDS involving trisomy 8 is closely related with increased inflammatory cytokine signaling pathways.

In the present case, recurrent periodic fever and lower abdominal pain were observed, indicating that our patient was complicated with FMF. In fact, our

Table 2. Reported cases with gastrointestinal involvement of Behçet's-like disease caused by MDS with trisomy 8.

Case No.	Age (years)	Sex	Type of MDS	HLA-B51	Preceding symptoms	Treatment	Intestinal ulcer		Outcome of BD (observation period)	First author, year
							Locations	Formations		
1	54	F	RCMD	–	BD	5ASA → 6-MP	Ileocecum	Oval	NC (6 years)	Yanai, 2016
2	41	M	RCMD	–	N.D.	PSL + Anakinra → PSL + AZA	N.D.	N.D.	PR	Fraison, 2016
3	69	M	RAEB2	–	N.D.	PSL→ AZA	N.D.	N.D.	CR	
4	79	F	RCMD	+	BD	PSL → ADA	Ileocecum	Punched out	PR (4 months)	Kimura, 2015
5	81	M	RARS	–	BD	PSL + CSA	Terminal ileum	Oval	Death	Kawano, 2015
6	45	M	RA int-1	+	BD	Surgery → PBSCT	Ileocecum	Punched out	Death	Endo, 2015
7	64	M	RA int-1	–	MDS	Immunosuppressive therapy→ CBT	Terminal ileum andascending colon	Oval	Death	
8	68	F	RCMD/RN	–	BD	PSL → AZA	Terminal ileum	Oval	CR (10 months)	Tanaka, 2013
9	36	M	RA	+	BD	Colchicine, PSL, SASP, MTX,CsA, IFX→surgery	Terminal ileum	Punched out	N.C.	Toyonaga, 2013
10	29	F	RA	–	BD	5-ASA, AZP, CsA,Tac, IFX	Terminal ileum and ascending colon	Punched out	N.C.	
11	24	F	RA	N.D.	BD	surgery	Terminal ileum and colon	Punched out	N.D.	Chen, 2012
12	4	F	N.D.	–	BD	BMT	Transverse and ascending colon	Round ulcers	CR	Shigeumra, 2011
13	34	F	RA		BD	PSL, AZP	N.D.		N.D.	Ahn, 2008
14	53	M	RCMD		BD	AZP	N.D.		N.D.	
15	31	F	RCMD-RS		BD	PBSCT	N.D.		CR	
16	46	F	MDS-U		BD	Total colectomy	N.D.		N.D.	
17	59	M	RCMD int-1	–	BD	Mesalazine, PSL, colchicine, CsA, IFX, AZP	Throughout the small and large intestines	N.D.	CR	Nonami, 2007
18	76	F	RA	+	BD	SASP	Ileocecum	Oval	PR	Kawabata, 2005
19	75	M	RAEB	–	MDS	SASP	Ileocecum	Oval	PR	
20	67	F	RAEB	–	MDS	colchicine, SASP	Ileocecum		Death	
21	28	F	RAEB-t	–	BD	Antibiotics → CBT	Throughout the small and large intestine	Multiple, oval →Longitudinal	CR (13 months)	Tsubota, 2005
22	69	M	RAEB-t	+	BD	5ASA	Ileocecum	N.D.	Death	Ando, 2005
23	64	M	RA	–	BD	PSL, surgery	Ascending colon and terminal ileum	Punched-out ulcers	NC	Fujita, 2005
24	49	M	RCMD	–	MDS	N.D.	N.D.	N.D.	N.D.	Adachi, 2003
25	25	M	RA	–	BD	PSL	Ileocecum	Punched-out	PR	Ogawa, 2001
26	41	F	RA	–	BD	PSL	Ileocecum	Punched-out ulcers	PR	
27	28	F	RA	–	MDS	PSL, SASP, steroid pulse → surgery	Ileocecum	N.D.	PR	Oh, 1999
28	39	F	RA	–	BD	SASP, PSL, steroid pulse, 5-ASA → surgery	Ileocecum	N.D.	N.D.	

No.: number; M: male; F: female; HLA: human leukocyte antigen; MDS: myelodysplastic syndrome; RCMD: refractory cytopenia with multilineage dysplasia; RAEB-1: refractory anemia with excess blasts type 1; RAEB-2: refractory anemia with excess blasts type 2; RARS: refractory anemia with ring sideroblasts; RA int-1: refractory anemia intermediate-1; RN: refractory neutropenia; RCMD-RS: refractory cytopenia with multilineage dysplasia and ringed sideroblasts; MDS-U: myelodysplastic syndrome, unclassified; RA: refractory anemia; RAEB: refractory anemia with excess blasts; RAEB-t: refractory anemia with excess blasts in transformation; BD: Behçet's disease; PSL: prednisolone; CsA: cyclosporine A; 6-MP: 6-mercaptopurine; AZP: azathioprine; AZA: azacitidine; MTX: methotrexate; IFX: infliximab; SASP: salazosulfapyridine; 5-ASA: 5-aminosalicylic acid; ADA: adalimumab; CBT: cord blood transplantation; BMT: bone marrow transplantation; PBSCT: peripheral blood stem cell transplantation; NC: no change; PR: partial response; CR: complete response; N.D.: not described.

patient had a heterozygous MEFV gene E148Q point mutation in exon 2. It is possible that our patient was complicated with FMF. The heterozygous MEFV gene E148Q point mutation was one of major mutations in Japanese FMF patient [10]. However, E148Q mutation is thought to be not enough to cause FMF and the pathogenic role of its mutation is still uncertain. It is very difficult to confirm whether the mutation of E148Q was pathogenic or benign polymorphism. In our patient, E148Q mutation might act as disease modifier to present periodic fever and abdominal pain. Inversely, recent reports showed that the MEFV gene mutations were more frequent in patients with MDS [11]. Recurrent inflammations and activation of NF-kB are known to be associated with the pathogenesis of MDS. Thus, MEFV gene mutations might be one of risk factors related to the pathogenesis of MDS. However, there is no data about relationship between MDS with trisomy 8 and MEFV gene mutations. Further studies are needed to clarify relationship between MEFV gene mutation and MDS.

Regarding therapy, intestinal Behçet's-like disease derived from MDS with trisomy 8 are refractory to conventional therapies, such as mesalazine, corticosteroids, and immunomodulators (Table 2). Currently, anti-TNFα agents, such as infliximab and adalimumab, are effective in common Behçet's disease patients with intestinal lesions [3,12]. However, treatments with anti-TNFα agents did not have a sufficient effect on controlling the disease activity for intestinal Behçet's-like disease comorbid with MDS involving trisomy 8. Therefore, we gave priority to treatment for the MDS itself and started a treatment with AZA not immunosuppressive agents next to colchicine. In our case, AZA treatment induced clinical and endoscopic remission. A few reports showed the efficacy of AZA for treating intestinal Behçet's-like disease associated with MDS involving trisomy 8 (Table 2) [13–16]. However, there was no report that AZA treatment induced and maintained complete both clinical and endoscopic remission of intestinal lesions ascribed to MDS involving trisomy 8. We consider early intervention of MDS itself as one of the factors for favorable efficacy of AZA for a long period. Our patient was scored as having intermediate-1 risk according to the International Prognosis Scoring System, and AZA therapy was started only 6 months after the onset of intestinal Behçet's-like disease. After eight cycles of treatment, anemia improved, and she became transfusion independent. Fluorescence in situ hybridization analysis of the bone marrow showed that the trisomy 8 signals also decreased. Those results indicated that in cases complicated with refractory intestinal lesions derived from MDS, early intervention of MDS itself might be more effective even if the patient does not have high-risk MDS. If the AZA treatment will become failure or leukemic change occur, we need to consider a bone marrow transplantation (BMT). Therefore, it is very important for decrease of adverse events of BMT to induce and maintain mucosal healing which there was no ulcers.

AZA is one of the DNA hypomethylating drugs that can improve the prognosis of high-risk patients with MDS, in whom it is difficult to perform allogenic stem cell transplantation. However, it is still uncertain whether AZA improves the prognosis of patients with low-risk MDS. In the immunological state of MDS, AZA has the effect of immunological suppression by induction of CD4+ FOXP3 + regulatory T cells [17]. The present case indicated that the immunoregulation by AZA therapy was effective for intestinal lesions associated with MDS trisomy 8.

In conclusion, we described a case of MDS-associated intestinal Behçet's-like disease in which mucosal healing was successfully induced by AZA treatment and its therapy maintained mucosal healing for a long period. Early intervention of causative therapies for MDS itself should be considered in patients with intestinal Behçet's-like disease complicated with MDS and might result in the better long-term course. Further studies are needed to clarify the pathogenesis of intestinal Behçet's-like disease associated with MDS involving trisomy 8 and to confirm the efficacy and safety of AZA treatment.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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References

[1] Voulgarelis M, Giannouli S, Ritis K, et al. Myelodysplasia-associated autoimmunity: clinical and pathophysiologic concepts. Eur J Clin Invest. 2004;34(10):690–700.
[2] Esatoglu SN, Hatemi G, Salihoglu A, et al. A reappraisal of the association between Behçet's disease, myelodysplastic syndrome and the presence

of trisomy 8: a systematic literature review. Clin Exp Rheumatol. 2015;33:S145–S151.
[3] Vallet H, Riviere S, Sanna A, et al. Efficacy of anti-TNF alpha in severe and/or refractory Behçet's disease: multicenter study of 124 patients. J Autoimmun. 2015;62:67–74.
[4] Kimura M, Tsuji Y, Iwai M, et al. Usefulness of adalimumab for treating a case of intestinal Behçet's disease with trisomy 8 myelodysplastic syndrome. Intest Res. 2015;13(2):166–169.
[5] Kawano S, Hiraoka S, Okada H, et al. Clinical features of intestinal Behçet's disease associated with myelodysplastic syndrome and trisomy 8. Acta Med Okayama. 2015;69:365–369.
[6] Toyonaga T, Nakase H, Matsuura M, et al. Refractoriness of intestinal Behçet's disease with myelodysplastic syndrome involving trisomy 8 to medical therapies – our case experience and review of the literature. Digestion. 2013;88(4):217–221.
[7] Nonami A, Takenaka K, Harada M, et al. Successful treatment of myelodysplastic syndrome (MDS)-related intestinal Behçet's disease by upfront cord blood transplantation. Intern Med. 2007;46(20):1753–1756.
[8] Aggarwal S, van de Loosdrecht AA, Alhan C, et al. Role of immune responses in the pathogenesis of low-risk MDS and high-risk MDS: implications for immunotherapy. Br J Haematol. 2011;153(5): 568–581.
[9] Chen G, Zeng W, Miyazato A, et al. Distinctive gene expression profiles of CD34 cells from patient with myelodysplastic syndrome characterized specific chromosomal abnormalities. Blood. 2004;15: 4210–4218.
[10] Migita K, Agematsu K, Yazaki M, et al. Familial Mediterranean fever: genotype-phenotype correlations in Japanese patients. Medicine (Baltimore). 2014; 93(3):158–164. May
[11] Oktenli C, Sayan O, Celik S, et al. High frequency of MEFV gene mutations in patients with myeloid neoplasm. Int J Hematol. 2010;91(5):758–761.
[12] Hisamatsu T, Naganuma M, Matsuoka K, et al. Diagnosis and management of intestinal Behçet's disease. Clin J Gastroenterol. 2014;7(3):205–212.
[13] Endo M, Sekikawa A, Tsumura T, et al. A case of myelodysplastic syndrome with intestinal Behçet's disease-like symptoms treated by prednisolone and azacitidine. Am J Case Rep. 2015;16:827–831.
[14] Tanaka H, Shimizu N, Nakaseko C, et al. Successful treatment by azacitidine therapy of intestinal Behçet's disease associated with myelodysplastic syndrome. Int J Hematol. 2013;97(4): 520–524.
[15] Fraison JB, Mekinian A, Grignano E, et al. Efficacy of azacitidine in autoimmune and inflammatory disorders associated with myelodysplastic syndromes and chronic myelomonocytic leukemia. Leuk Res. 2016;43:13–17.
[16] Frietsch JJ, Dornaus S, Neumann T, et al. Paraneoplastic inflammation in myelodysplastic syndrome or bone marrow failure: case series with focus on 5-azacytidine and literature review. Eur J Haematol. 2014;93(3):247–259.
[17] Goodyear OC, Dennis M, Jilani NY, et al. Azacitidine augments expansion of regulatory T cells after allogeneic stem cell transplantation in patients with acute myeloid leukemia (AML). Blood. 2012;119(14):3361–3369.