

# Clinical Association Between Behçet Syndrome, Cytopenia, and Acquired Trisomy 8: a New Clinical Syndrome?

Yan Shen (✉ [shenyan1212@sina.com](mailto:shenyan1212@sina.com))

Fudan University Hua Dong Hospital Division of Rheumatology Allergy and Immunology <https://orcid.org/0000-0002-9744-3224>

**Dan Luo**

Huadong Hospital Affiliated to Fudan University

**Hai-fen Ma**

Huadong Hospital Affiliated to Fudan University

**jian-fei Cai**

Huadong Hospital Affiliated to Fudan University

**Jun Zou**

Huadong Hospital Affiliated to Fudan University

**Zhi-jun Bao**

Huadong Hospital Affiliated to Fudan University

**Jian-long Guan**

Huadong Hospital Affiliated to Fudan University <https://orcid.org/0000-0002-6481-480X>

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## Research Article

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## Abstract

**Objectives:** Behçet syndrome (BS) is heterogeneous with clinical variability across ethnicities and geographic locations. This study analyzed the clinical characteristics of BS associated with cytopenia and trisomy 8.

**Methods:** This was a retrospective study of Chinese BS patients in the Shanghai Behçet's disease database who were diagnosed with cytopenia and trisomy 8 between October 2012 and April 2019. All subjects fulfilled the International Study Group (ISG) criteria or the International Criteria for Behçet's Disease (ICBD).

**Results:** Twenty-one patients with BS had cytopenia with trisomy 8; 16 (16/21, 76.2%) were diagnosed with myelodysplastic syndrome (MDS). Compared with 1,147 patients with BS without cytopenia, patients with BS and trisomy 8/cytopenia were more likely to be female (23.8% vs 51.8%,  $p = 0.011$ ), older ( $37.9 \pm 12.8$  vs  $45.1 \pm 12.0$ ,  $p = 0.007$ ), have fewer skin lesions (33.3% vs 56.7%,  $p = 0.033$ ), fever (52.4% vs 1.1%,  $p < 0.001$ ), have higher C-reactive protein, have higher erythrocyte sedimentation rate (ESR), and display a higher rate of gastrointestinal (GI) ulceration (61.9% vs 9.2%,  $p < 0.001$ ). By contrast, they had a lower leukocyte count, lower hemoglobin levels, and a lower platelet count ( $p < 0.05$  for all comparisons). Ulcers in the ileocecal region were more frequently seen in intestinal patients with BS with trisomy 8 than in patients with BS without cytopenia (100.0% vs 41.8%;  $p = 0.002$ ). Compared with 54 patients with MDS without BS symptoms, those with BS and trisomy 8-cytopenia were more likely to be female (23.8% vs 70.4%,  $p < 0.001$ ) and younger ( $37.9 \pm 12.8$  vs  $67.2 \pm 12.4$ ,  $p = 0.001$ ). In the follow-up, three patients with BS with trisomy 8 (3/21, 14.3%) died, which is a higher rate than in patients with BS (5/1147, 0.44%) and much lower than in patients with MDS (13/54, 24.1%).

**Conclusions:** The data on patients with BS with cytopenia and trisomy 8 were different from BS or MDS in epidemiology, clinical performance, and prognosis. BS with cytopenia and acquired trisomy 8 may be a new clinical syndrome.

## 1. Introduction

Behçet syndrome (BS) is a variant of vasculitis. Its basic clinical feature is recurrent oral ulcers as an initial symptom, which is gradually associated with vulvar ulcers, nodular erythema, and other skin and mucous membrane lesions. It may be selective for ophthalmitis, intestinal ulcer, aortic regurgitation, venous thrombosis, arterial stenosis, aneurysm, arthritis, or cytopenia. BS was first comprehensively described by the dermatologist Hulusi Behçet in 1937. The disease has a high prevalence in countries along the ancient Silk Road, a route of travel and commerce extending from the eastern Mediterranean to East Asia [1].

Not much attention has been paid to changes in the blood system and rheumatism, which are common manifestations of the disease. Some diseases begin with hematological abnormalities while others occur simultaneously or successively with hematological abnormalities, which may be partially related to drug use. There has been a recent increase in the number of case reports showing an association between trisomy 8 and intestinal BS with myelodysplastic syndrome (MDS) [2, 3]. MDS is a blood disorder characterized by impaired generation and maturation of hematopoietic cells in the bone marrow, leading to peripheral blood cytopenia [4]. It may also progress into acute leukemia [4]. Previously, BS and MDS were considered two different diseases. However, there may be some connection between them since patients with MDS can develop autoimmune diseases such as BS, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), relapsing polychondritis, and vasculitis [5–8]. Indeed, most patients with BS and MDS have GI ulcers [2, 9]. It is also unclear whether immunosuppressive agents might affect this association [10].

Our team reported 16 patients with BS with MDS and found that gastrointestinal (GI) ulceration and trisomy 8 were more common in these patients [11]. In this study, we focused on patients with BS with cytopenia and trisomy 8 and investigated those patients' characteristics.

## 2. Materials And Methods

### 2.1. Study Design

This was a retrospective follow-up study of patients with BS in the Shanghai Behçet Syndrome database who had hematologic abnormalities and trisomy 8 and was diagnosed between October 2012 and April 2019. All patients had active BS and underwent endoscopic examination. This work was conducted in accordance with the Declaration of Helsinki (2000). The Institutional Review Board of Huadong Hospital approved the study protocol. The Board waived the need for individual consent.

### 2.2. Patients

During the study period, 1,168 patients with BS (with complete clinical and laboratory data) received medical care at Fudan University Huadong Hospital. All patients had active BS and were diagnosed according to the International Criteria for Behçet Disease (ICBD) [12] (the 1990 criteria were used because the 2014 criteria [13] were established during the study period). BS was diagnosed in the presence of recurrent oral ulceration and two of the following criteria: 1) recurrent genital ulceration; 2) anterior uveitis, posterior uveitis, cells in vitreous or retinal vasculitis; and 3) a positive pathergy test [12]. This retrospective study also included a cohort of 54 patients with MDS diagnosed from January 2016 to April 2020. MDS was diagnosed and classified according to the WHO classification [14], which takes into consideration morphologic, immunophenotypic, cytogenetic, fluorescence in situ hybridization (FISH), and molecular data.

### 2.3. Endoscopy

Two experienced gastroenterologists performed endoscopic examinations using GIF H260 and CF-H260A1 endoscopes (Olympus, Tokyo, Japan) for upper and lower GI tract examinations, respectively. During endoscopy, two biopsies were taken from the gastric antrum for rapid urease tests and histological examination.

## 2.4 Description of Cytopenia

A hemoglobin count of < 13 g/dL in men and < 12 g/dL in women was defined as anemia, and leukocyte counts of < 4,000/mm<sup>3</sup> ( $\geq 2$  occasions) were defined as leucopenia. Likewise, an absolute neutrophil count of < 1,500/mm<sup>3</sup> ( $\geq 2$  occasions) was defined as neutropenia, and a platelet (PLT) count of < 100,000/mm<sup>3</sup> was defined as thrombocytopenia. The presence of any such values was acknowledged as meeting the criteria for cytopenia.

## 2.5. Cytogenetics

Bone marrow chromosome analysis was performed using chromosome-banding procedures. At least 20 metaphases were analyzed. Abnormal clones were described according to the 2006 International System for Human Cytogenetic Nomenclature (ISCN) [15], and aberrations were counted following the International Working Group on MDS Cytogenetics (IWGMC) consensus guidelines [16]. FISH analysis was performed on short-term cultured bone marrow. Sample preparations and hybridizations were performed according to the manufacturer's recommendations, using commercially available probes (Vysis Inc., Downers Grove, IL, USA). At our hospital, systematic screening for trisomy 8 was performed on patients with BS with hemocytosis. Karyotyping was performed on these patients based on clinical suspicion of trisomy 8. Blood marrow aspiration was done to perform karyotyping, and a minimum of 500 interphase cells were analyzed. If the cells with an abnormal signal were < 5%, 1,000 interphase cells were screened. Normal control values were previously established using five normal samples of bone marrow donors and 15 bone marrow samples of patients with iron deficiency anemia but with normal karyotype.

## 2.6. Clinical Evaluation and Laboratory Findings

The presence of GI symptoms, such as abdominal pain, melena/hematochezia, diarrhea, weight loss, perforation, ileus, or bleeding, and extra-GI symptoms, such as genital ulcers, uveitis, dermatological lesions, neurological involvement, peripheral vasculitis, and joint involvement, were recorded at the time of diagnosis. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, and peripheral blood counts were also recorded.

## 2.7. Statistical Analysis

Continuous data were tested for normal distribution using the Kolmogorov–Smirnov test. Normally distributed continuous data were presented using mean  $\pm$  standard deviation and analyzed using Student's *t*-test. Nonnormally distributed data were presented as a median (range) and analyzed using the Mann–Whitney U test. Categorical data were presented as frequencies and analyzed using the chi-squared test or Fisher's exact test, as appropriate. Factors found to be significantly different between the groups were integrated into a logistic regression model to identify independently associated factors for hematologic abnormality development. SPSS 22.0 (IBM Corp., Armonk, NY, USA) was used for statistical analyses. Two-sided *p*-values < 0.05 were considered statistically significant.

## 3. Results

### 3.1. Patient Characteristics

Of the 1,168 patients with BS, there were 21 with BS and trisomy 8 and 1,147 with BS without trisomy 8. One female with BS presented with MDS and cervical cancer. Among the 21 patients with BS with cytopenia, 16 were diagnosed with MDS (76.2%). BS was diagnosed before hematologic abnormality in eight (38.1%) patients, after hematologic abnormality in six (28.6%), and concomitantly with hematologic abnormality in seven (33.3%) (Table 1).

Table 1  
Clinical characteristics of 21 patients with Behçet disease and hematologic disorder.

Case No.	Age/sex	BD symptoms	MDS type	Karyotype and FISH	Endoscopic findings	Distribution pattern	BD duration (years)	MDS duration (years)	Treatment	Cytoto prior to
1	47/F	IOGA	MDS-RCMD	47XX + 8	Terminal ileum, rectum, CU	Multi-segmental	20	20	Prednisone Cyclosporine Thalidomide Infliximab	-
2	35/F	IOGS	MDS-U	47XX + 8	Terminal ileum	Multi-segmental	6	10	Prednisone Cyclosporine Thalidomide Infliximab	-
3	35/M	IOG	MDS-U	47XX + 8	Terminal ileum	Single	5	1	Prednisone Infliximab	Cyclosporine Thalidomide
4	68/F	IOSA	Anemia	47XX + 8	Terminal ileum, ileocecal valve	Multi-segmental	40	1	Prednisone Cyclosporine Infliximab	MMF Thalidomide
5	46/F	IOGPA	MDS-U	47XX + 8	Ileocecal valve	Single	10	10	Prednisone Cyclosporine Thalidomide Infliximab	-
6	65/M	IOG	MDS-RAEB	48,XY,+8,+19,del(20)(q11.2)	Terminal ileum, CU	Multi-segmental	5	0.5	Prednisone Cyclosporine Thalidomide Infliximab	-
7	56/F	IOPS	MDS-RCUD-RN	47XX + 8	Ileocecal valve	Single	14	20	Prednisone Cyclosporine Thalidomide Infliximab	-
8	58/F	IOGS	MDS-RCMD	47XX + 8	Terminal ileum, CU, small intestine	Multi-segmental	36	20	Prednisone Cyclosporine Infliximab	Thalidomide
9	48/F	IOGP	MDS-RCMD	47XX + 8	Ileocecal valve	Single	8	7	Prednisone Cyclosporine Thalidomide Infliximab	-
10	34/F	IOG	MDS-RCUD	47XX + 8,-20,add(21)(q21)	Terminal ileum, CU	Multi-segmental	4	4	Prednisone Cyclosporine Thalidomide Infliximab	-
11	36/F	OG	Leucopenia	47XX + 8	-	-	4	10	Thalidomide Colchicine	-
12	44/F	OGP	MDS-U	47XX + 8	-	-	10	20	Thalidomide Colchicine	-

I: Intestinal involvement; O: oral ulcer; G: genital ulcer; S: skin lesion; A: arthritis; P: pathergy. MDS-U: MDS-unclassifiable, RCMD: refractory cytopenia with multilineage dysplasia, RAEB: refractory anemia with excess of blasts, RCUD: refractory cytopenia with unilineage dysplasia. CU: colonic ulcers. MMF: mycophenolate mofetil.

Case No.	Age/sex	BD symptoms	MDS type	Karyotype and FISH	Endoscopic findings	Distribution pattern	BD duration (years)	MDS duration (years)	Treatment	Cytoto prior to
13	40/F	OG	Leucopenia + thrombocytopenia	47XX + 8	-	-	10	10	Cyclosporine Thalidomid	-
14	59/M	OGA	MDS-U	47XX + 8	-	-	10	1	Prednisone Cyclosporine Thalidomide	-
15	30/F	IOGS	Leucopenia + thrombocytopenia	47XX + 8	Terminal ileum	Single	5	5	Prednisone Cyclosporine Thalidomide Infliximab	Thalidomide
16	42/F	OGS	MDS-RAEB	47XX + 8	-	-	3	5	Prednisone Cyclosporine Thalidomide	-
17	46/F	OGS	MDS-RAEB	47XX + 8	-	-	10	1	Prednisone Cyclosporine Thalidomide	-
18	25/F	OG	MDS-RCMD	47XX + 8	-	-	10	10	Prednisone Cyclosporine Thalidomide	-
19	52/M	IOG	MDS-U	47XY + 8	Terminal ileum, CU	Multi-segmental	7	2	Prednisone Cyclosporine Thalidomide Infliximab Tocilizumab	Thalidomide
20	56/F	IOA	MDS-RCMD	48XX + 8 + 9	Terminal ileum, small intestine	Multi-segmental	5	0.5	Prednisone Cyclosporine Thalidomide Tocilizumab	-
21	39/M	OGP	Leucopenia + thrombocytopenia	47XX + 8/46XY	-	-	10	7	Thalidomide	-

I: Intestinal involvement; O: oral ulcer; G: genital ulcer; S: skin lesion; A: arthritis; P: pathergy. MDS-U: MDS-unclassifiable, RCMD: refractory cytopenia with multilineage dysplasia, RAEB: refractory anemia with excess of blasts, RCUD: refractory cytopenia with unilineage dysplasia. CU: colonic ulcers. MMF: mycophenolate mofetil.

All patients were clinically and cytogenetically evaluated once when BS was active, with or without treatment. Based on the WHO classification, six patients had MDS-unclassifiable (MDS-U), five had refractory cytopenia with multilineage dysplasia (RCMD), three had refractory anemia with excess of blasts (RAEB), and two had refractory cytopenia with unilinear dysplasia (RCUD). Among the other five patients with undiagnosed MDS, one had anemia, one had leucopenia, and three had leucopenia and thrombocytopenia.

### 3.2. Clinical Features of MDS, BS with Trisomy 8, and BS without Trisomy 8

Table 2 shows the demographic and clinical features of patients with BS, BS with trisomy 8, and MDS. Among the 21 patients, five were male and 16 were female. The mean age at diagnosis was 37.9 ± 12.6 years for BS, 45.1 ± 12.0 years for BS with trisomy 8, and 67.2 ± 12.4 years MDS. There were great differences in gender and age between the three groups ( $p < 0.05$ ).

Table 2  
Clinical characteristics between BS patients and BS with/without hematologic disorder and trisomy 8 and MDS patients.

	<b>BS with hematologic disorder and trisomy 8 (n = 21)</b>	<b>BS without hematologic disorder and trisomy 8 (n = 1147)</b>	<b>MDS (n = 54)</b>
Age, years mean (SD)	45.1 ± 12.0*	37.9 ± 12.8	67.2 ± 12.4**
Male (%)	5 (23.8) *	594 (51.8)	38 (70.4) **
Oral ulcer	21 (100)	1051 (91.6)	-
Genital ulcer	18 (85.7)	796 (69.4)	-
Ocular lesion	0 (0)	157 (13.7)	-
Arthritis	6 (28.6)	243 (21.2)	-
Skin lesions	7 (33.3) *	650 (56.7)	-
Positive pathergy test	5 (23.8)	55 /125 (44.0)	-
Central nervous system	1 (4.8)	18 (1.6)	-
Vascular lesions	0 (0)	35 (3.1)	-
GI involvement	13 (61.9) *	110 (9.2)	0 (0) **
Fever	11 (52.4) *	13 (1.1)	10 (18.5) **
<b>Laboratory findings at diagnosis of BS or MDS</b>			
ESR (mm/h)	52.7 ± 33.9*	22.1 ± 24.4	
CRP (mg/L)	34.9 ± 34.5*	12.9 ± 21.5	
WBC (10 <sup>9</sup> /L)	3.2 ± 1.2*	7.4 ± 2.5	
Hemoglobin (g/L)	99.4 ± 18.8*	132.4 ± 19.4	
Platelets (10 <sup>9</sup> /L)	52.7 ± 33.9*	240.1 ± 72.8	
*P < 0.05. BS with hematologic disorder and trisomy 8 compared to BS.			
** P < 0.05. BS with hematologic disorder and trisomy 8 compared to MDS.			
GI, gastrointestinal; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; WBC, white blood cells.			

In the BS with trisomy 8 group, oral ulcers were the most common finding (100%), followed by genital ulcers (87.5%), GI involvement (61.9%), fever (52.4%), and skin lesions (33.3%). Uveitis and vascular lesions, which are common features of BS, were not recorded in the BS with trisomy 8 group. In the univariate analyses, BS with trisomy 8 patients were significantly more likely to be female, older, have a fever, display GI involvement, and have fewer skin lesions than patients with BS without trisomy 8 ( $p < 0.01$ ) (Table 2). Leukocyte count, hemoglobin levels, and platelet count were significantly lower, and ESR and CRP significantly higher, in BS with trisomy 8 patients than in those with BS without trisomy 8 ( $p < 0.05$ ).

### 3.3. Characteristics of Patients with BS with or without Trisomy 8 in GI Involvement

Among the 1,147 patients with BS, 110 had GI BS without cytopenia, and 13 had GI BS with cytopenia and trisomy 8. Table 3 shows the demographic and clinical features of the two groups. In patients with GI BS and trisomy 8, oral ulcers were the most common finding (100%), followed by genital ulcers (80.0%), fever (60.0%), skin lesions (40.0%), positive pathergy tests (30.0%), and arthralgia (30.0%). Patients with GI BS and trisomy 8 were significantly more likely to have intestinal ulcers in the ileocecal region than patients with BS with GI without MDS (100.0% vs 48.9%;  $p = 0.032$ ). Figure 1 shows the typical colonoscopy results of patients with GI BS and trisomy 8. In the univariate analyses, patients with GI BS and trisomy 8 were more likely to be female and older than patients with GI BS but no trisomy 8 ( $p < 0.01$ ) (Table 3). The former were likely to have a lower leukocyte count, hemoglobin level, and platelet count, and higher ESR levels, than the latter ( $p < 0.05$ ). There was no statistically significant difference in GI symptoms and CRP level between the two groups.

Table 3  
Symptoms and laboratory findings in patients with intestinal BS according to hematologic abnormality and trisomy 8

	Intestinal BS with hematologic abnormality trisomy 8 (n = 13)	Intestinal BS without hematologic abnormality (n = 110)	P
Age at diagnosis of intestinal BS (years)	48.3 ± 12.4	36.5 ± 15.1	0.008*
Male (%)	3 (23.1)	58 (52.7)	0.041*
Duration (years)	10.2 ± 9.5	9.3 ± 9.2	0.129
Systemic signs			
Oral ulcer	13 (100)	108 (98.2)	> 0.99
Genital ulcer	11 (84.6)	69 (62.7)	0.708
Ocular lesion	0 (0)	3 (3.2)	> 0.99
Arthralgia	3 (23.1)	22 (23.4)	0.694
Skin lesions	4 (30.8)	42 (44.7)	> 0.99
Positive pathology test	3 (23.1)	20 (21.3)	0.608
Central nervous system	0 (0)	1 (0)	-
Symptoms of GI involvement			
Abdominal pain	8 (61.5)	82 (87.2)	0.184
Melena/hematochezia	4 (30.8)	30 (31.9)	0.717
Diarrhea	5 (38.5)	46 (48.9)	> 0.99
Weight loss	8 (61.5)	44 (46.8)	0.083
Fever	9 (69.2)	8 (8.5)	0.002*
Perforation	0 (0)	8 (8.5)	> 0.99
Ileus	1 (7.7)	8 (8.5)	> 0.99
Location of intestinal ulcers			
Esophagus	0 (0)	18 (19.1)	0.336
Ileocecal	13 (100)	46 (41.8)	0.002*
Small intestine	1 (7.7)	6 (6.4)	0.548
Colon	1 (7.7)	24 (25.5)	0.426
Laboratory findings at BS diagnosis			
ESR (mm/h)	51.14 ± 31.19	26.78 ± 23.64	0.005*
CRP (mg/L)	29.03 ± 33.53	21.21 ± 33.07	0.327
WBC (10 <sup>9</sup> /L)	3.7 ± 2.5	6.8 ± 2.9	0.003*
Hemoglobin (g/L)	89.7 ± 17.7	129.4 ± 19.9	< 0.001*
Platelets (10 <sup>9</sup> /L)	163.9 ± 116.4	243.1 ± 92.7	< 0.001*

\*P < 0.05. BD: Behçet disease; GI: gastrointestinal; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; WBC: white blood cells.

### 3.4. Treatment and Outcome of BS with Cytopenia and Trisomy 8

Overall, 21/21 (100%) patients with BS with trisomy 8 had received treatment, 17 (81.0%) with steroids (prednisone, median dose 30 mg/day [IQR 20–48]). Along with steroids, the immunosuppressive drugs that were used included thalidomide (n = 18), cyclosporine (n = 17), infliximab (n = 11), and colchicine (n = 2). In a median follow-up of 37 months (range, 17 to 72 months), 3/21 (33.3%) cases showed complete responses to first-cycle therapy (about three months) and achieved clinical improvements for BS and hematologic abnormalities. Meanwhile, 2/21 (9.5%) cases showed no improvement, not only in BS but also in hematologic abnormality. Several cases (14/21; 66.7%) showed stability in BS and cytopenia. In total, 3/21 (mortality rate: 14.3%) patients died during follow-up: one from infectious complications, one from hematological complications, and one with an undetermined cause of death. From the follow-up data, three

patients with BS with trisomy 8 (3/21, 14.3%) died, which is a much higher rate than patients with BS (5/1147, 0.44%) and much lower than patients with MDS (13/54, 24.1%) ( $p < 0.01$ ).

## 4. Discussion

In this retrospective study, we focused on a unique group of patients with BS that had a prominent feature of cytopenia and trisomy 8. This study is the first to report on patients with BS with trisomy 8 from the Shanghai Behçet Syndrome Database. In terms of gender and age, patients with BS with cytopenia and trisomy 8 were more likely to be female and older than patients with BS and much younger than patients with MDS. The incidence of gastrointestinal (GI) ulceration was much higher than in BS and patients with MDS, and ulcers in the ileocecal region were more frequently seen in intestinal patients with BS and trisomy 8. More than half of the patients were diagnosed with MDS. The mortality rates of BS patients with trisomy 8 were different from those of BS and MDS patients, which were much higher than those of patients with BS and much lower than those of patients with MDS.

BS is a complex, multisystemic disorder with unknown etiology and unique geographic distribution. There has been controversy over whether to call it a "disease" or "syndrome." Many studies have shown that it is composed of multiple phenotypes, such as skin-mucosa, eye, gastrointestinal, vascular, and neurological involvement [17]. Hematologic involvement or hematologic malignancies are frequently encountered in rheumatic diseases, such as systemic lupus erythematosus (SLE) and Sjögren syndrome (SS) [18]. Until now, however, no paper has reported hematologic involvement as a particular phenotype in BS, and there has been little research on hematologic involvement in large BS samples. Some studies have even referred to it as a "Behçet-like disease" [19, 20]. Analyses of several case reports have shown an association between trisomy 8 and intestinal BD with MDS [2, 3, 21, 22]. Indeed, trisomy 8 in BD and MDS has been reported in 87% of patients [2], compared to 5–7% of patients with primary MDS but without BD [23]. Trisomy 8 with BD but without MDS has also been reported [24, 25].

Trisomy 8 is considered a secondary or late event in the MDS transformation process [26, 27]. The precise mechanisms underlying the tumorigenesis remain unclear, although a relationship has been observed between trisomy 8 and symptoms related to BD, both in the present study and in the literature. As BD-MDS patients have high frequencies of intestinal lesions and trisomy 8, as well as a higher expression of several cytokines controlled by genes located on chromosome 8, trisomy 8 may predispose patients with cytopenia to BD.

According to our data, most of the BS with trisomy 8/cytopenia patients were isolated trisomy 8 (19/21, 90.5%). Some patients lacking morphological criteria in the bone marrow were not considered as patients with MDS. Isolated trisomy 8 has been discussed in some studies [28, 29]. It can be a constitutional condition as a constitutional mosaicism (cT8M) in healthy people, and it was not considered a tumor marker in certain studies. Some studies have suggested that trisomy 8 could be present as a cT8M in myeloid malignancies. In our retrospective study, we found that BS associated with trisomy 8/cytopenia had a particular clinical phenotype, mainly represented by frequent gastrointestinal involvement, less ocular and central neurological impairment, and unique characteristics in terms of gender, age, and survival rate. We suggest that BS with cytopenia and trisomy 8 could be a new entity characterized by ulcerative gastrointestinal involvement. Newer genomic technologies, such as single-nucleotide polymorphism array and next-generation sequencing, may reveal the heterozygous deletions resulting in haploinsufficient gene expression involved in the pathogenesis of these GI-BS patients with trisomy 8.

## 5. Conclusion

BS with trisomy 8 can be associated with a particular phenotype of ulcerative digestive disease, which has unique characteristics in terms of gender, age, and survival rate. Thus, it should be considered a distinct disease. Differential diagnosis may sometimes be difficult. Further studies are needed to determine the role of overexpressed trisomy 8 genes, identify the underlying mechanisms, and determine the best treatment regimen.

## Declarations

## Conflicts of interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

## Funding

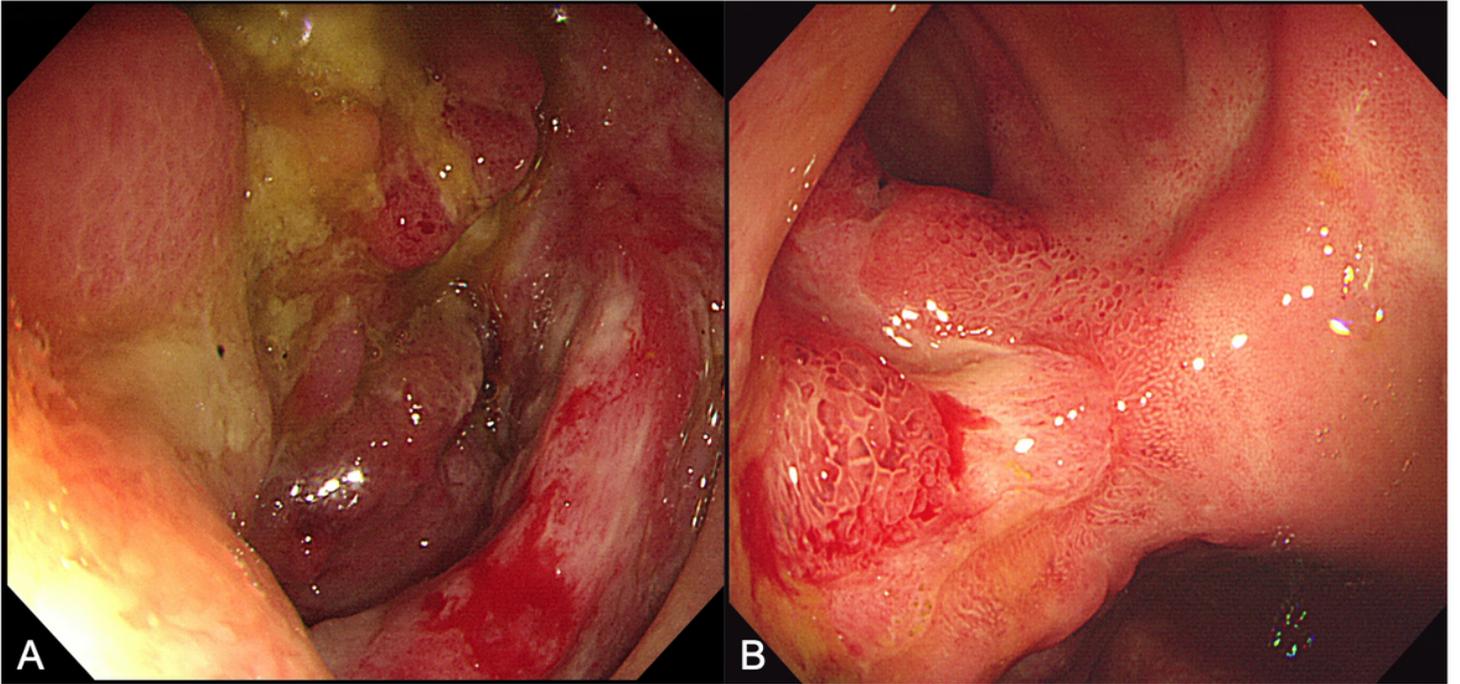
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## Figures



**Figure 1**  
In two BS patients with trisomy 8, typical colonoscopy results of gastrointestinal involvement showed severe open ulcers in the ileocecal area (A), huge round edema at the end of the ileum, deep layer and diffuse erosion ulcer (B).