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ORIGINAL ARTICLE

Aplastic anemia associated with Crohn's disease: a tertiary center retrospective study

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Abstract

Aplastic anemia (AA) has been reported to be associated with inflammatory bowel disease (IBD), but mostly with ulcerative colitis (UC). Little is known about the associations between AA and Crohn's disease (CD). We aim to determine the portraits of patients with AA-CD. Among a total of 657 patients with CD registered in Xijing Hospital of Digestive Diseases IBD center from January 2008 to October 2018, the patients diagnosed with concurrent AA were reviewed. Clinical presentation, medical history, endoscopic features, response to treatment, and prognosis in this set of patients were collected. Six male patients confirmed as CD associated with AA were identified. The incidence rate was 0.91% for CD associated with AA in our series. Average age at diagnosis of CD and AA was 41.5 and 39.2 years old, respectively. Abdominal pain and hyperpyrexia were the most common symptoms. Endoscopic findings showed discontinued severe inflammation, and all these patients presented with deformed ileocecal valve. Conventional pharmacotherapy failed to achieve a favorable effect. Four of six patients died from CD progression and its complications. None of these patients received bone marrow transplantation treatment because of poverty. Concurrence of AA and CD is a relatively rare condition. Immunologic impairment may play an important pathogenic role and deserves further attention. Males are more susceptible to this condition. Patients with AA-CD are prone to a severe clinical course and poor prognosis. Conventional therapy achieves no potent effect, and allogeneic stem cell transplantation may be a potentially efficient therapy.

Keywords Crohn's disease · Aplastic anemia · Incidence · Stem cell transplantation

Introduction

Aplastic anemia (AA) is a clinical syndrome with bone marrow hematopoietic failure. The symptoms of AA include bone marrow hypoplasia, pancytopenia and anemia, bleeding, and infection syndrome. The possible pathogenic factors of AA include medicine like mesalazine and sulfasalazine, chemical toxicant, radiation, immune dysfunction, and hereditary reasons. In most patients, T cell-mediated immune destruction of hematopoietic cells contributes to peripheral blood pancytopenia and bone marrow hypoplasia [1].

Crohn's disease (CD) is an idiopathic inflammatory bowel disease (IBD) which potentially affects any position of the gastrointestinal tract, mainly in the terminal ileum and right colon. Clinically, CD is characterized by a malabsorption syndrome including abdominal pain, diarrhea, and weight loss. Pathologically, it is featured by discontinuous inflammation of bowel segments and involvement of full intestinal layers.

Song Su, ZhenZhen Liu, Fang Wang contributed equally to this work.

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Previous case reports [2–4] showed that there was an association between AA and IBD, but mostly with UC. The possible connections between AA and CD have still not been well recognized nor are the clinical features and endoscopic findings of CD patients with AA. Also, despite use of antibiotics, cyclosporine and glucocorticosteroid in the management of CD associated with AA have been described in case reports, little is known about the response to typical treatment and prognosis of this coexistence. Hence, we aim to characterize the clinical features, endoscopic findings, and response to treatment in patients with CD and concomitant AA (CD-AA).

Methods

This was a retrospective descriptive study conducted at Xijing Hospital of Digestive Diseases affiliated to Air Force Medical University, an IBD tertiary referral center. This center was established in the year of 2006. There have been a total of 3042 patients with IBD registry in this center, comprising of CD patients 657, UC patients 2136, and indeterminate type patients 249. Among the CD patients, 417 are male and 240 are female. Patients with both CD and AA from January 2008 to October 2018 were searched and reviewed by two physicians (Song Su and ZhenZhen Liu). Coexistent medical conditions were ascertained from endoscopic features and histological findings. Confirmed histological evaluation of both bowel lesions and bone marrow aspirate was obtained by two specialist histopathologists, respectively. Initial evaluation for each confirmed case included a full clinical history and a total colon endoscopy including terminal ileum, three-dimensional computed tomography (3DCT), and hematologic examination. A retrospective analysis of medical records was performed to extract demographic data, medical history, clinical features, serological markers, endoscopic characteristics, histological findings, and treatment for CD and AA. Additionally, the response to treatment and prognosis so far were followed up by telephone and/or outpatient clinic. Follow-up time for CD and AA was defined as the period between diagnosis and the last inpatient or outpatient record.

A CD diagnosis was confirmed by standard histological criteria and a combination of clinical manifestation, endoscopic or surgical features, and/or radiological findings [5]. The diagnosis of AA was based on the international consensus diagnostic criteria, specifically hematologic findings and bone marrow aspirate [6]. In addition, other causes of anemia accompanied by insufficient myeloproliferation were excluded, including paroxysmal nocturnal hemoglobinuria (PHN), lymphoma, myelodysplastic syndrome (MDS), autoantibody mediated pancytopenia, and primary myelofibrosis.

Results

Demographics

In total, we identified 6 patients with a confirmed diagnosis of CD associated with AA. The incidence rate of CD associated with AA is 0.91% (6/657). All the patients were male, and none of them had a family history of inflammatory bowel disease, AA, or other autoimmune diseases. Besides, a history of exposure to myelotoxic agents and a recent infection history such as acute hepatitis were denied. Regarding CD, mean follow-up was 36.0 months (range 10–87 months). Mean age at diagnosis was 41.5 years (range 25–74 years). As for AA, mean age at diagnosis was 39.2 years old (range 14–74 years old) while mean follow-up was 62.0 months (range 10–206 months, case 1 was excluded due to death during the first admission). The mean interval between the diagnoses of CD and AA was 6 years (range 0–12) (Tables 1 and 2).

Clinical presentation

The most common symptoms for this set of patients were abdominal pain (100% of patients) and hyperpyrexia (66.7%). The pain was mostly presented as intermittent dull pain which was tolerable. One patient complained of the pain in the lower right abdomen and received laparoscopic right-sided colectomy following an ambiguous diagnosis of ileocecal junction malignancy in his local hospital. Four patients suffered fever with temperature higher than 39 °C with or without rigors. Additionally, five of six patients had a change in stool trait (rigid one, pasty two and diarrhea two). Moreover, case 1 and case 3 experienced controllable hematochezia. Case 5 complained of fatigue because of coexistent anemia (Table 1). Based on the results of bone marrow examination, AA in case 2 preceded the diagnosis of CD by 12 years and the rest patients of this set were identified as AA simultaneously with the diagnosis of CD. No patients were classified as severe type AA based on the Camitta criteria [7] (Table 2).

Endoscopic and CT findings

Colonoscopy revealed discontinuous severe inflammation with ulceration and stenosis formation. Cecum and ileum were frequently found to be ulcerative with friability and nodularity. Of note, all the patients in this series manifested with a deformed ileocecal valve. Lesion biopsy showed chronic full-thickness colitis with ulceration and non-caseating granuloma. Figure 1 shows the typical appearance of stomas, colon, cecum, ileocecal valve, and ileum. All the six patients received small intestinal 3DCT evaluation and discontinued, and various degrees of thickening were found. Four of the six were

Table 1 Demographics and clinical characteristics of CD in patients with coexistent AA: current series

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Gender	M	M	M	M	M	M
Age at diagnosis	59	28	34	29	25	74
Clinical presentation	Abdominal pain; high fever (40 °C); bleeding; pasty stool	Right lower abdominal pain; high fever (39 °C)	Abdominal pain; high fever (39.6 °C); diarrhea; bleeding	Abdominal pain; high fever (39 °C); diarrhea	Abdominal pain; pasty stool; fatigue	Abdominal pain; rigid stool
Extension	Ileocecal valve deformed; cecum; ascending colon	Stomas	Ileocecal valve deformed; cecum	Ileocecal valve deformed; ileum	Ileocecal valve deformed; ileum; whole colon	Ileum; remaining colon
Histology	Inflammatory granulation tissue; ulceration; chronic inflammation	Inflammatory granulation tissue; ulceration; chronic inflammation; glandular epithelium atypical hyperplasia	Inflammatory granulation tissue; chronic inflammation	Inflammatory granulation tissue; chronic and acute inflammation; bleeding; glandular epithelium atypical hyperplasia	Inflammatory granulation tissue; chronic inflammation; ulceration; glandular epithelium atypical hyperplasia	Inflammatory granulation tissue; chronic inflammation; ulceration; full-thickness lymphocytic infiltration
Montreal classification	A3L3B3	A2L2B2p	A2L3B2	A2L3B3p	A2L3B3	A3L3B2
Virus infection	EBV(−)	EBV-IgG(+) and CMV-IgM(±)	EBV-IgG(+) and CMV-IgM(±)	CMV-IgG(+)	EBV-IgG(+) and CMV-IgG(±)	EBV-IgG(+)
Surgery	Ileum perforation neoplasty; ileum stoma	Right-sided colectomy; appendicectomy	NA	NA	NA	Right-sided colectomy
Follow-up (months)	10	62	87	20	31	18

M male, *EBV* Epstein-Barr virus, *CMV* cytomegalovirus, *NA* none

Table 2 Clinical features and diagnostic criteria of AA in patients with coexistent CD: current series

	Case 1	Case 2	Case 3	Case 4	Case	Case 6
Gender	M	M	M	M	M	M
Age at diagnosis	59 (Simultaneous with CD)	14 (14 Years before CD)	34 (Simultaneous with CD)	29 (Simultaneous with CD)	25 (Simultaneous with CD)	74 (Simultaneous with CD)
Severity classification	Non-severity	Non-severity	Non-severity	Non-severity	Non-severity	Non-severity
Hematologic test						
HGB (g/L)	107	72	58	79	76	40
ANC (10^9/L)	1.43	1.42	2.19	0.77	1.41	1.8
PLT (10^9/L)	21	97	6	29	27	42
RET (10^9/L)	30	32	29	25	36	31
Bone marrow aspirate	Insufficient myeloproliferation; megakaryocyte absence; granulocyte series 0.78; erythrocyte series 0.08; non-hematopoietic cell mass presence	Not obtained	Insufficient myeloproliferation; megakaryocyte absence; granulocyte series 0.25; erythrocyte series 0.12; non-hematopoietic cell mass presence	Insufficient myeloproliferation; megakaryocyte count 2granulocyte series 0.15; erythrocyte series 0.30; non-hematopoietic cell mass presence	Insufficient myeloproliferation; megakaryocyte count 18; granulocyte series 0.20; erythrocyte series 0.40; non-hematopoietic cell mass presence	Insufficient myeloproliferation; megakaryocyte count 12, very few platelet; granulocyte series 0.37; erythrocyte series 0.26; increased non-hematopoietic cells
Bone marrow biopsy	Extremely low bone marrow hyperplasia; very few megakaryocyte; mainly medium and late phase erythrocytes; normal granulocytes; no fibrous tissue hyperplasia	Not obtained	Extremely low bone marrow hyperplasia; very few megakaryocyte, granulocyte or erythrocyte; no fibrous tissue hyperplasia reticular fiber Gomori staining (−)	Extremely low bone marrow hyperplasia; very few megakaryocyte, granulocyte and medium/late phase erythrocyte; no fibrous tissue hyperplasia reticular fiber Gomori staining (−)	Extremely low bone marrow hyperplasia; very few megakaryocyte, granulocyte or erythrocyte; no fibrous tissue hyperplasia; reticular fiber Gomori staining (−)	Extremely low bone marrow hyperplasia; very few megakaryocyte, granulocyte or erythrocyte; no fibrous tissue hyperplasia
Virus infection	EBV(−)	EBV-IgG(+) and CMV-IgM(±)	EBV-IgG(+) and CMV-IgM(±)	CMV-IgG(+)	EBV-IgG(+) and CMV-IgG(±)	EBV-IgG(+)
Autoantibody	Negative	Not obtained	Not obtained	Negative	ANA: 1:320	Negative
Transfusional history						
Erythrocyte	0	0	10	8	7	8
Platelet	1	0	16	6	0	2
Follow-up (months)	10	206	87	20	31	18

HGB hemoglobin, *ANC* absolute neutrophil count, *RET* reticular cell, *EBV* Epstein-Barr virus, *ANA* antinuclear antibody

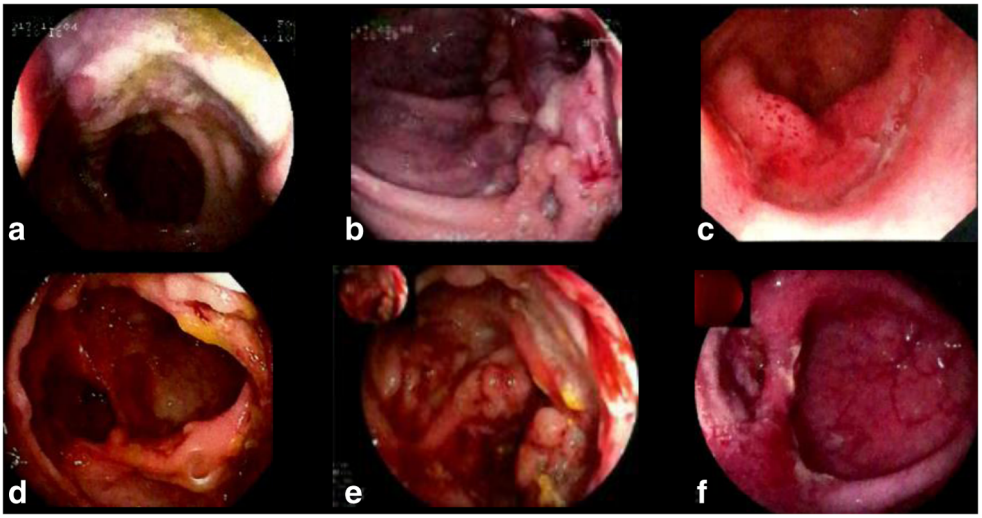

Fig. 1 Typical endoscopic findings of the presented patients. **a** Formation of a large ulcer in the terminal ileum (case 1). **b** A stoma with severe inflammation complicated with hyperplastic nodularity (case 2). **c** Ulcer formation in the ileum (case 3). **d** Severely deformed ileocecal junction (case 4). **e** Grossly deformed ileocecal junction with nodularity (case 5). **f** Deformed ileocecal valve (case 6)

identified with enlargement of lymph nodes. In addition, the rest of the extension was summarized in Table 1 to facilitate a Montreal classification.

Treatment and response

Medical therapy, comorbidities, and prognosis for each patient are summarized in Table 3. On admission, all patients received supportive therapy simultaneously with laboratory and imaging evaluation, including smoking cessation, antibiotics, nutrition support, and symptom relief treatment. Following definite diagnosis of CD with AA, medicines for CD like glucocorticosteroid, mesalazine, infliximab, cyclosporine, and medicines for AA including glucocorticosteroid, cyclosporine, stanozolol, and granulocyte stimulating factor were prescribed. The medicine and duration of each individual are summarized in Table 3. Comorbidities in these patients can be divided into three categories as follows: local complications like intestinal obstruction and bleeding, extraintestinal disorder including anal fistula, sacroiliitis, and thrombosis, as well as medicine-induced adverse events such as femoral head necrosis. Of them, one patient (case 5) was initially treated with cyclosporine but suffered apparent side effect. Consequently, five cycles of infliximab were administrated but, unfortunately, tuberculosis was followed requiring antituberculotic tetralogy. This finding may suggest a potential side effect of immunosuppression during infliximab treatment. Regarding the prognosis, four of six died from comorbidities or CD progression. Among them, one patient (case 2) suicided in the second month after discharge because of poor quality of life. Notably, due to the severe symptoms of CD, one patient (case 1) poorly responded to the treatment and died from comorbidities including pulmonary infection, bleeding, and perforation. Only two patients (case 3 and 6) survived until the latest follow-up.

Discussion

To our knowledge, this is the largest study of patients with CD associated with AA. A striking male predominance was found. The majority of patients suffered a manifestation with abdominal pain and hyperpyrexia. Moreover, most patients presented a severe clinical course pattern characterized by serious intestinal inflammation, multi-comorbidities, as well as poor response to conventional medical treatment. Endoscopic findings revealed deformed ileocecal valve, ulcerations, and severe inflammation in both colon and ileum. 3D-CT showed discontinued thickening of intestinal wall and enlargement of lymph nodes. Four of six patients died from disease progression and comorbidities. Only two patients have survived up to date.

Regarding the coexistence of IBD and hematopoietic disorders, relationship between UC and hematologic disease like myelodysplastic syndrome and leukemia has been described as they share an underlying immune dysfunction that can damage the function of T-lymphocytes [2]. Also, previous literature has reported a clinical association between ulcerative colitis (UC) and AA [2–4, 8, 9]. However, few articles reported the associations between CD and AA. As we know, only two cases [10, 11] were reported and little is known about the mechanism of concurrence, clinical features of this rare entity, as well as the treatment for these patients.

Although the association between CD and AA may be coincidental, previous and recent literature suggests certain relations between these two diseases rather than only a coincidence. Concerning the mechanism for development of both AA and CD, three assumptions seem plausible. Firstly, CD and AA may share an immunologic impairment underlying both diseases. Previously reported cure function of hematopoietic stem cell transplantation for patients with AA and IBD suggests that immunologic irregularities be a key point to reverse the disease [12]. Several studies also have

Table 3 Treatment and prognosis for these patients

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Medicines for CD						
Glucocorticosteroid	√ 2008.06–2009.04		√ 2010.03–2013.03	√ 2008.10–2018.-03		
Mesalazine	√ 2008.08–2009.03	√ 2009.04–2013.10	√ 2010.03–2013.03	√ 2016.10–2018.-03		√ 2017.09–2018.08
Infliximab					√ 5 times	
Cyclosporine	√ 2008.06–2009.04					
Medicines for AA						
Glucocorticosteroid	√ 2008.06–2009.04	√ 2000.09–2006.05	√ 2010.03–2013.03	√ 2016.10–2018.-03		
Cyclosporine	√ 2008.06–2009.04	√ 2000.09–2006.05		√ 2008.10–2012.-04	√ 2017.01 (8 days in total)	
Stanozolol	√ 2008.06–2009.04	√ 2000.09–2006.05		√ 2018.03–2018.-06		
Granulocyte stimulating factor				√ 2018.03–2018.-06		
Final remission status of AA						
HGB (g/L)	68	71	61	69	78	80
ANC (10^9/L)	0.12	1.42	2.07	0.47	0.78	1.6
PLT (10^9/L)	5	43	20	19	25	45
RET (10^9/L)	25	30	30	25	20	32
Comorbidities	Pulmonary fungal infection; respiratory failure; hemorrhagic shock	Anal fistula; bleeding; sacroiliitis	Femoral head necrosis	Sacroiliitis; anal fistula	Intestinal tuberculosis	Lower limbs thrombosis; incomplete intestinal obstruction
Prognosis	Died from comorbidities	CD symptoms remained; AA slowly progressed; suicided on the second month after discharge	CD symptoms relieved; AA no progression	Died on the third month after discharge	Complicated with tuberculosis; died from disease progression	CD symptoms relieved; AA no progression

CD Crohn's disease, *AA* aplastic anemia

demonstrated that allogeneic bone marrow transplantation had an ability to resolve CD [13]. Some investigators speculated that NOD-2 gene mutations, which may lead to increased risk of CD, possibly could alter the NF-kB-mediated regulation of hematopoietic progenitor cell development and subsequently resulted in the development of CD and AA [10]. In addition, immunosuppression caused by either CD may result in the occurrence of AA and vice versa. It has been reported that functional impairment of neutrophils due to AA may lead to chronic bowel infection which subsequently may play a significant pathogenic role in CD. On the other hand, intestinal wall ischemia due to anemia of AA can also contribute to the development of CD. Moreover, medicines like mesalazine, azathioprine (AZA), 6-mercaptopurine (6-MP), and sulfasalazine have been reported to potentially induce the development of AA [8, 14, 15]. When the AZA/6-MP was prescribed to children with UC, the incidence of adverse effects (mainly myelosuppression) could be up to 40%. Mesalazine-induced severe aplastic anemia in patients with UC has also been reported [8]. In the presented cases, all the AA were diagnosed before or simultaneously with CD, indicating medicine for CD does not account for the onset of AA in this set of patients.

Interestingly, we noticed that all the patients in this case series were male. It is not surprising because CD is of a male predominance, and the incidence of AA has no difference between male and female according to the epidemiologic data in China [16, 17]. However, we believe CD associated with AA was not restricted to male as one female patients with AA complicated with CD was reported [11].

Of note, despite the non-severity trait of AA in this patient set, most patients in the present patient set suffered a severe clinical course. Abdominal pain and hyperpyrexia (range from 39.0 to 40.0 °C) were the most common symptoms. The reason of hyperpyrexia may be attributed to severe inflammation and potential intestinal infections like Epstein-Barr virus (EBV) infection, because only case 1 was identified with pulmonary infections which may lead to fever. In contrast, none of the rest patients were found with fever source, including infections, autoimmune disease, or tumors.

When we reviewed the endoscopic images of these patients, some typical findings are illustrated in Fig. 1. We found a deformed ileocecal valve in every patient with interest, except case 1 whose right-sided colon had been resected due to perforation earlier. Although CD frequently affected the ileocecal junction, all the patients demonstrated with a grossly deformed ileocecal valve may indicate an underlying function role of this location in the development of CD. Since ileocecal is plentiful of lymphocytes which is essential for the immunologic activity. Thus, we hypothesize that deformed ileocecal valve may be a clinical characteristic for patients with concomitant CD and AA. In addition, deformed ileocecal valves were identified in previous reported cases [10]. Moreover, 3D-CT revealed serious intestinal inflammation. Discontinued thicken of intestine and terminal colon were noted. Three patients (Table 3) demanded surgical intervention for intestinal obstruction or perforation.

Currently, treatment for CD should be specified according to site, activity, and behavior of the disease. The medications mainly include steroids like prednisolone and budesonide, mesalazine, and immunosuppressants like azathioprine and intramuscular methotrexate; anti-TNF agents like adalimumab and infliximab; and other treatment methods like nutritional supplementation, antibiotics, omega-3 fatty acids, probiotics, cytopheresis, and autologous stem cell transplantation [5]. With regard to AA, the treatment generally comprises of supportive care like blood transfusion, prophylactic platelet transfusion and antibiotics, immunosuppressive therapy (IST) comprising of antithymocyte globulin (ATG) and cyclosporine (CSA), and hematopoietic stem cell transplantation (HSCT). However, little is known about the appropriate treatment strategy for patients with CD and concomitant AA. Of the two previous cases, only Mori M et al. described a treatment with prednisolone achieved remission, whereas no treatment and prognosis was reported in the other one. Similarly, we provided classic treatment for the present set of patients, in which medications including steroids, mesalazine, infliximab, cyclosporine, stanozolol, and support care were used following respective consensus of treatment associated with our experience. However, unfortunately, traditional medical therapy failed to achieve potent effect in four of six patients. Case 1 died due to perforation and bleeding despite received proper surgical intervention. Case 2 suicided in the second month after discharge because of maintained symptoms and low quality of life. Case 4 died from progressed CD and its complications including bleeding, malabsorption, infection, and cachexia. Case 5 died from progressed CD with local and systematic comorbidities including bleeding, perforation, malabsorption, and intestinal tuberculosis. In addition, we found that the final hematologic results of dead cases were seriously poor, which suggested that the AA in these patients were deeply ignored and this ignorance may further accelerate the progression of disease and final death by exacerbating infection, bleeding, and impairing the tolerance capability of anemia. Considering the positive effects of allogeneic stem cell transplantation (ASCT) for patients with CD [18] as well as ASCT being well-established treatment for AA, we propose that ASCT may be a potentially curative therapy for patients with both CD and AA. Also, perianal fistulas in CD patients were reported to benefit from bone marrow derived or adipose-derived mesenchymal stem cells (MSCs). Local administration of MSCs into the fistula is an effective and safe treatment for patients who did not respond to conventional and/or biological therapy. But, due to poverty, none of our patients choose to receive ASCT treatment. Otherwise, ATG and bone marrow transplantation treatment can be taken into

consideration during the early process of AA in spite of the severity form, in order to acquiring early control of disease. As for CD, currently, the treatment for general CD cases comprises a gradual elevation process in choosing medications from 5-ASA, glucocorticosteroid, immunomodulator to biologics. However, when it comes to CD cases associated with high risk factors, top-down therapy has been recommended by the guideline, which means biologics becomes the first-line choice for these high-risk cases. Although AA has not yet been classified as the high-risk factor group in guideline, we believe the value of top-down therapy for CD cases associated with AA deserve further exploration. But due to poverty, the amount of medical fund that these patients could afford was badly limited. Until start specialized and regular treatment, they have commonly spent the majority of medical cost on the diagnostic and initial therapeutic course, especially for CD, of which the symptoms were easily to be serious and obvious including abdominal pain, diarrhea, bleeding, infection, anal fistulas, and so on. Consequently, CD has huger impact on the quality of life; thus, these patients tend to spend more money on the treatment of CD. Further, as the CD and AA progressed, there was little fund left for following treatment, and when we discuss with these patients that bone marrow transplantation treatment is a potentially effective therapy with uncertain efficiency, also, the expense of bone marrow transplantation is high and they need to wait a matching donor; all these patients rejected ASCT treatment.

As a retrospective evaluation, this study has some limitations. First, evaluation of clinical response to treatment was conducted retrospectively. However, to ensure accurate information, treatment and response of each patient were collected by their treating physicians. Further, to reduce the risk of recall bias, all the patients were re-followed up and responses at different time points were compared with previous records and confirmed with patient himself or his family. Second, no bone marrow evaluation was available in case 2. Because the AA condition was stable during our hospital, we did not repeat the bone marrow evaluation. But considering following facts, on one hand, the diagnosis of AA in case 2 was made at another famous tertiary medical center; on the other hand, hematologic evaluation of HGB 72 g/L, ANC 1.42×10^9/L, PLT 97×10^9/L, and RET 32×10^9/L also supports the diagnosis of AA; therefore, we believed the diagnosis of AA in case 2 was reasonable and recruited this case in the reported group. Third, life quality outcomes were not available in this set of patients due to patients passing away. Otherwise, upper digestive tracts in these patients were not evaluated and should be assessed in future patients.

In conclusion, CD associated with AA is a rare clinical condition with poor prognosis. A common pathogenic link between CD and AA is suggested in the presented patients, which may be a shared underlying immunologic dysfunction in both diseases. Most patients are likely to suffer a severe clinical course. Endoscopy and 3D-CT frequently identify discontinuous severe inflammation. Deformed ileocecal valve due to lymphocytes impairment may be a typical endoscopic finding. High incidence of bleeding, perforation, intestinal obstruction, and potential malignancy increases the risk of surgical intervention. Conventional treatment for these patients may fail to achieve potent effect while ASCT may have curative potential for patients with both CD and AA which needs further studies.

Authors' contribution Song Su: Conception and design of the study, Acquisition of data, Analysis and interpretation of data, Drafting the article. ZhenZhen Liu: Acquisition of data, Analysis and interpretation of data, Drafting the article. Fang Wang: Acquisition of data, Analysis and interpretation of data. YuJie Zhang: Conception and design of the study, Revising the article. Yi Chu: Acquisition of data. MingZuo Jiang: Acquisition of data. Nan Wu: Acquisition of data, Analysis and interpretation of data. JunChao Lin: Acquisition of data. Bing Xu: Conception and design of the study, Revising the article. XianMin Xue: Acquisition of data. YongQuan Shi: Conception and design of the study, Analysis and interpretation of data. Shaoqi Yang: Revising the article. KaiChun Wu: Conception and design of the study, Analysis and interpretation of data. Jie Liang: Conception and design of the study, Analysis and interpretation of data, Revising the article

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This is a retrospective observational study. This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Although this is a retrospective study, informed consent was obtained from all individual participants included in the study during the follow-up process.

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