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CLINICAL CASE REPORT

Spontaneous Intra-Abdominal Hemorrhage Due to Rupture of Jejunal Artery Aneurysm in Behcet Disease
Case Report and Literature Review

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Abstract: Rupture of jejunal artery aneurysm is a very rare event resulting in life-threatening hemorrhage in Behcet disease (BD). We report a case of ruptured jejunal artery aneurysm in a 35-year-old patient with BD. The patient had a 1-year history of intermittent abdominal pain caused by superior mesenteric artery aneurysm with thrombosis. Anticoagulation treatment showed a good response. Past surgical history included stenting for aortic pseudoaneurysm. On admission, the patient underwent an urgent operation due to sudden hemorrhagic shock. Resection was performed for jejunal artery aneurysm and partial ischemia of intestine. The patient was diagnosed with BD, based on a history of recurrent oral and skin lesions over the past 6 years. Treatment with anti-inflammatory medications showed a good response during the 8-month follow-up.

An increased awareness of BD and its vascular complications is essential. Aneurysms in BD involving jejunal artery are rare, neglected and require proper management to prevent rupture and death. To our knowledge, this is the first reported case of jejunal artery aneurysm caused by BD.

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Abbreviations: BD = Behcet disease, CECT = contrast-enhanced CT, CRP = C-reaction protein, CT = computed tomography, ESR = erythrocyte sedimentation rate, EVAR = endovascular repair, ICBD = International Criteria for Behcet Disease, IMA = inferior mesenteric artery, MR-angiography magnetic resonance angiography, PT = Prothrombin time, PTT = partial thromboplastin time, SMA = superior mesenteric artery, TCAE = transcatheter arterial embolization, UK = unknown, US = ultrasound.

INTRODUCTION

Behcet disease (BD) is classified as an inflammatory vascular disease, affecting vessels of all kinds and sizes, characterized by a relapsing and remitting course. The aetiopathogenesis of the disease remains unknown.[1] The prevalence of BD is global. However, it shows marked geographical variation, and occurs more commonly in regions along the Silk Road, from the Mediterranean and the Far East.[2] It manifests oral and genital ulcerations, skin lesions, uveitis, and involves vascular, central nervous system, and gastrointestinal systems.

Vascular involvement occurs in about 14.3% of patients and is more common in males.[3] The most common features are superficial thrombophlebitis and deep vein thrombosis, whereas only 7% affect the arterial system. Arterial aneurysms are rare in BD and generally involve large arteries, such as the abdominal aorta, the pulmonary and femoral arteries. Aneurysmal degeneration of the visceral branches of the abdominal aorta is a rare and potentially life-threatening disease with a documented prevalence of 0.1% to 2%.[4] We report a rare case of a patient with fatal rupture of jejunal artery aneurysm secondary to BD who had multiple arterial aneurysms. To our knowledge, this is the first reported case of rupture jejunal artery aneurysm caused by BD. We compare our new case with the results of a literature review involving 24 previously reported cases and discuss the main characteristics, diagnosis, treatment, and outcome of visceral arterial aneurysm secondary to BD.

PATIENTS AND METHODS

Patient and Literature Review

We performed a PubMed (National Library of Medicine, Bethesda, MD), EMBASE (Excerpta Medica Database), and ScienceDirect search using the terms "Behcet AND aneurysm" and "vasculo-Behcet," retrieving all articles published in English up to June 2015. We provided a flow chart outlining the process of identification of eligible case studies (Figure 1). We combined these data with the new case reported here discussing visceral arterial aneurysm secondary to BD. The patient signed the permission for the publication when he was admitted in our hospital. Written informed consent was obtained, and the study was approved by the research ethics committee of the Tianjin Medical University General Hospital.

CASE REPORT

A 35-year-old man was admitted to our hospital because of paroxysmal upper abdominal pain in October 2014. He had a 1-year history of intermittent abdominal pain due to superior mesenteric artery aneurysm with thrombosis. One year ago, the patient manifested gastrointestinal symptoms, such as abdominal pain, occasional nausea but no vomiting, hematochezia or
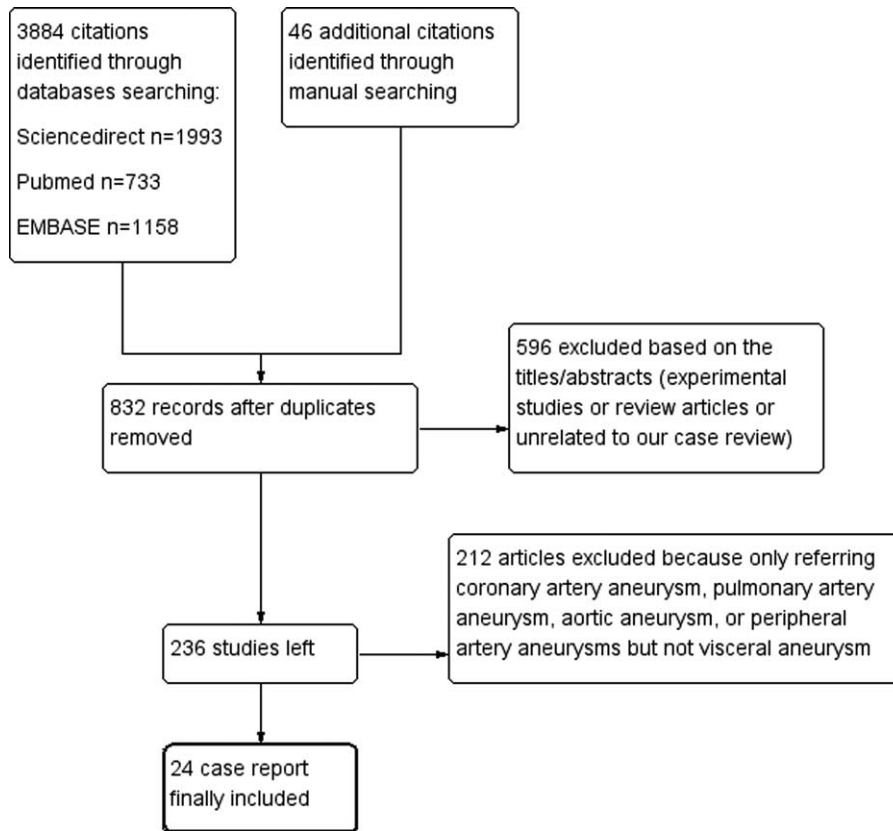
FIGURE 1. The flow chart outlining the strategy identifying eligible case studies.

dark stools. CT revealed an aneurysm of the superior mesenteric artery (SMA) with thrombosis. There were no signs of bowel ischemia. The symptoms were alleviated with warfarin treatment. The patient's past surgical history included percutaneous aortic stenting due to aortic pseudoaneurysm diagnosed at another hospital in May 2009. The patient was acutely ill at admission, but with stable vital signs. Physical examination showed tenderness and rebound pain in left upper quadrant. A tender, palpable pulsatile mass, measuring 5 cm in diameter, was observed in his left groin. Laboratory analysis revealed leukocytes 24.38×10^9/L, and an elevated percentage of neutrophils (93.5%), CRP was 60 mg/L (normally less than 6 mg/L), ESR was 40 mm/h, and PT and PTT were within normal limits. D-dimer was 3462 ng/mL. Other routine blood tests were normal. Antinuclear antibody, rheumatoid factor, and other autoantibodies were all negative. Contrast-enhanced CT (CECT) of the whole abdomen demonstrated a 9.4-mm-diameter aneurysm involving the SMA (Figure 2), a 4.8-mm-diameter distal jejunum artery aneurysm (Figure 3), splenomegaly and renal infarction, and no signs of bowel ischemia.

The patient developed hypotension along with a sudden drop in hematocrit after admission. We carried out exploratory laparotomy urgently and observed hematoma on jejunum with active blood extravasation and about 2000 mL hemorrhagic seroperitoneum. We resected a small intestinal mass and performed intestinal anastomosis. Histological examination (Figure 4) of the aneurysm wall demonstrated fibrosis and chronic perivascular inflammation of adventitia. Inflammatory cells included monocytes and plasmacytes, along with an abundance of neutrophils in the vessel wall. These findings

may possibly be compatible with chronic nonspecific vasculitis. Combined with clinical manifestations, jejunal artery lesions were found to cause the bleeding.

The patient revealed a long history of recurrent aphthous oral ulceration, lower limb bilateral erythema nodosa, and pustules. Ophthamologic examination revealed no obvious eye pathology. The above findings (Table 1) indicated a diagnosis of BD-based on international clinical criteria. The patient was stable after the procedure, and a follow-up CT (Figure 5) showed good blood flow to visceral arteries without increase in the size of SMA aneurysm. Anti-inflammatory medications, including steroids, *Tripterygium wilfordii* and thalidomide were given postoperatively. During the 8-month follow-up no signs of disease activity such as anastomotic or other aneurysms were found. Aphthous mouth ulcers, erythema nodosa, and pustules were in remission. The CRP levels and the ESR were within the normal range. The results showed a disease under control.

RESULTS

Comparison with Literature

Visceral arterial aneurysm secondary to BS is rare, with only 24 cases reported in the literature. Including the new case, a visceral arterial aneurysm secondary to BS has been reported in males. The mean age of patients at diagnosis was 33.5 (19–50) years.

Clinical Features and Diagnosis

In 25 cases, the multisystem disorder involved oral aphthosis,[5–22] genital aphthosis,[5,6,9,10,12–17,19,21,22] skin lesions,[7,10,12,14,16,19] ocular
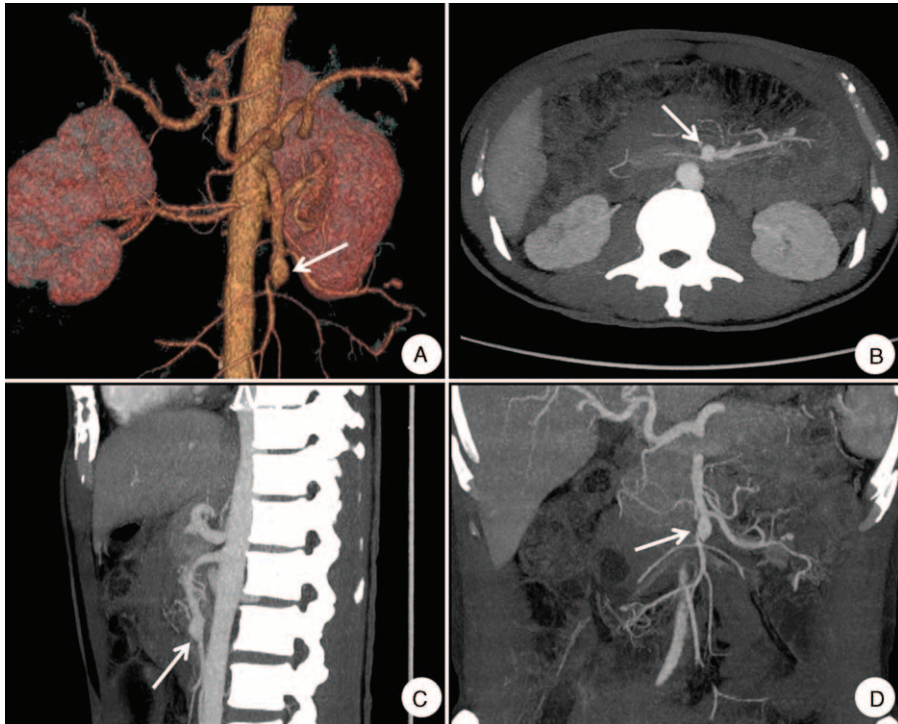
FIGURE 2. Three-dimensional volume rendering (A), the axial (B,C) arteriography (D) images show a 9.4-mm-diameter aneurysm at the superior mesenteric artery.

lesions,[6–9,14,15,17,19–21,23] vascular involvement,[5,9,11,15,17,24] and positive pathergy test.[6,15,16,23] The BD symptoms do not necessarily involve or manifest simultaneously. Patient characteristics are summarized in Table 2.

We diagnosed 25 patients with arterial involvement radiologically including ultrasound,[6,7,9,13,15,18,25] angiography,[8,9,13,14,16,18,19,24–28] CT,[5,6,8,10–12,15,17,18,20–23,25–28] and magnetic resonance angiography.[23] The most common imaging
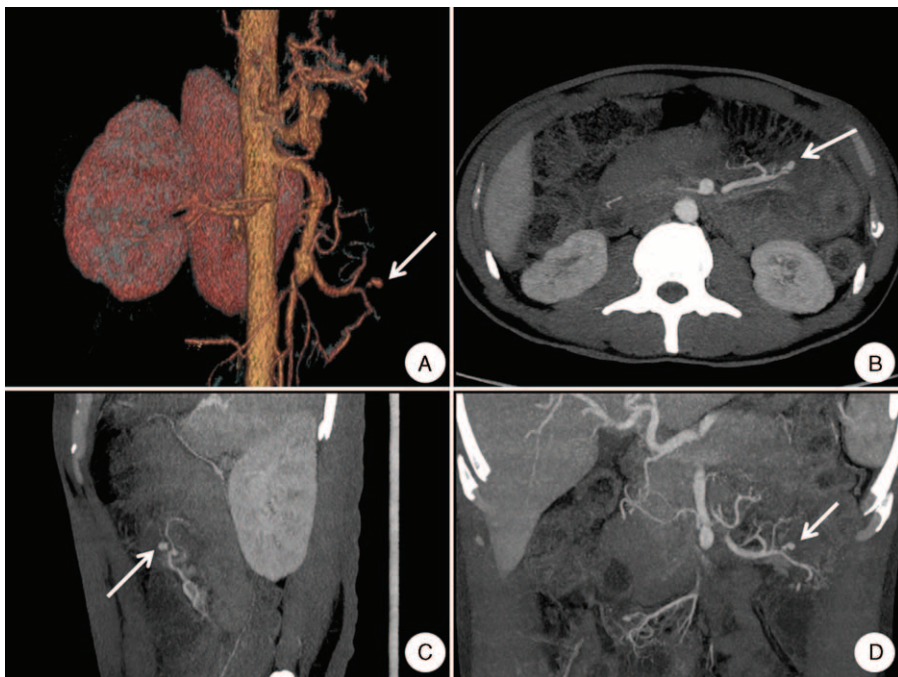

FIGURE 3. Three-dimensional volume rendering (A), the axial (B,C) arteriography (D) images show a 4.8-mm-diameter distal jejunum artery aneurysm.
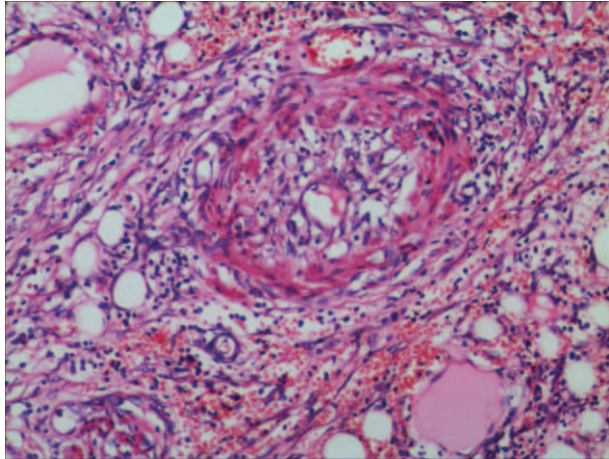

FIGURE 4. Aneurysm wall fibrosis and chronic perivascular inflammation of adventitia; inflamed cells including monocytes and plasmacytes, and neutrophils in the vessel wall (×100).

modality used was CT (76.0%) and secondary angiography (48.0%).

Treatment and Outcomes

In this review, aneurysms of the hepatic artery and renal artery were the most frequent types of visceral aneurysm. Twelve patients underwent transcatheter arterial embolization (TCAE),[5,6,8–10,16,19–21,25,27] 1 patient was successfully treated surgically but died from pneumonia,[8] and another patient developed segmental pancreatitis after embolization.[25] The success rate of TCAE was 92% in this review. Nine patients underwent open surgical repair, and 1 patient received endovascular repair (EVAR). Eight patients showed relapsed aneurysm despite anti-inflammatory treatment.[5,9,16,17,22,24,26,28]

Corticosteroids (methylprednisolone and prednisone) were used as the initial and first-line immunosuppressive therapy in 15 patients (93.8%). Immunosuppressive therapy with methotrexate, colchicine, cyclophosphamide, chlorambucil, cyclosporine

A, and sulfasalazine was used in 11patients (68.8%), always in combination with corticosteroids. The efficacy of immunosuppressive therapy is questionable because of the recurrent nature of BD. Eight patients received anticoagulation therapy[9–12,15,23,24] including our case and another case[15] with a bleeding disorder secondary to anticoagulation. Treatments administered to the 25 cases are summarized in Table 3.

DISCUSSION

BD is a chronic, relapsing, inflammatory vascular disease with no pathognomonic test. Arterial complications occur in only 1% to 7% of patients with BD.[27] The risk of developing vascular complications is 5 times higher in males.[23] Arterial complications include aneurysms, stenosis, and occlusions.[29] The artery most often affected is the abdominal aorta followed by the pulmonary, femoral, subclavian, popliteal, and common carotid arteries.[30] The severity and prognosis of BD are variable. In most patients, it has a relapsing, remitting chronic course. Vascular involvement is the major life-threatening manifestation.[31] Involvement of visceral vessels is rare. Our case is the first reported case of jejunal artery involvement in BD.

The pathogenetic mechanisms are still incompletely known. However, the interaction between genetic background and environmental or infectious factors certainly contributes to the immune dysregulation that characterizes this disease.[1] The arterial lesions involve inflammation of the media and adventitia, comprising aseptic infiltration of tissues with neutrophils and mononuclear cells. In affected arteries, active arteritis occurs initially, followed by medial destruction and fibrosis. Therefore, perforation of the arterial wall is the most common lesion, predisposing to pseudoaneurysm or rupture, possibly as a result of endothelial dysfunction, necrosis of the elastic and muscle cells in the medium. Open surgical repair is difficult, and anastomotic pseudoaneurysms often occur because of vessel wall fragility.

BD diagnosis is mainly based on clinical criteria because of lacking a universally recognized pathognomonic test. The revised International Criteria for Behcet Disease (ICBD) published in 2014 is the latest diagnosis/classification criteria.[32] The new criteria include oral aphthosis, genital aphthosis, ocular lesions, neurological manifestations, skin lesions, vascular manifestations, and positive pathergy test. Oral aphthosis, genital aphthosis, ocular lesions each gets 2 points, whereas skin lesions, vascular manifestations, neurological manifestations, and positive pathergy test each gets 1 point. A patient scoring 4 points or above is classified/diagnosed as BD. However, the various symptoms in BD do not necessarily manifest themselves at the same time. In 6.8% of the cases, vascular involvement preceded or occurred during the diagnosis of BD and 33.7% of the patients developed vascular disease within 5 years of diagnosis.[3] Early diagnosis of BD in young males with aneurysms is critical to avoid any ruptured aneurysms. Early diagnosis may be based on radiographic imaging such as ultrasound angiography, CT, and magnetic resonance angiography. CECT has become the procedure of choice in evaluating patients with aneurysm. Selective angiography has proven useful for both the diagnosis and treatment of intestinal bleeding.

BD with vascular disease should be distinguished from Takayasu's arteritis, giant cell arteritis, Cogan's syndrome, and syphilitic arteritis. Takayasu's arteritis is usually seen in people aged less than 40 years. Absence of glomerulonephritis, myalgia, polyneuropathy, or polyneuritis does not confirm periarteritis nodosa diagnosis. Absence of headache, temporal artery

TABLE 1. Patient Profile

| Characteristic	
Recurrent oral ulceration	Positive
Genital ulcers	Negative
Cutaneous pustules	Positive
Positive pathergy test	Untested
Ocular involvement	Negative
Musculoskeletal involvement	Negative
Neurology	Negative
Vascular involvement	Aortic pseudoaneurysm, SMA aneurysm, anastomotic pseudoaneurysm, jejunum artery aneurysm
Gastrointestinal ulcers	Negative
Inflammatory markers	Leukocytes, neutrophils, CRP, ESR were elevated
Specific diagnostic markers	Negative
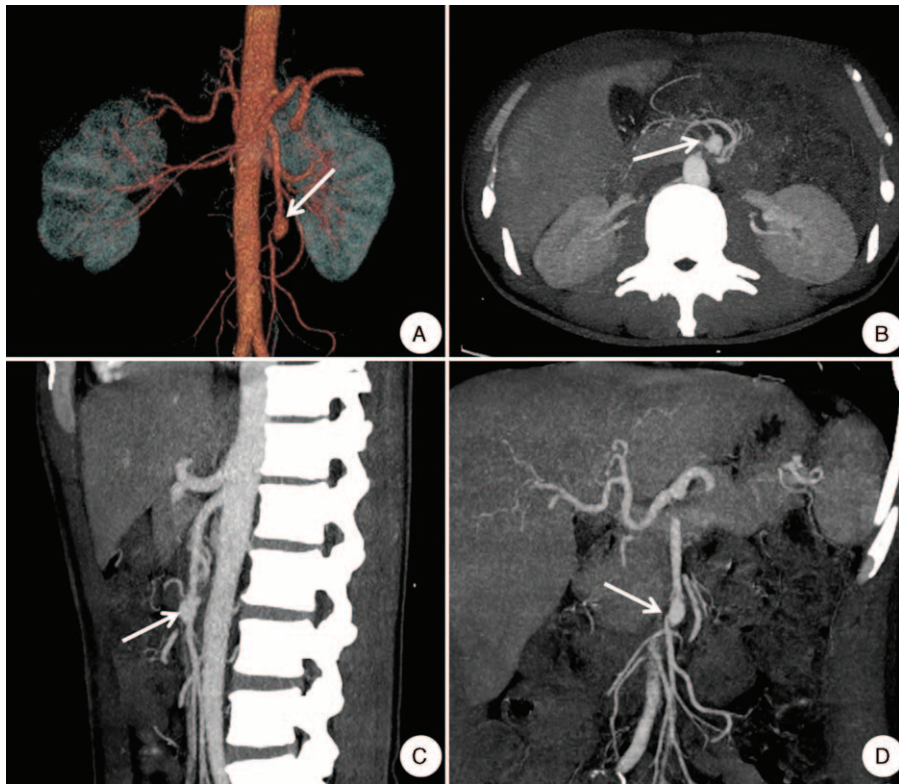
FIGURE 5. Three-dimensional volume rendering (A), the axial (B,C) arteriography (D) images show good blood flow to visceral arteries and no increase in superior mesenteric artery aneurysm size.

tenderness, or abnormality excludes giant cell arteritis. Syphilitic aneurysms are usually located in the ascending aorta or aortic arch due to infection with *Treponema pallidum*.

The traditional treatment of vascular lesions in BD consists of surgical repair and graft insertion, with a high frequency of graft occlusion and anastomotic pseudoaneurysm formation.[33] Our patient had anastomotic pseudoaneurysms in the left iliac artery due to percutaneous aortic stenting. Percutaneous stenting may provide a safer alternative to open repair although this approach also carries risk. Recently, endovascular repair (EAVR) of arterial disease has become popular because of its greater safety and patient tolerance compared with open surgical repair.[34] Stent-graft placement has been used for the treatment for aortic and arterial aneurysm or pseudoaneurysm in patients with vascular BD. In particular, patients with anastomotic complications or contraindications for surgical reconstruction are candidates for hybrid surgeries,[35] such as combined bypass grafting. TCAE is indicated for both ruptured and intact aneurysms, and is considered safe and effective for arterial aneurysms in BD.[20] In our review, the success rate of TCAE was 92%. However, rupture warrants an emergent open surgery to ligation in most cases. Of course, currently, few people prefer open surgery for aneurysm and evacuation of the thrombus.[36] In vascular BD, surgical and endovascular interventions alone increased the incidence of pseudoaneurysm.

Early initiation of prednisone in combination with aggressive immunosuppressive therapy, cyclophosphamide, or anti-TNF therapy is critical for inhibiting the progression of vascular lesions and provides a good prognosis.[37] Aggressive therapy prior to any surgical correction is essential, and surgical intervention should be avoided whenever possible.[38] Persistent inflammation suggests recurrent lesions. One case reported disease exacerbation in addition to anticoagulation by warfarin-induced nontraumatic subcapsular hematoma of the right kidney. Endothelial damage may be related to disease predisposition to thrombophilia. Anticoagulant fibrinolytic or anti-platelet aggregation may increase the risk of aneurysm rupture, causing severe bleeding resulting in death. No evidence of benefit with anticoagulant management of arterial lesions was seen. Anticoagulation therapy is not recommended. Aggressive treatment of the primary disease improves the aneurysm to prevent acute vascular surgery. Close follow-up with anti-inflammatory medications, and periodic surveillance are the only current methods for the prevention of arterial complications in patients with BD.

TABLE 2. Patient Characteristics (n = 25)

Characteristic	n (%)
Oral aphthosis n (%)	19/19 (100%)
Genital aphthosis n (%)	14/19 (73.7%)
Skin lesions n (%)	6/18 (33.3%)
Ocular lesions n (%)	11/18 (61.1%)
Artery and vein involvement n (%)	7/25 (28.0%)
Positive pathergy test n (%)	4/6 (66.7%)
Duration (yr)	4.7

TABLE 3. Diagnostic Method and Treatment of Visceral Arterial Aneurysm in BD

References	Age	Localization	Diagnostic Method	Surgical Procedure	Medication
Present case	35	Jejunal artery	CECT	Open surgery for Aneurysmectomy	Steroids, tripterygium wilfordii and thalidomide
Planer[4]	20	Renal artery	CT	TCAE	Corticosteroids and methotrexate
Kwon[25]	40	Renal artery	CT, aortography, CT angiography	open surgical repair	Steroids and colchicines
Ozkurt[5]	20	Renal artery	US, CT	TCAE	UK
Fukuda[6]	31	Renal artery	CECT	UK	UK
Sueyoshi[7]	42	Renal artery	CECT, angiography	TCAE	UK
Sherif[8]	36	Renal artery	US, arteriography	TCAE	Steroids and chlorambucil
Adams[9]	22	celiac artery	CECT	TCAE	Prednisone, cyclophosphamide, colchicines and dalteparin sodium
Maeda[22]	UK	celiac artery	CT, MR-angiography	Conventional open bypass surgery	Prednisolone, methotrexate, warfarin and aspirin
Ullery[10]	19	celiac artery	CT angiography	open surgical repair	Immunosuppressive therapy
Bautista-Hernandez[11]	37	celiac artery	CT, CECT	stent-graft repair	Cyclosporine A, prednisone, clopidogrel, warfarin, cyclosporine A
Men[12]	23	SMA	US, angiography	UK	UK
Chubachi[13]	37	SMA	Aortography	Open surgery for Aneurysmectomy	Methylprednisolone
Yokota[14]	24	celiac and SMA	US, CT	UK	Prednisolone
Güven[23]	39	SMA	Angiography	TCAE	colchicin, aspirin, and prednisolone
Hong[15]	50	ileocolic artery	Angiography	TCAE	Prednisolone and sulfasalazine
Morimoto[16]	48	IMA	CT	Aneurysmectomy and reimplantation	Prednisolone, cyclophosphamide, and mizoribine
Cekirge S[17]	25	Hepatic artery	Doppler sonography, angiography, CT	EVAR	UK
Hatzidakis[18]	40	Hepatic artery	Angiography	TCAE	UK
Ahmed[19]	39	Hepatic artery	CECT	TCAE	Steroids and cyclophosphamide
Hotta[26]	34	Hepatic artery	CECT, angiography	TCAE	UK
Jung[20]	33	Hepatic artery	CECT	TCAE	UK
Oto[24]	23	Hepatic artery	US, angiography, CT	TCAE	UK
Saiki[21]	50	SMA	CT	Aneurysmectomy and bypass surgery	Prednisolone
Ozveren[27]	36	SMA	CT, angiography	Aneurysmectomy and vein graft surgery	Prednisolone

CECT = contrast-enhanced CT, CT = computed tomography, EVAR = endovascular repair, IMA = inferior mesenteric artery, MR = angiography magnetic resonance angiography, SMA = superior mesenteric artery, TCAE = transcatheter arterial embolization, UK = unknown, US = ultrasound.

CONCLUSIONS

A patient with vascular BD may present with multiple arterial abnormalities with diverse clinical features, warranting early identification and prompt treatment for proper management. Systemic arterial aneurysms in BD should be surgically corrected because of the risk of ruptured aneurysms. Early diagnosis and prompt immunosuppressive therapy prevent life-threatening complications in BD.

In conclusion, we report the treatment of aneurysm secondary to BD. To our knowledge, this is the first report of a case of ruptured distal jejunum artery aneurysm caused by Behcet's syndrome. There were no signs of recurrence during 8-month follow-up. We will continue to monitor the patient closely because of the recurrent nature of BD.

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