Clinical Case Report

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Intestinal brucellosis associated with celiac artery and superior mesenteric artery stenosis and with ileum mucosa and submucosa thickening

A case report

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Abstract

Rationale: Brucellosis is a multisystem infection found worldwide that has a broad range of characteristics, which range from acute fever and hepatomegaly to chronic infections that most commonly affect the central nervous system, cardiovascular system, or skeletal system. Gastrointestinal and splanchnic artery involvements in brucellosis are relatively uncommon.

Patient concerns: We report a case of brucellosis in an adolescent presenting as intermittent abdominal pain, diarrhea, and fever, with intestinal tract involvement. And stenosis of the celiac artery and the superior mesenteric artery was found after exposed to risk factors of Brucella infection. Splanchnic vessels stenosis and an endothelial lesion may exacerbate the prevalent symptom of abdominal pain, as a form of colic pain, occurring after eating.

Diagnoses: The patient was diagnosed as brucellosis. The narrowing of the SMA and CA was suspected to be vasculitis secondary to the brucellosis.

Interventions: The patient was treated with minocycline and rifampicin for 12 weeks totally.

Outcomes: The gastrointestinal manifestations of brucellosis recovered rapidly under intensive treatment. However, follow-up imaging revealed that the superior mesenteric artery and celiac artery stenosis was unimproved.

Lessons: In brucellosis, gastrointestinal manifestations may be the only observable features of the disease. Splanchnic arterial stenosis is a rare complication of brucellosis. Sonography and computed tomography may be useful for both diagnosis and follow-up.

Abbreviations: ANA = antinuclear antibody, BMI = body mass index, CA = celiac artery, CT = computed tomography, CTA = computed tomographic angiography, IBD = inflammatory bowel disease, IMA = inferior mesenteric artery, PET = positron emission tomography, PSV = peak systolic velocity, SMA = superior mesenteric artery, STA = standard tube agglutination, TB = tuberculosis, US = ultrasound.

Keywords: Artery, brucellosis, endothelium, ileum, imaging, stenosis

1. Introduction

Brucellosis is a common zoonosis that is caused by gram-negative bacteria, *Brucella* spp. The spleen, liver, and bone marrow are the most frequently involved sites. In addition, cardiovascular, osteoarticular, gastrointestinal, urogenital, hematological, and neurological complications may arise.[1]

In this case, an adolescent was diagnosed with brucellosis, whose initial manifestations included abdominal pain, diarrhea, followed up by fever and constipation. Further colonoscope showed an intestinal inflammation lesion and ultrasound (US) suggested vasculitis of abdominal arteries. The purpose of this case report is to introduce the clinical features, imaging results, management strategy, and prognosis of a rare manifestation of brucellosis.

2. Case report

A 15-year-old male patient was admitted to a hospital due to a 4-week history of fever and intermittent, diffuse abdominal pain.

The patient had first presented with diffuse, intermittent abdominal pain and diarrhea after eating barbecue many times over the course of 2 weeks. Two days after the first presentation of these symptoms, he had a high fever, with a maximum temperature of 39°C. His symptoms did not remit after 4 weeks. So he went to a local hospital and was treated with an unidentified antibiotic. His diarrhea was relieved, but the fever and abdominal pain did not improve. Approximately 10 days later, he was transferred to our hospital for further investigation and management of suspected inflammatory bowel disease (IBD).

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Table 1

Laboratory data.

Variables	Reference range	2 wk before admission	On admission	1 mo after admission	2 mo after admission	4 mo after admission
HGB, g/L	120–160	118↓	118↓	127	142	148
White cell count, ×10S9/L	3.5–9.5	15.2↑	6.5	5.4	5.5	4.3
Differential count, %						
Neutrophils	50.0–75.0	81.5↑	65.9	63.2	64.5	55.5
Lymphocytes	20.0–40.0	10.0	25.1	24.1	24.0	35.3
Monocytes	3.0–8.0	6.8	5.6	8.1	8.1	6.2
ESR, mm/h	0–15	22↑	17↑	5	6	1
CRP, mg/L	0–8	28↑	12↑	7	13↑	<1
Antinuclear antibody	–	–	–	–	–	–
OB	–	+	+	+	–	–

CRP = C-reactive protein, ESR = erythrocyte sedimentation rate, HGB = hemoglobin, OB = occult blood test.

He was living in a village in Heilongjiang Province, a northern province in China where the incidence of human brucellosis has increased substantially. In addition, the patient had a history of eating barbecue. He denied having a history of exposure to contaminated water or going to epidemic areas. His mother had suffered from pulmonary tuberculosis about 10 years ago. He had lost approximately 5 kg of weight over the previous month and he was only 41 kg in weight and 174.5 cm in height (body mass index [BMI] 13.5) when admitted to our hospital.

On physical examination, his temperature was 37.2°C, intestinal peristalsis had decreased to 2 to 3 times per minute, and suspicious tenderness was detected in the right and left upper quadrants of the abdomen. Other vital signs and elements of the examination were normal. The laboratory investigations revealed anemia, a high erythrocyte sedimentation rate, and an elevated C-reactive protein level; the laboratory test results are shown in Table 1. A stool specimen was positive for occult blood. A tuberculin skin test was negative, as was an interferon gamma

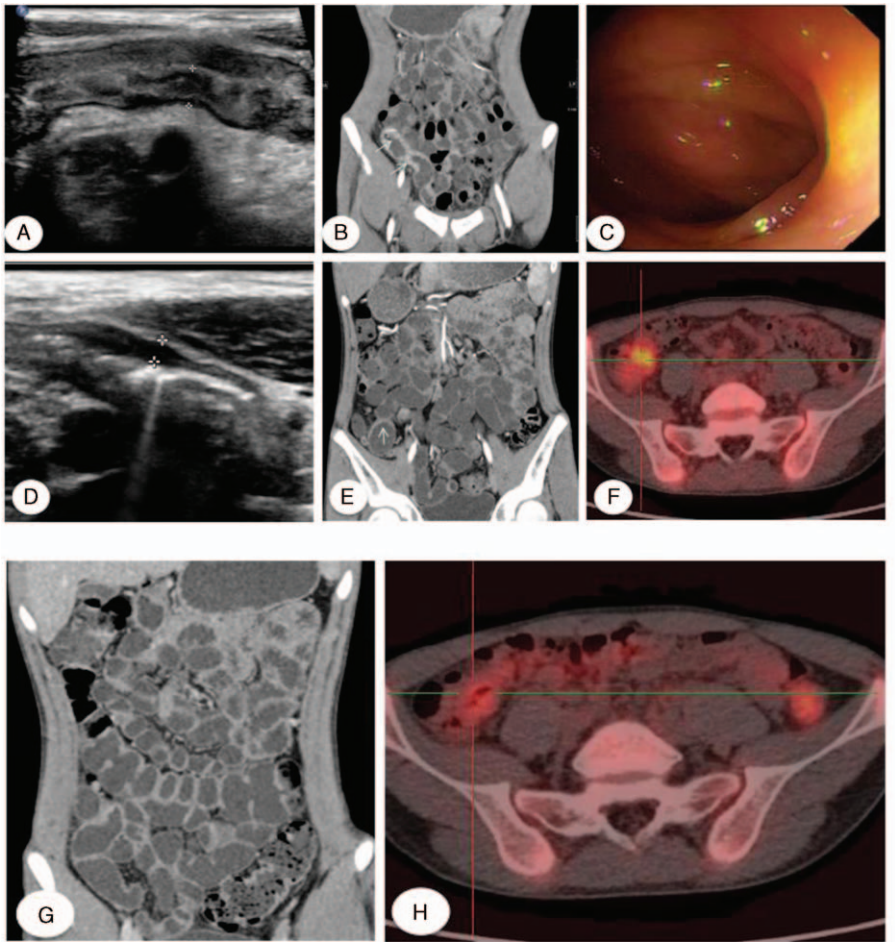

Figure 1. Intestinal brucellosis. (A) Initial US results revealed a thickened hypoechoic bowel wall in the terminal ileum, where mainly the mucosal and submucosal layers were thickened. The 5-layered structure of the bowel wall remained identifiable. (B) CT results showed thickened bowel walls in the ileocaecal area and the terminal ileum, with abnormally enhanced mucosa. (C) An endoscopic examination showed irregular ulcers in the distal ileum and mucosal edema. (D–F) After 1 month of treatment, sonogram (D), CT (E), and PET/CT (F) results revealed remarkable improvements in the bowel. (G, H) Both the ileocaecal area and the terminal ileum appeared normal after 3 mo of treatment. CT = computed tomography, PET = positron emission tomography, US = ultrasound.

release assay (T-spot. tuberculosis) for *Mycobacterium tuberculosis*. A Widal-Felix test was negative. Negative test results were found for antibodies to IBD, antinuclear antibody, and extractable nuclear antigens.

A transabdominal US examination was performed to investigate the cause of the abdominal pain. The US showed a thickened hypoechoic bowel wall in the terminal ileum (0.55 cm), with thickening mainly in the mucosal and submucosal layers. The 5-layer structure of the bowel wall remained identifiable (Fig. 1). Additionally, color Doppler US showed increased flow signals in the bowel walls and luminal narrowing. The ileocaecal structure was intact. Notably, multiple hypoechoic lymph nodes (maximum diameter: 1.8 cm) with a thickened cortex were detected in the abdominal cavity, especially in the right lower quadrant; some of these lymph nodes were fused together. Furthermore, a spectral analysis of the Doppler signals of arteries supplying the gastrointestinal tract (i.e., celiac trunk and superior mesenteric arteries) was performed. The results showed a dramatically increased flow velocity (peak systolic velocity: 643 cm/s) in the origin of the superior mesenteric artery (SMA) and celiac artery (CA) (Fig. 2), which suggested significant stenosis. A computed tomography (CT) scan of the intestine confirmed the above findings; the scan showed a thickened bowel wall in the ileocaecal area and terminal ileum, with an abnormal enhancement of the mucosal surface (Fig. 1) and remarkably enlarged lymph nodes near the iliac vessels in the right lower quadrant of the abdomen. An aortic computed tomographic angiography showed moderate narrowing in the beginning of the SMA and slight narrowing in the beginning of the CA (Fig. 2). Incidentally, the CT scan revealed an enlarged spleen with multiple wedged areas of low attenuation under the membrane (Fig. 3), and a similar lesion was also found in the inferior pole of the left kidney; these were suspected to be areas of infarction.

The patient underwent an endoscopic examination. The examination revealed many irregular ulcers in the narrowed lumen of the terminal ileum. Additional pathological features of the terminal ileum included inflammatory exudate, granulation tissue, and mucosal lymphoid hyperplasia, which collectively suggested severe acute and chronic inflammation of the intestinal mucosa.

Due to the patient's signs and symptoms, he was considered to be suffering from an intestinal infection rather than from IBD. Subsequently, additional history was obtained. He had eaten undercooked roast lamb and beef many times during the 2 weeks before he began to feel uncomfortable. No pathogenic microorganism was found in endoscope biopsy tissues of the patient. Cytomegalovirus DNA and IgM antibody were negative on multiple blood tests. In addition, cytomegalic inclusion body was not present in the tissue sample from endoscopic biopsy.

Brucellosis was suspected because the patient came from Heilongjiang Province, which is a northern province in China where the incidence of human brucellosis has risen substantially. A blood sample was sent for serological testing, and the Brucella standard tube agglutination (STA) test was twice positive at a dilution of 1:160. In addition, the Rose-Bengal plate test was positive for brucellosis. Two *Brucella* spp. blood cultures were collected and all results were negative.

According to his symptoms (i.e., fever, abdominal pain), imaging results (i.e., splenomegaly, splenic and renal infarction), history of eating undercooked roast lamb and beef, and STA continuously twice positive at a dilution of 1:160 and Rose-Bengal test results, Brucellosis was highly suggestive. Unfortunately, multiple *Brucella* spp. blood culture were undertaken and

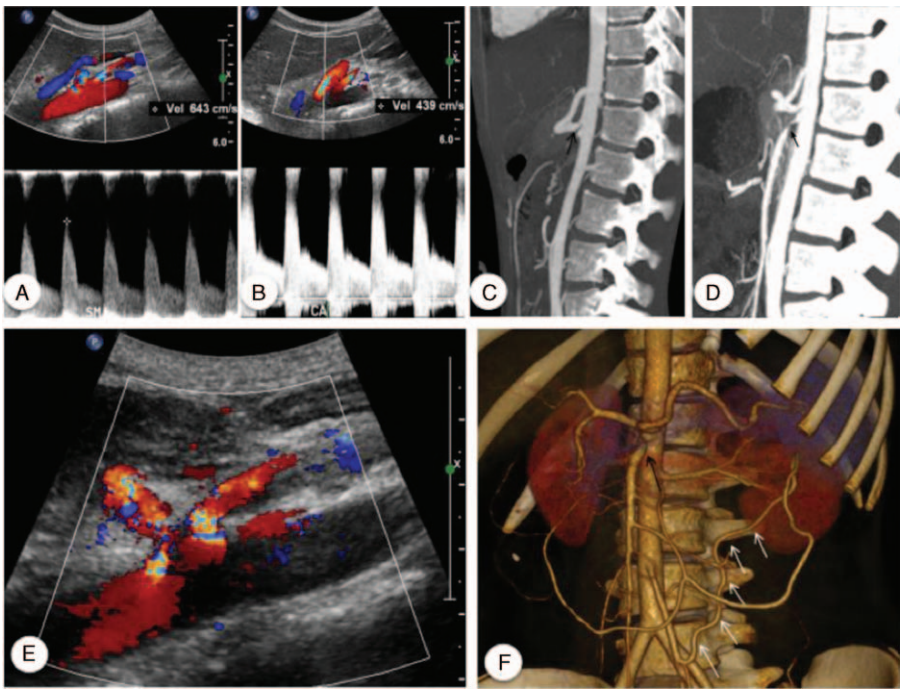

Figure 2. Brucellosis complicated with SMA and CA involvement. (A, B) Color Doppler images showing elevated peak systolic velocity in the SMA (PSV: 64 cm/s) and CA (PSV: 439 cm/s). (C, D) CTA results confirming moderate stenosis in the CA and SMA (black arrow). (E, F) In the follow-up examination (1 mo later), the US (E) and CTA (F) results showed that the SMA stenosis had not improved. The Riolan artery, collateral circulation between the SMA and IMA, had opened (white arrows). CA = celiac artery, CT = computed tomography, CTA = computed tomographic angiography, IMA = inferior mesenteric artery, PSV = peak systolic velocity, SMA = superior mesenteric artery.

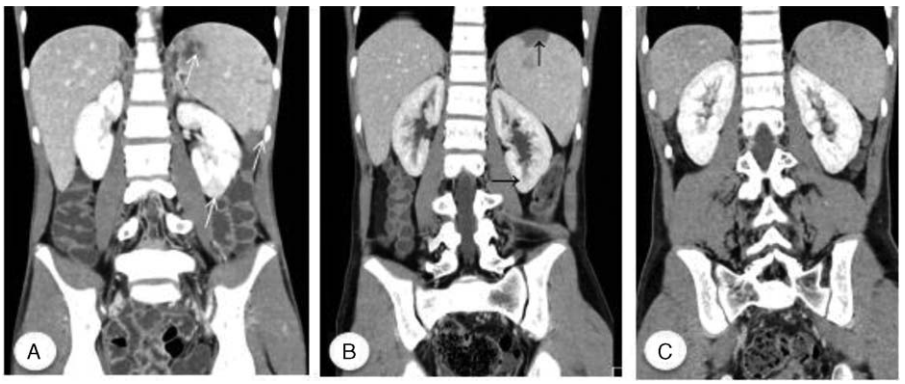

Figure 3. Areas of infarction in the spleen and left kidney in the case of brucellosis. (A) Abdominal computed tomography showing areas of low attenuation in the lower pole of the left kidney and an enlarged spleen with multiple wedged lesions under the capsule (white arrows). (B) After 1 mo of treatment, the renal lesions were barely perceptible and the splenic lesions had become smaller (black arrows). (C) Both the kidneys and the spleen appeared normal after 3 mo of treatment.

turned out to be negative. Neither Brucella Coombs test nor PCR analysis was further undertook. For the suspicion of that the abdominal artery stenosis was caused by embolism from endocarditis, a transthoracic echocardiogram was performed. There was no sign of endocarditis. No cardiac murmur or sign of embolism was found in physical examination. The patient received minocycline (doxycycline was unavailable) plus rifampicin to treat brucellosis and there was a significantly improvement after 4 weeks treatment. Further transesophageal echocardiogram has not been arranged. Finally, the patient was diagnosed as brucellosis. The narrowing of the SMA and CA was suspected to be vasculitis secondary to the brucellosis.

Doxycycline is considered as the first-line therapy for Brucellosis; however, it is currently unavailable in Beijing. Minocycline combined with rifampicin were used instead. The patient was given oral minocycline and rifampicin for 12 weeks totally. After 3 weeks of treatment, he had no fever or abdominal pain. After another 7 weeks, follow-up CT and US examinations showed remarkable improvements in the bowel. Positron emission tomography (PET) was used for further investigation of the intestine inflammation. The results showed mildly increased metabolic activity in the terminal ileum and adherent lymph nodes (Fig. 1), which was indicative of an inflammatory disease instead of a malignancy. The areas of splenic infarction were smaller than they were previously, and renal perfusion appeared normal (Fig. 3). The CT results showed that the narrowed lumens of the SMA and CA had not improved. However, the Riolan artery, a collateral circulation between the SMA and inferior mesenteric artery (IMA), had opened (Fig. 2). Two months later, the splenic and renal lesions were barely perceptible. Due to the suspected secondary vasculitis, he was treated with minocycline and rifampicin for another 8 weeks, but there was little improvement in the noted arterial stenosis (Fig. 2). Additional laboratory test results are shown in Table 1.

3. Method

This study was approved by the Institutional Review Board of the Peking Union Medical College Hospital, Beijing, China. The patient provided written informed consent for the use of his information.

4. Discussion

Brucellosis is a zoonosis that occurs worldwide and is caused by gram-negative bacteria, *Brucella* spp. In China, this disease is particularly endemic in the provinces of Inner Mongolia, Heilongjiang, Hebei, Jilin, and Shanxi.[2] Brucellosis spreads to humans by the consumption of infected dairy products or meat of domestic livestock (e.g., sheep, goats, cattle, water buffalo, camels, pigs) and by close contact with their secretions and carcasses.[2–4]

Brucellosis may lead to a variety of clinical presentations. Fever and arthralgia of the large joints are the most common manifestations, followed by cough, malaise, myalgia, sweating, rash, and cardiac involvement.[3,4] Gastrointestinal manifestations are diverse and maybe the only symptoms of brucellosis that occur. These features range from relatively milder complaints, such as anorexia, diarrhea, or constipation, to more serious complications, such as mesenteric lymphadenitis, liver or spleen involvement, or cholecystitis; rarely, even life-threatening complications can occur, such as colitis, pancreatitis, peritonitis, or intestinal obstruction.[5]

As the clinical symptoms and signs of this disease are not specific, it can be difficult to diagnose. There have been few reports of the imaging results of a Brucella infection involving the intestinal tract. For our case, the diagnosis was confirmed by history, clinical feature, serology, and response to treatment. Differential diagnoses include Q fever and other infection such as cytomegalovirus. Q fever is also a zoonosis with varied manifestations, but Q fever in human is not common in China, which usually present with acute and self-limited pneumonia and hepatitis, chronic infection is rare. We did not find any intracellular organism in the biopsy tissue or any similar case in Chinese literatures. Cytomegalovirus DNA and IgM antibody were negative on multiple blood tests. Accordingly, Q fever and cytomegalovirus infection or coinfection was excluded. As with other types of infectious enterocolitis, the sonographic signs of intestinal brucellosis are characterized by the symmetric and homogeneous thickening of the wall in the terminal ileum and proximal colon, in association with enlarged regional mesenteric lymph nodes. *Brucella melitensis* is able to spread systemically from the digestive tract after infection, most likely through M cells of the mucosa-associated lymphoid tissue, which may correlate with the image of the ileal mucosa shown in Fig. 1.[6] In this case, many irregular ulcers were observed in the narrowed lumen of the terminal ileum endoscopically. These ulcers could explain the patient's severe and persistent abdominal pain and high fever. In addition, the imaging patterns could help to differentiate this condition from IBD. In the differential diagnosis between infectious ileocolitis and Crohn disease, the latter is

characterized by transmural inflammation and intestinal complications. Therefore, the bowel wall is usually thicker than it is in infectious ileocolitis, and the normal stratified pattern may disappear due to the transmural inflammation. The thickened bowel wall may be surrounded by mesenteric hypertrophy and other complications, such as abscesses or fistulas. None of these features are present in infectious ileocolitis.

In addition, SMA syndrome may be one of the reasons of his constellation of symptoms of intermittent abdominal pain and diarrhea after eating.[7] This patient lost approximately 5 kg (10% of weight) over the previous month and he was only 41 kg in weight and 174.5 cm in height (BMI 13.5) in admission. There appears to be a reduction of body mass in the computerized tomographic images. This may have been due to decreased caloric intake or cachectic or due to abdominal angina of 4 weeks duration. The fat padding between the aorta and the origin of the SMA was decreased from normal. This can be the underlying cause of an acute aortomesenteric angle and external compression on the duodenum. Figure 2 shows the SMA in a computerized tomographic angiogram, the angle between the aorta and the SMA, the aortomesenteric angle appears to be more acute than normal. This angle appears to be approximately 30°, which is less than the normal range of 38° to 50°. Such an acute angle would be consistent with SMA syndrome.

Vasculitis is rarely reported as a clinical manifestation of brucellosis. A summary by Herrick indicated that a total of 34 cases of brucellosis complicated with vascular involvement have been reported, including of the aorta in 23 cases (68%), of upper limb vessels in 6 cases (18%), of lower extremity vessels in 3 cases (9%), of the SMA in 2 cases (6%), and of the carotid artery in 1 case (3%).[8] In many of these cases and for unknown reasons, the vasculitis progressed even under intensive therapy.[9–12] One case of brucellosis endocarditis complicated by disease in the SMA was reported by Erbay.[13] There is a case report of multiple mycotic aneurysms in the aorta due to brucellosis, with apparent extension into the SMA.[14] In our case, the SMA and CA were significantly narrowed, which may explain the commonly prevalent symptom of abdominal pain, as a form of abdominal angina, occurring after eating food. We speculate that the SMA and CA stenosis in our case was due to infectious vegetation, while the diagnosis of "vasculitis" in general can include autoimmune or rheumatologic diseases. For further clarification of the situation, the "radiological vasculitis" instead of vasculitis was used as a description of radiological features. The stenosis in the lumens of the CA and the SMA might be possibly due to vegetation due to Brucella, since Brucella can directly infect vascular endothelial cells.[15,16] And the narrowing did not improve with 20 weeks of oral minocycline and rifampicin treatment. The Riolan artery, collateral circulation between the SMA and IMA, opened to relieve the intestinal ischemia. Sonography combined with color Doppler flow imaging and CT were used to identify changes in the intestinal walls and the main splanchnic vessels. These techniques were useful for both diagnostic and follow-up purposes.

Brucella is known as a causative agent of infectious endocarditis, capable of affecting the aortic or mitral valves. The patient's *Brucella* spp. blood culture was negative consecutive 2 times. The negative blood cultures raised the possibility of a clinical diagnosis of "culture-negative" endothelial infection or "culture-negative" infectious endocarditis, particularly since *Brucella* species are known as one of the causes of "culture-negative" infectious endocarditis. The presence of visible endothelial lesions in the CA and the SMA are evidence for an endothelial infection in general, of which endocarditis is a subset.

Recommended treatments have included doxycycline plus rifampicin or doxycycline plus trimethoprim–sulfamethoxazole, or fluoroquinolone plus rifampicin, for 6 weeks. In cases of localized involvement, such as spondylitis or endocarditis, treatment for a longer duration has been recommended. In cases involving the central nervous system, antibiotic penetration through the blood–brain barrier must be considered. This case had imaging evidence of endothelial infection and because of this was prescribed a 12-week course of antibiotics.

In conclusion, gastrointestinal manifestations may be the only observable features of the disease. Brucellosis should be suspected when a patient is from endemic areas, has been exposed to risk factors, for example, has consumed undercooked meat products, and presents with abdominal pain, fever, and diarrhea. Splanchnic vasculitis is a rare complication of brucellosis. Imaging modalities can distinguish changes in the intestinal walls and the main splanchnic vessels, which are very important both for diagnosis and during follow-up examinations. The gastrointestinal manifestations of brucellosis recovered rapidly under intensive treatment, while the noted arterial stenosis remained unchanged even with a long-term drug treatment.

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