Surg Today (2005) 35:671–676
DOI 10.1007/s00595-004-2975-2

SURGERY TODAY

Esophagobronchial Fistula in a Patient with Behçet's Disease: Report of a Case

Yoshikazu Morimoto[1], Yasuhiro Tanaka[1], Toshinori Itoh[2], Shigetaka Yamamoto[1], Youjiro Kurihara[1], and Kazuhiro Nishikawa[1]

[1]Department of Surgery, Osaka General Medical Center, 3-1-56 Bandaihigashi, Sumiyoshi-ku, Osaka 558-8558, Japan
[2]Department of Surgery E1, Osaka University Graduate School of Medicine, Suita, Japan

Abstract
Esophageal involvement in Behçet's disease is generally considered to be very uncommon. So far, six cases of esophageal ulcers associated with perforation, penetration, or fistula in Behçet's disease have been described in the English literature. This report describes esophagobronchial fistula in a patient with intestinal Behçet's disease. A 62-year-old man was transferred to our hospital for peritonitis due to a small intestinal perforation after an appendectomy. At the age of 14 years he had had recurrent oral ulcers. Ulcerations of the ileum and epididymitis were found, and a pathological examination revealed nonspecific inflammation. Furthermore, an esophageal ulcer with esophagobronchial fistula was diagnosed. The fistula required not only endoscopic treatment but also surgical intervention. The patient's clinical features were consistent with the active phase of intestinal Behçet's disease. The symptoms gradually resolved without any treatment. Four years after remission, however, the symptoms recurred with gastrointestinal hemorrhage and polyarthritis. In the ileocolic region, punch-out ulcerations were noted. The clinical history and features led to a diagnosis of Behçet's disease associated with recurrent gastrointestinal ulcerations. Steroid therapy (prednisolone, 20 mg daily) was started, and led to a rapid resolution of the symptoms. The patient is now being followed up as an outpatient while receiving prednisolone (10 mg per day), without complaint of any gastrointestinal symptoms.

Key words Intestinal Behçet's disease · Esophageal involvement · Esophagobronchial fistula

Reprint requests to: Y. Morimoto
Received: January 21, 2004 / Accepted: November 16, 2004

Introduction

Behçet's disease was first reported as a triple symptom complex consisting of oral ulcers, genital ulcers, and ocular inflammation, as described by Behçet in 1937.[1] Intestinal Behçet's disease, which is one of the entities of Behçet's disease, is often due to nonspecific ulcers, especially in the distal ileum and cecum, but rarely in the esophagus.[2–5] Esophageal involvement in Behçet's disease is very uncommon and to date less than 50 cases have been reported.[5–10] This report describes esophagobronchial fistula in a patient associated with intestinal Behçet's disease.

Case Report

A 62-year-old man was transferred to Osaka General Medical Center due to peritonitis after appendectomy on December 27, 1996. At the age of 14 years, he had experienced recurrent oral ulcers, which usually resolved spontaneously after several days. The patient had no past history of genital ulceration or thrombophlebitis. No demonstrable pathology had been found on a previous examination of his upper alimentary tract. On December 20, 1996, acute right lower abdominal pain occurred. The patient was diagnosed to have acute appendicitis and he thus underwent an appendectomy at a different hospital. His drainage tube revealed contaminated fluid containing digestive juices. He was diagnosed to have panperitonitis and was transferred to our hospital on postoperative day 7. On physical examination, his abdomen was hard with rebound tenderness. We at first considered this patient to have peritonitis due to an intestinal perforation after surgery, and treated him with intravenous hyperalimentation. During hospitalization, an extended subcutaneous abscess in the scrotum was also determined. The patient underwent an excision of the right testis and drainage

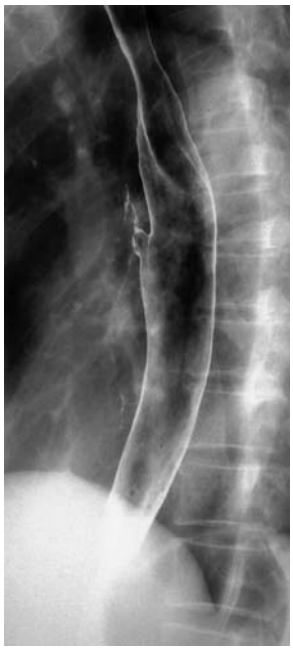


Fig. 1. Esophagobronchial fistulogram. A barium swallow revealed a fistula between the mid-esophagus and the right main bronchus

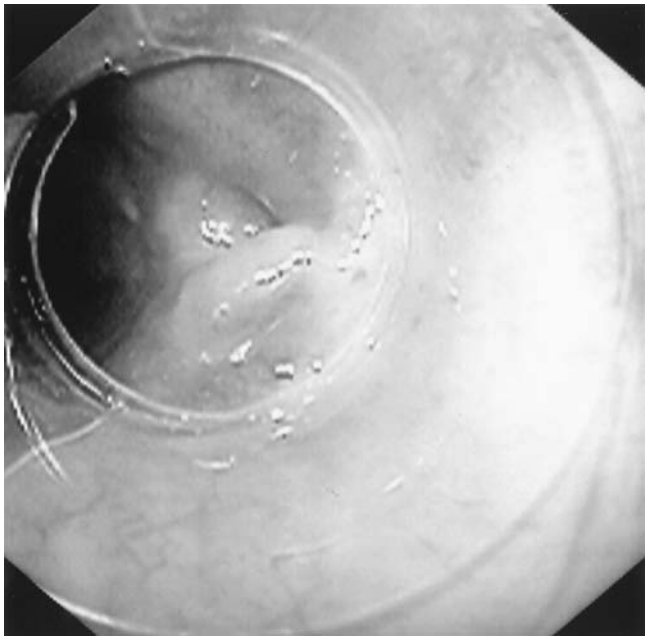


Fig. 2. Esophgogastroscopic examination. A small ulcerate area was found on the anterior wall of the esophagus 30 cm from the incisors. 99% Ethanol was injected around the ulcer

on January 14, 1997. The pathological examination revealed nonspecific inflammation with epididymitis. The patient's symptoms due to peritonitis did not resolve with conservative treatment, and we performed an ileostomy at the left lower abdomen on February 5, 1997. On postoperative day 21, massive gastrointestinal bleeding and pneumonia developed. A barium swallow revealed a fistula between the mid-esophagus and the right main bronchus (Fig. 1). Upper gastrointestinal endoscopy revealed a small, ulcerated area on the anterior wall of the esophagus, 30 cm from the incisors (Fig. 2), but no ulcers in the stomach or duodenum. Neither massive esophageal hemorrhage nor eroded vessels were noticed, but we treated the patient with 99% ethanol injection around the esophageal ulcer to occlude the fistula. The pneumonia improved after this interventional therapy. Almost simultaneously, small intestinal ulcers were also found at the site of ileostomy (Fig. 3). A histological examination of the ulcers revealed nonspecific inflammatory reaction, and an infiltrate consisting mainly of lymphocytes and some plasma cells into the muscularis propria (Fig. 4a,b). According to his clinical features, the symptom complex was consistent with the active phase of intestinal Behçet's disease. The patient's symptoms gradually resolved after several weeks without any subsequent medical treatment. He thereafter could eat well without any symptom of pneumonia, and was discharged (Table 1).

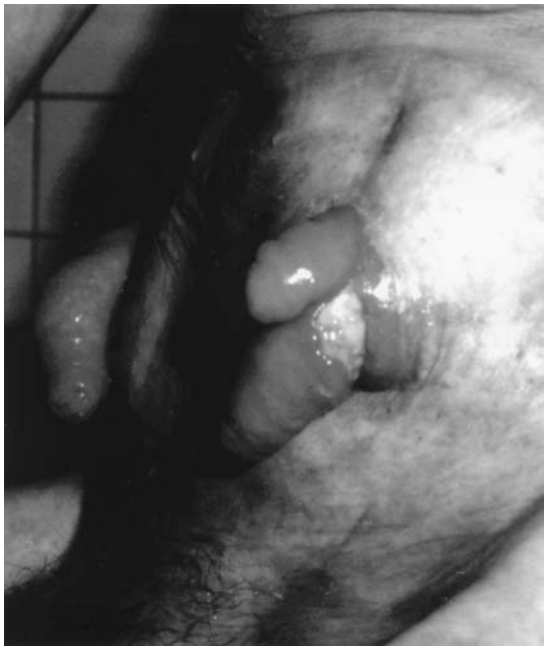


Fig. 3. Punch-out ulcerations were observed in the intestinal mucosa at the ileostomy site

On November 5, 1997, he was readmitted for the purpose of a surgical intervention for an esophagobronchial fistula. A fistulous communication between the esophagus and the right bronchus beneath the azygos vein was found by video-assisted thoracoscopic

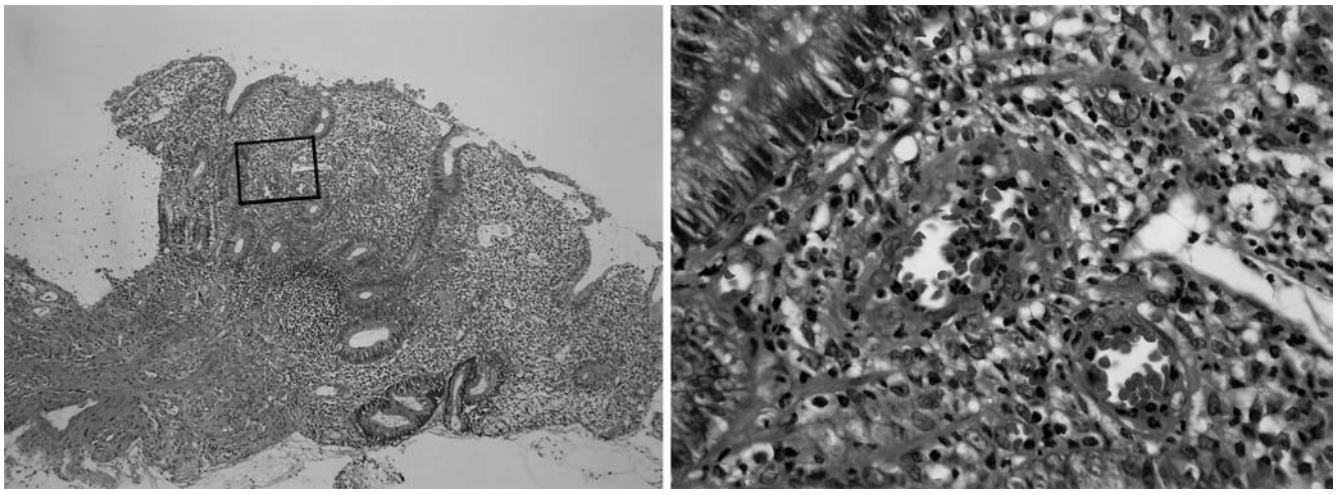
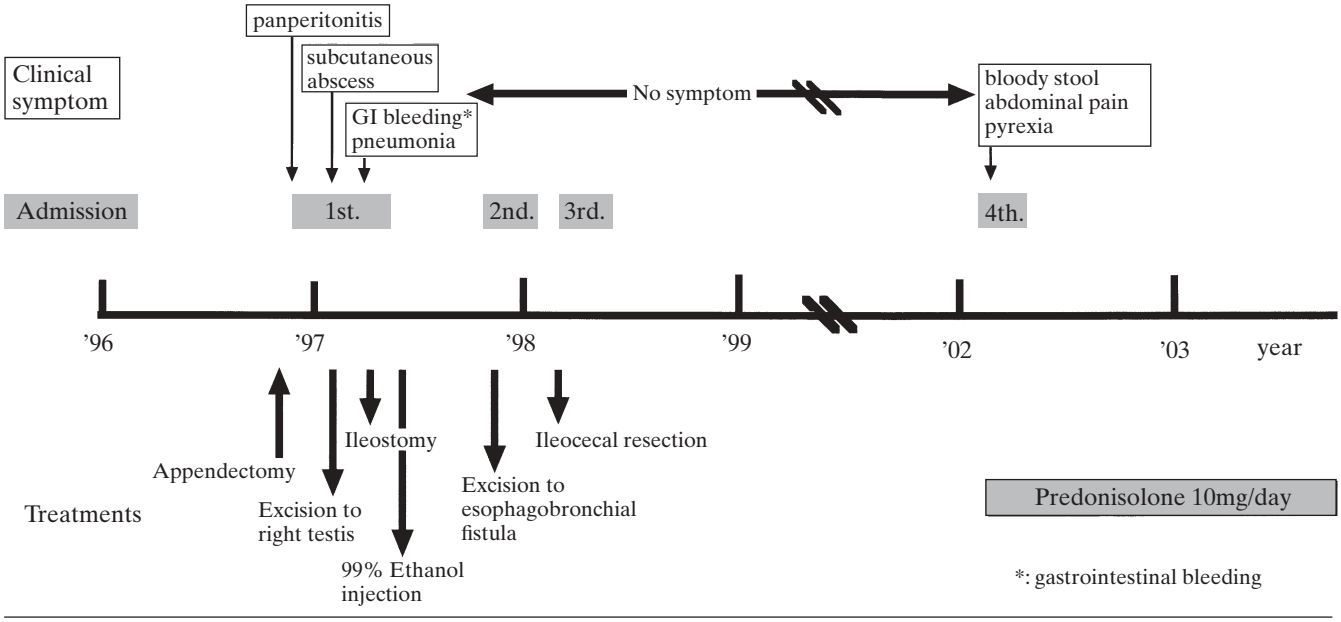


Fig. 4a,b. Histological examination. **a** A stained section of an active ulcer shows a diffuse cellular infiltrate mainly consisting of lymphocytes and plasma cells in the muscularis propria. No granulation can be seen (H&E, ×20). **b** A higher power view, framed with solid lines in **a**, shows a submucosal vessel with wall thickness and perivascular inflammatory infiltrate (H&E, ×160)

Table 1. Clinical course



surgery (Fig. 5). This communication, measuring 20 mm in length and 5 mm in diameter, was excised using Endo-GIA (Tyco Healthcare, Mansfield, MA, USA). Two months later, he underwent an ileocecal resection, ileocolonic reanastomosis, and repair of the abdominal wall defect with a femoral musculocutaneous flap. The clinical course after these procedures was uncomplicated, and for the next 4 years the patient remained healthy and did not require any treatment (Table 1).

On February 5, 2002, he was again admitted to our hospital due to a recurrence of symptoms with bloody stools, abdominal pain, and pyrexia. He also complained of lumbago, right coxalgia, and neck pain. On physical examination he was noted to have ulcers of varying size on his lip, tongue, and buccal mucosa.

Laboratory studies revealed hemoglobin, 8.4 g/dl; hematocrit, 25.3%; white blood cell count, 7700/mm^3; C-reactive protein (CRP), 12.3 mg/dl; erythrocyte sedimentation rate (ESR), 138 mm/1st hour. HLA-B51 was not present. Conservative treatment with intravenous hyperalimentation resolved the gastrointestinal hemorrhage and oral ulcers, but he developed a fever of up to 38°C daily. To evaluate the other abnormalities, colonoscopy was performed. In the region of ileocolic anastomosis, there was a localized area of severe inflammatory bowel disease characterized by punch-out ulcerations. An ophthalmic examination did not reveal any ocular inflammation and a pathergy test was negative.

The patient's clinical history and features showed not only ulcerations of the small intestine, esophagus, and colon but also recurrent oral ulcers, epididymitis, and polyarthritis. Accordingly, he was diagnosed to have Behçet's disease with gastrointestinal ulcerations. Steroid therapy (prednisolone 20 mg daily) was started and led to a rapid resolution of symptoms. Furthermore, the levels of CRP and ESR decreased to within the normal range. The patient showed a remarkable recovery 14 days after commencement of steroid therapy. He is now being followed up as an outpatient while receiving prednisolone (10 mg daily). Steroid therapy has prevented a recurrence of any gastrointestinal symptoms during the follow-up period of 23 months (Table 1).

Discussion

Behçet's disease is a disorder characterized by multisystem vasculitis and inflammatory tissue damage of unknown etiology. It occurs most commonly along the ancient Silk Road that extended from the Far East to the Mediterranean Sea. The prevalence of this disease differs widely among races, being 10 in 100 000 in Japan, and only 0.3 per 100 000 in the Western countries.[11] The cause of Behçet's disease is unknown, and the leading etiologic theories include infectious, autoimmune, and genetic mechanisms. Currently, a streptococcal

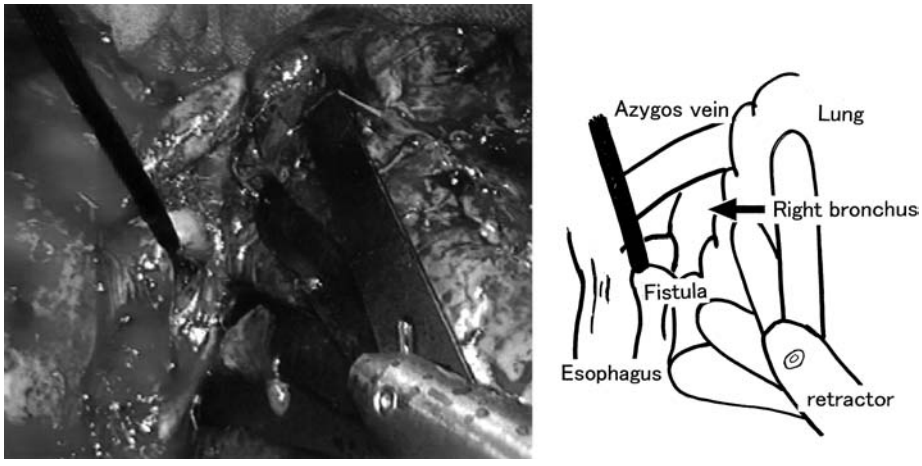


Fig. 5. Operative findings. An esophagobronchial fistula, measuring 20 mm in length and 5 mm in diameter, was seen

Table 2. Esophageal ulcers associated with perforation, penetration, or fistula in Behçet's disease: review of the literature

No.	Year	First author[Ref.]	Age	Sex	Clinical symptoms							
					Oral	Eye	Skin	Genital	Neural	Vascular	Articular	Others
1	1973	Brodie[2]	71	M	+	–	+	+	–	+	+	None
2	1975	Parkin[3]	52	F	+	–	+	–	–	–	–	None
3	1977	Lebwohl[4]	16	F	+	–	–	+	+	–	–	None
4	1979	Levack[16]	42	M	+	–	–	+	–	+	+	None
5	1983	Mori[9]	39	M	+	–	+	+	–	–	+	None
6	2004	Present case	62	M	+	–	–	–	–	–	+	Epididymitis

+, present; –, absent; GI, gastrointestinal

infection may be considered to affect the onset of this disease.[3]

The diagnosis is based only on clinical features. Some sets of refined diagnostic criteria are now being established to more accurately diagnose this disease. However, there is no universally accepted definition for Behçet's disease. The generally accepted criteria, derived from an international study group (ISG),[12] are as follows: presence of oral ulceration plus any two of genital ulceration, typically defined eye lesions, typically defined skin lesions, or a positive pathergy test finding. Although gastrointestinal symptoms are common in Behçet's disease, the occurrence of gastrointestinal ulcers is rare. So-called intestinal Behçet's disease accounts only for 1%–3% of cases.[12,13] Furthermore, the diagnosis of intestinal Behçet's disease is especially difficult. The major difficulty lies in the considerable overlap between the features of Behçet's disease and those of inflammatory bowel disease.

Retrospective consideration of our case showed that peritonitis after an appendectomy might play a role in a perforation of the terminal ileum. During hospitalization, an esophageal ulcer also developed and led to an esophagobronchial fistula. After a 4-year remission, punch-out ulcerations at the site of ileocolic anastomosis recurred and induced melena with severe anemia (Table 1). When the patient's clinical features were compared with the ISG's criteria, he did not fulfill the major criteria except for the recurrent oral ulcers. Other clinical manifestations, such as epididymitis and polyarthritis, defined as minor criteria by the Behçet's Disease Research Committee of Japan,[14] were identified in this patient. The same patient may be classified as having complete Behçet's disease by one set of criteria while being considered to have incomplete disease based on other criteria. Therefore, some authors have suggested that intestinal Behçet's disease should be considered a classification of its own.[11,15]

Esophageal involvement in Behçet's disease, however, is very uncommon and less than 50 cases have been reported in the literature.[5–7,9,10,14] According to these reports, the esophageal lesions are mainly nonspecific ulcers in the middle and/or the lower esophagus, and serious complications such as erosions, perforations, esophagitis, stenosis, and varices have been rarely described.[8] Brodie and Ochsner reported the first case of esophageal penetration in Behçet's disease in 1973.[2] Since then, to our knowledge, five cases of life-threatening esophageal involvement, such as perforation, penetration, or fistula, have been reported.[2–4,9,16] The characteristics of these patients are shown in Table 2; all had oral ulcers but none showed eye lesions. Three patients underwent surgical intervention for esophageal involvement, two underwent fistula excision, and one underwent an esophagectomy. Two patients had other gastrointestinal manifestations except for esophagus and underwent intestinal resection. Two patients who remained untreated died of sudden collapse or severe infection. Three were still alive, and one patient was only treated conservatively.

In our case, esophagobronchial fistula required not only endoscopic treatment but also surgical intervention. Because of an increase in morbidity and mortality after a resection,[8] invasive treatment should be avoided during the acute phase. We therefore first administered endoscopic therapy using 99% ethanol injection and then performed less invasive surgical excision with video-assisted thoracoscopic surgery during remission. Our patient's recurrent symptoms improved after steroid therapy, but we should strictly follow up his condition because the natural course of this entity may be characterized by recurrent exacerbations and remissions.

Esophageal involvement does not significantly correlate with the disease duration, disease activity, or any other aspect of Behçet's disease. As a result, any

Table 2. *Continued*

Esophageal ulcer	Treatment	Other GI ulcer	Operation for GI ulcer	Prognosis	Cause of death
Penetration (mediastinum)	Esophagectomy	—	—	Died	Pulmonary emboli
Perforation (left pleural cavity)	—	Stomach, duodenum, jejunum, ileum	Excision for perforated jejunum	Died	Sudden collapse
Penetration (mediastinum)	Conservative	Cecum, ascending colon	—	Alive	
Fistula (esophagotracheal)	Excision (deltopectoral flap)	—	—	Alive	
Fistula (esophagobronchial)	—	—	—	Died	Infection
Fistula (esophagobronchial)	Ethanol injection and excision	Ileocolonic anastomosis	Ileocecal resection for perforated ileum	Alive	

esophageal ulceration which appears to be a manifestation of Behçet's disease should be considered as one of the possible entities for this disease in patients with gastrointestinal symptoms.

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