

Case report

Esophageal tuberculosis presenting with an appearance similar to that of carcinoma of the esophagus

YUSHI FUJIWARA, HARUSHI OSUGI, NOBUYASU TAKADA, MASASHI TAKEMURA, SHIGERU LEE, MASAKATSU UENO, KENICHIRO FUKUHARA, YOSHINORI TANAKA, SATOSHI NISHIZAWA, and HIROAKI KINOSHITA

Department of Gastroenterological Surgery, Osaka City University Graduate School of Medicine, 1-4-3 Asahi, Abeno, Osaka 545-8585, Japan

A case of esophageal tuberculosis presenting with an appearance similar to that of esophageal cancer is reported. The patient was an 82-year-old man with progressive dysphagia. Barium swallow and esophagoscopy revealed an elevated lesion with deep ulceration in the middle thoracic esophagus. Esophageal carcinoma, in particular, an undermining type of undifferentiated carcinoma, was suspected fluoroscopically and endoscopically. Histological examination of biopsy specimens revealed no malignancy, but there were epithelioid granulomas and a few Langhans' type multinucleated giant cells. Endoscopic ultrasonography clearly demonstrated an extramural lesion with calcification and direct infiltration of enlarged subcarinal lymph nodes into the esophageal wall. Ultrasonographic and histological findings indicated the possibility of esophageal tuberculosis. Although no bacteriological evidence was obtained, a therapeutic trial for tuberculosis, using anti-tuberculous drugs, was started. After 2 weeks, the enlarged subcarinal lymph nodes were markedly reduced in size. The patient's symptoms improved gradually and had disappeared 8 weeks after he started treatment, when tubercle bacilli were isolated from sputum. A connection between the esophageal wall and its adjacent structures was clearly demonstrated by endoscopic ultrasonography. For patients with findings indicative of esophageal tuberculosis on endoscopic ultrasonography, a therapeutic trial for tuberculosis should be considered, even if polymerase chain reaction assay or culture is negative.

Key words: esophageal tuberculosis, endoscopic ultrasonography (EUS), antituberculous chemotherapy

Introduction

Among the various types of extrapulmonary tuberculosis, esophageal tuberculosis is extremely rare.^{1,2} A confirmed diagnosis of esophageal tuberculosis requires the isolation of tubercle bacilli, which is seldom achieved.³ Caseous necrosis, which is indirect evidence of tuberculosis, is not usually detected.³ Therefore, in some patients, a diagnosis was only obtained after an unnecessary esophagectomy, because malignancy could not be ruled out.^{4,5} A case of esophageal tuberculosis, presenting with an appearance similar to that of esophageal cancer, fluoroscopically and endoscopically, is reported. The patient was treated with antituberculous drugs. The utility of endoscopic ultrasonography (EUS) in diagnosing the disease is discussed.

Case report

An 82-year-old man was admitted to our hospital with progressive dysphagia. He had not complained of fever, night sweat, or any respiratory symptoms. Although he denied contact with tuberculous patients, a tuberculin skin test was positive (18mm after 48h). The initial bacteriological examination and polymerase chain reaction (PCR) assay of sputum were negative for tubercle bacilli. Laboratory examination showed that the leukocyte count and hematocrit were within the reference ranges, while the concentration of C-reactive protein was slightly elevated (2.5mg/dl). The erythrocyte sedimentation rate was 74mm in the first hour. Serum concentrations of carcinoembryonic antigen and squamous cell carcinoma-related antigen were within the reference ranges.

A chest X-ray revealed no abnormal lesions in the pulmonary field, and no effusion. Barium swallow showed an elevated lesion with a central ulcer in the right wall of the middle thoracic esophagus (Fig. 1).



Fig. 1. Barium swallow showed an elevated lesion with a central ulcer (*arrow*) in the right wall of the middle thoracic esophagus

Esophagoscopy revealed an elevated lesion, covered with intact mucosa, except for a deep central ulceration, on the right wall 30cm from the incisors. This lesion was stained with iodine, except for the center of the ulcer (Fig. 2). These findings suggested that the lesion could be esophageal carcinoma, in particular, an undermining type of undifferentiated carcinoma. However, although histological examination of biopsy specimens obtained from the ulcer margin failed to demonstrate any malignancy, despite the taking of three biopsy specimens, epithelioid granulomas and a few Langhans' type multinucleated giant cells were revealed (Fig. 3). A Ziehl-Neelsen stain of the biopsy specimen did not reveal any acid-fast bacilli. PCR assays, repeated twice, and the initial culture of the biopsy specimens were negative for tubercle bacilli. Chest computed tomography (CT) showed thickening of the middle thoracic esophagus and enlarged subcarinal lymph nodes (30×20 mm) with thin peripheral enhancement and central low-density areas (Fig. 4). EUS revealed an extramural low-echoic lesion, 15.0×7.5 mm in diameter adjacent to the right side of the esophagus 33cm from the incisors. The lesion had fine central calcification with no border echo be-

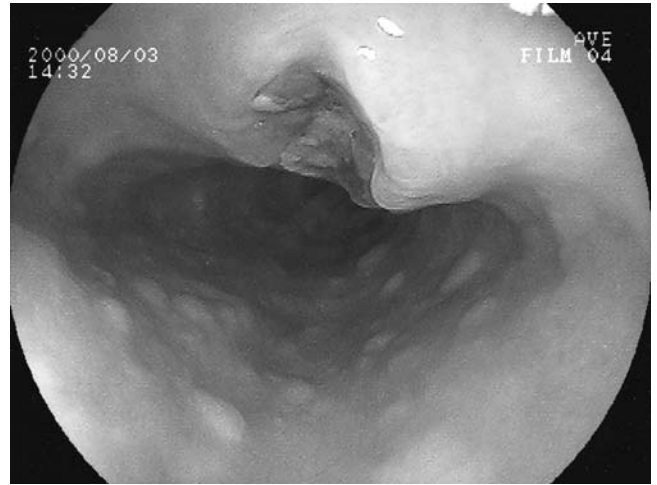


Fig. 2. Esophagoscopy findings of the lesion in the middle thoracic esophagus showed an elevated lesion, covered with intact mucosa, with deep ulceration in the center, on the right wall 30cm from the incisors. This lesion was stained with iodine, except for the center of the ulcer

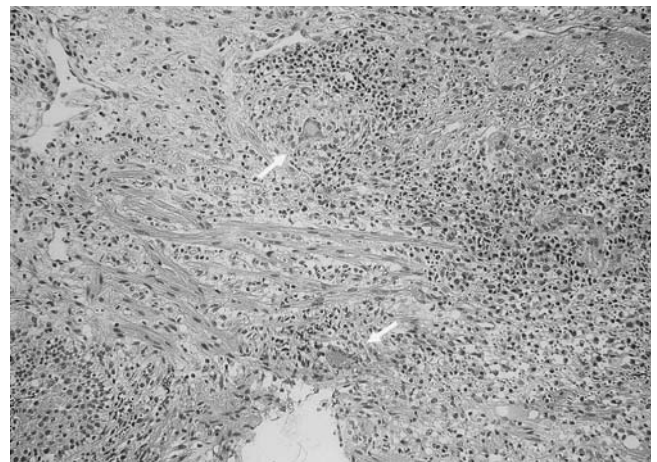


Fig. 3. Histological examination of a repeat biopsy specimen revealed epithelioid granulomas and a few Langhans' type multinucleated giant cells. H&E, $\times 100$

tween the lesion and the esophageal wall. No lesion suspected as originating from the esophageal mucosa was demonstrated (Fig. 5A,B). Ultrasonographically, no other mediastinal nodes were seen to be enlarged. Summing up these findings, we suspected the esophageal lesion to be secondary to infiltration of the tuberculous change of the mediastinal lymph nodes into the esophageal wall, although esophageal cancer still remained as the differential diagnosis.

Although no bacteriologic evidence was obtained, a therapeutic trial for tuberculosis, using isoniazid (300mg per day), rifampicin (450mg per day), and ethambutol (750mg per day) was started. After 2 weeks,

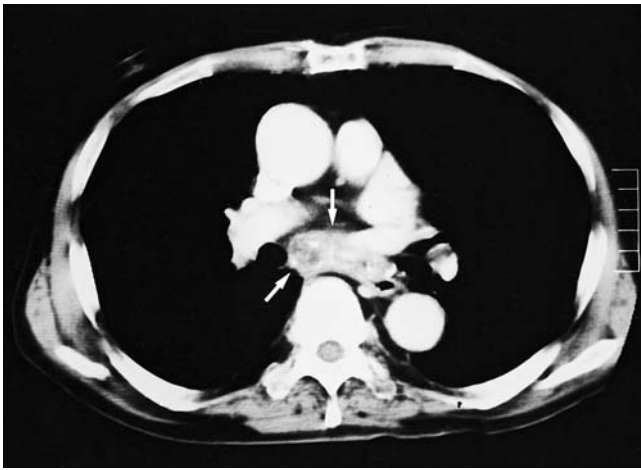


Fig. 4. Chest computed tomography (CT) showed thickening of the middle thoracic esophagus and enlarged subcarinal lymph nodes, with thin peripheral enhancement and central low-density areas (arrows)

chest CT revealed that the enlarged subcarinal lymph nodes were markedly reduced in size (22×15 mm; Fig. 6A,B). The patient's symptoms subsided gradually and had disappeared 8 weeks after he started the treatment. Bacteriologic culture of sputa at 8 weeks was positive for tubercle bacilli and the treatment was continued for 9 months. Although the patient has refused follow-up endoscopy, fluoroscopy, and CT, he is well and symptom-free 15 months after starting the treatment.

Discussion

The esophagus is the least frequently involved organ in gastrointestinal tuberculosis.^{1,2} Lockard¹ reported that esophageal tuberculosis accounted for a mere 0.15% in a series of 16489 autopsies of tuberculous subjects. Until 1997, 52 cases had been reported in the Japanese literature, including 16 autopsies.⁶ Several mechanisms have been proposed to explain the spread of infection to the esophagus:^{1,2,5,7-10} (1) infection of the esophageal mucosa from swallowed tuberculous sputum; (2) contiguous extension from laryngeal and pharyngeal lesions; (3) contiguous extension from other adjacent infected structures, such as the mediastinum, hilar lymph nodes, or vertebrae; (4) hematogenous infection in the course of generalized disseminated miliary tuberculosis; (5) and retrograde lymphatic spread. The esophagus at the tracheal bifurcation is commonly involved, because the most frequent mechanism of esophageal tuberculosis is the direct extension of tuberculous lymphadenitis from the hilar and/or mediastinal lymph nodes.^{1,7-9}

Esophageal tuberculosis can be surmised when dysphagia or odynophagia develops in patients with signs of pulmonary or systemic tuberculosis.^{8,11} However, in patients with no such signs, the diagnosis is hard to confirm and it is difficult to differentiate from esophageal cancer. In some patients, a diagnosis has been obtained after an unnecessary esophagectomy, because malignancy could not be ruled out.^{4,5}

A confirmed diagnosis of esophageal tuberculosis requires the isolation of tubercle bacilli.³ Gordon and Marshall¹² reported that Ziehl-Neelsen staining and culture of the biopsy specimen were helpful in making a correct diagnosis of esophageal tuberculosis. However, tubercle bacilli can seldom be isolated from esophageal lesions, sputum, gastric juice, or stool.³ Recently, PCR assays of sputum and biopsy specimens have been used for an immediate diagnosis of the presence of tubercle bacilli.¹³ In our patient, the initial biological examination and PCR assay of sputum and the biopsy specimen were all negative for tubercle bacilli, and histological examination of the biopsy specimen demonstrated epithelioid granulomas and Langhans' type multinucleated giant cells.

In evaluating mediastinal lesions, CT and/or EUS are commonly used. EUS is superior to CT scanning for assessing close-proximity imaging of the esophageal wall and its adjacent structures.^{14,15} The presence of nodes with central low-density areas and peripheral rim enhancement, and findings of homogeneous and calcified nodes on CT are helpful in differentiating tuberculous lymphadenitis from other causes of mediastinal lymphadenopathy.¹⁶⁻¹⁸ However, findings specific for tuberculous lymphadenopathy on EUS have not been reported yet. In our patient, EUS demonstrated the extramural lesion clearly. The lesion was delineated as a low-echoic lesion, 15.0×7.5 mm in diameter, with fine central calcification. There was no border echo between the lesion and the adjacent esophagus. The lesion had infiltrated into the wall and there was no layer structure of the esophageal wall. The mucosal lesion of the esophagus was therefore suspected to be merely the result of infiltration of mediastinal lymphadenopathy.

The other probable alternative was undifferentiated carcinoma of the esophagus, which is not common, but often has an undermining growth pattern with mediastinal lymph node involvement. However, the carcinoma metastasizes commonly not only to the nodes at the tracheal bifurcation but also to the nodes at the recurrent laryngeal nerve and celiac axis.¹⁹ Moreover, repeated biopsy was negative for malignancy, but detected epithelioid granulomas and Langhans' type multinucleated giant cells. These findings confirmed that the lesion could be tuberculous, but malignancy could not be ruled out. As the patient had progressive symptoms and further investigations were thought to be

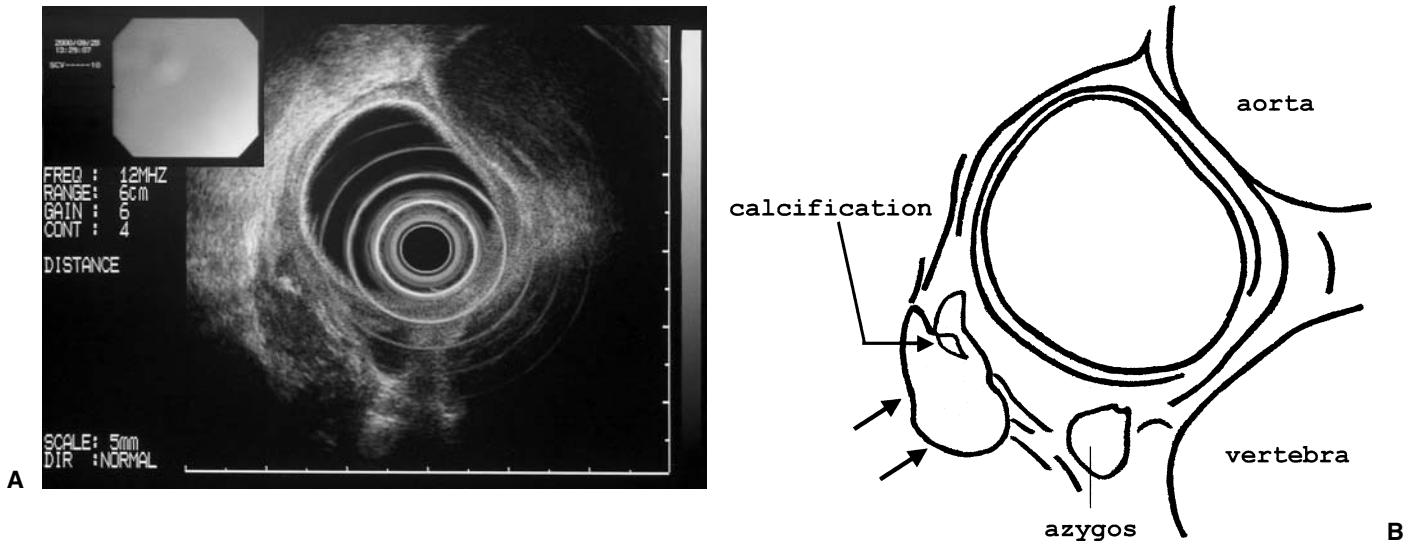


Fig. 5. **A** Endoscopic ultrasonography (EUS) revealed an extramural low-echoic lesion adjacent to the right side of the esophagus 33 cm from the incisors. **B** Schema of **A** shows that the lesion had a central calcification and there was no border echo between the lesion and the esophageal wall (*arrows*)

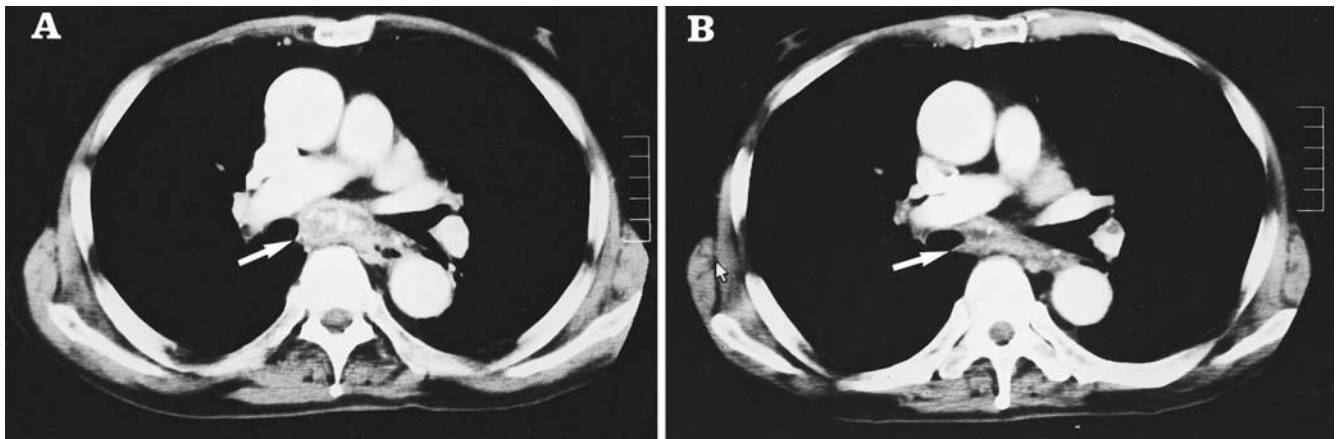


Fig. 6A,B. Findings of chest CT. **A** Finding on July 28, 2000. **B** Finding on August 30, 2000, 2 weeks after the initiation of treatment. Chest CT revealed that the subcarinal lymph nodes were markedly reduced in size. *Arrows* show the subcarinal lymph nodes

uninformative, a therapeutic trial was started, with great care for the possibility of malignancy. We used isoniazid, rifampicin, and ethambutol. The combined administration of these agents has been proven to be effective.^{5,9} An immediate response to the treatment was confirmed by CT, before the positive culture was obtained from sputum. The patient became asymptomatic immediately and has been in good condition after completion of the treatment.

Many reports state that esophageal tuberculous lesions, even if they are causing a stricture, can be healed with antituberculous treatment and that surgical intervention is not necessary.⁹ Therefore, a diagnostic strategy that takes account of tuberculosis is essential to

avoid an unnecessary esophagectomy for patients with an esophageal lesion that is histologically unproven to be malignant. As most esophageal tuberculosis is a direct extension of tuberculous lymphadenopathy, EUS seems to be the best diagnostic tool, delineating the extramural condition of the lesion. For patients with EUS, findings indicative of esophageal tuberculosis, a therapeutic trial for tuberculosis should be considered, even if PCR assay or culture is negative.

References

1. Lockard LB. Esophageal tuberculosis: a critical review. *Laryngoscope* 1913;23:561–84.

2. Carr DT, Spain DM. Tuberculosis in a carcinoma of the oesophagus. *Am Rev Tuberc Pulm* 1942;46:346-9.
3. Savage PE, Grundy A. Oesophageal tuberculosis: an unusual cause of dysphagia. *Br J Radiol* 1984;57:1153-5.
4. Sinha SN, Tesar P, Seta W, Sengupta SK. Primary oesophageal tuberculosis. *Br J Clin Pract* 1988;42:391-4.
5. Fahmy AR, Guindi R, Farid A. Tuberculosis of the oesophagus. *Thorax* 1969;24:254-6.
6. Kasajima H, Mikami Y, Nozaki T, Kawashima H, Mikami M, Suzuki H, et al. A case of esophageal tuberculosis presenting as a submucosal tumor of the esophagus. *J Jpn Surg Assoc* 1997;58:1781-5.
7. Rosario MT, Raso CL, Comer GM. Esophageal tuberculosis. *Dig Dis Sci* 1989;34:1281-4.
8. Rubinstein BM, Pastrana T, Jacobson HG. Tuberculosis of the esophagus. *Radiology* 1958;70:401-3.
9. Dantew B, Frengley D, Wolinsky E, Spagnuolo PJ. Esophageal tuberculosis: mimicry of gastrointestinal malignancy. *Rev Infect Dis* 1987;9:140-6.
10. Furuya Y, Kobayashi S, Higuchi Y. A case of tuberculosis of the esophagus. *Nippon Acta Radiol* 1970;29:1408-14.
11. Schneider R. Tuberculous esophagitis. *Gastrointest Radiol* 1976;1:143-5.
12. Gordon AH, Marshall JB. Esophageal tuberculosis: definitive diagnosis by endoscopy. *Am J Gastroenterol* 1990;85:174-7.
13. Goel MM, Ranjan V, Dhole TN, Srivastava AN, Mehrotra A, Kushwaha MR, et al. Polymerase chain reaction vs conventional diagnosis in fine needle aspirates of tuberculous lymph nodes. *Acta Cytol* 2001;45:330-40.
14. Holscher AH, Dittler HJ, Siewert JR. Staging of squamous esophageal cancer: accuracy and value. *World J Surg* 1994;18:312-20.
15. Van Dam J. Endosonographic evaluation of the patient with esophageal cancer. *Chest* 1997;112(4 Suppl):184S-190S.
16. Williford ME, Thompson WM, Hamilton JD, Postlethwait RW. Esophageal tuberculosis: findings on barium swallow and computed tomography. *Gastrointest Radiol* 1983;8:119-22.
17. Im JG, Song KS, Kang HS, Park JH, Yeon KM, Han MC, et al. Mediastinal tuberculous lymphadenitis: CT manifestations. *Radiology* 1987;164:115-9.
18. Moon WK, Im JG, Yeon KM, Han MC. Mediastinal tuberculous lymphadenitis: CT findings of active and inactive disease. *AJR Am J Roentgenol* 1998;170:715-8.
19. Bancewicz J, Osugi H. Oesophagus: epidemiology, investigation, and surgical management. London: BMJ Publishing Group, 1996.