

Advanced esophageal carcinoma without obvious superficial mucosal alteration

Zhu Jiang^{1,2}, Xiangnan Li^{1,2}, Yang Yang^{1,2}, Song Zhao^{1,2}

¹. Department of Thoracic surgery, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan 450052, China

². Lung cancer diagnosis and treatment research center, Zhengzhou University, Zhengzhou, Henan 450052, China
zhaosong@zzu.edu.cn

Abstract: Objective: To explore the diagnosis, etiology, clinical feature and treatment of advanced esophageal carcinoma with no obvious superficial mucosal alteration. Method: Between December 2004 to December 2009, we treated eight patients who suffered advanced esophageal cancer but were not found obvious superficial mucosal alteration by fiber-esophagoscopy. The bulging mucosa was smooth and biopsy examination showed chronic mucosal inflammatory. Without definite diagnosis, the patients (five men and three women) underwent esophagectomy in our department. Clinic data and tumor characteristics of them were analyzed retrospectively. Result: Two patients died after the operation, while the other six recovered uneventfully. Postoperative histological examination confirmed six squamous carcinoma (SCC) and two adenocarcinoma (ADC) and the tumor originated in the lamina propria mucosa, muscularis mucosae or submucosa, while mucous epithelium found no tumor cells. Until now, one patient is still alive more than five years, one survived about five years, three survived less than five years, and another one had been dead within two years. Conclusion: As the symptom of this kind tumor is mild and the diagnosis is difficult before surgery, the surgeons should be patient when they encounter these patients. Long time follow up is very important.

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1. Introduction

Esophageal carcinoma mainly originates from the mucosal epithelium. The mucosal alteration is always obvious under the fiber-esophagoscopy or upper gastrointestinal barium meal, especially in advanced esophageal carcinoma. But in clinic, there are a small number of patients having no obvious superficial mucosal alteration that can lead to misdiagnosis or missed diagnosis. The cases are rarely reported in medical literature. In this text, we will analyze our patients' data and explore this issue.

2. Material and Methods

From 2004 to 2009, we treated a total of 936 cases with advanced esophageal carcinoma and underwent esophagectomy with lymph node dissection on them. Eight patients (5 men and 3 women) were found no significant changes on the surface of the esophageal mucosa, accounting for 0.85%. The mean age was 59.7 years (range from 49 to 72 years). None had received preoperative treatment, including irradiation and chemotherapy. One case had no subjective symptom, while four suffered progressive dysphagia sensation for 7-10 months (mean 8.5 months). Other three patients complained retrosternal pain in chest after eating for 1-7 months (mean 6 months).

All these eight patients underwent fiber-esophagoscopy performed by an experienced

endoscopist. He found unilateral esophageal wall bulging in five cases with lumen stenosis. Three cases showed esophageal wall circular stenosis, accompanied with mucous membrane stiffness and poor expanding ability. However, all eight cases' mucosa were smooth and in normal color. The endoscopist couldn't find pallor, congestion or ulcer mass under the high solution endoscope. Their biopsy examination indicated chronic mucosal inflammatory. To make the clearly diagnosis, another fiber-esophagoscopy biopsy was taken in 5 patients, in which we still couldn't find mucosal tumor tissue. Other three patients took the endoscopic ultrasonography (EUS), which showed the lesions were hypo-echoic changing, seemingly originating from the submucosa or muscularis.

Upper gastrointestinal barium meal showed five cases' esophageal lumen external pressed changing with the esophageal mucosa surface smooth. We also performed preoperative computed tomography scan which indicated five cases could see that tumors were related to the esophagus and the mass were close to the esophagus lumen or the wall, while the other three showed wall thickening. Because of the indeterminate performances, we considered five patients of esophageal carcinomas, while the other three were misdiagnosed as esophageal leiomyoma.

One case's tumor was located at the upper thoracic esophagus, three were at the middle thoracic esophagus and others were at the lower thoracic esophagus. We took some tissue of the mass and sent the intraoperative frozen section which indicated tumors, so all eight patients underwent surgical resection by left transthoracic approach, including subtotal esophagectomy with stapled anastomosis after aortic arch in four cases and esophagogastric resection, staple anastomosis under the aortic arch in three cases. One case underwent hand-sewn anastomosis at the left neck. The surgery procedure was successful.

3. Results

There were two in-hospital deaths after the operation. One patient had a sequence of pneumonia, respiratory failure while another patient died as a result of anastomotic leak that led to mediastinitis during the hospital stay. The other six recovered uneventfully. All the resected specimens with intact mucous membrane were fixed in formalin, and cut into 5mm sections along the mid portion of the tumor. Then they were stained with hematoxylin and eosin and examined by light microscopy to find the relationship between the tumor and the epithelia of mucous membrane. All lymph nodes were examined at the long axis. Histological examination confirmed six of squamous carcinomas (SCC) and two of adenocarcinoma (ADC). Five patients had para-esophageal lymph nodes metastasis and one case had perigastric lymph nodes metastasis with no cervical lymph node metastasis. According to the TNM (UICC 2009) classification, the tumors were categorized as the followings: one patient was at Stage I b (T2 N0 M0), 3 at the Stage II b (T2 N1 M0), 2 patients at Stage II a (T3N0 M0) and 2 at the Stage IIIa (T3N1M0). The tumor originated from lamina propria mucosa, mucosae muscularis or submucosa, while the epithelium of superficial mucous found no obvious lesion or tumor cell.

One month later, all of them took four cycle neoadjuvant chemotherapy: Oxaliplatin (130mg/m²) and Tegafur (500mg/m²), which repeated every 21 days. All patients were followed up regularly at our hospital with routine physical and laboratory examination after discharge. Until now, one case still be alive more than 5 year, one patients survived about five years, three cases survived less than 5 years, and one patients had been dead within 2 years.

4. Discussions

As we all know, esophageal carcinoma is a major cause of cancer-related deaths around the world (Parkin and Bray, 2005), the depth of the tumor penetration is a crucial factor determining the

prognosis of patients with carcinoma (Tachibana et al, 1999, Ando et al, 2000, Ando et al, 1999). The majority of the carcinoma mucous membrane has obvious pathological changes, especially in advanced esophageal cancer. However, the tumor originated and grew from the lamina propria mucosa, mucosae muscularis and submucosa, mucous membrane has no obvious alteration in these eight cases. The reason of these particular cases is associated with tumor growth pattern (Ohno et al, 1991). Tumor originates in the lamina propria mucosa or submucosa and grows in a down growth pattern locating on one side of the wall. They don't grow into the lumen, but in contrast to the submucosa and muscularis. Cancer cells grow and reproduce in the submucosa and form a submucosa mass which oppresses the esophageal membrane wall. They further invade the esophageal muscle. At last, it can be seen the distant metastasis of lymph or invasion of vessels. As a result of this growth, the membrane surface is often smooth without pale color, so we can't find any significant changing in esophageal mucous membrane surface. They were called late submucosal esophageal cancer which is extremely uncommon type.

Esophageal peristalsis is less affected by early lesion and the contra-lateral esophageal wall can still expand without causing serious difficulty in swallowing. So the dysphagia sensation of this type is slight, the average medical history is 10 months or more. The mucous membrane can be motivated which is similar to the esophageal leiomyoma.

The diagnosis rate of upper gastrointestinal barium meal is more than 95% in terminal cancer patients. X-ray characteristics can be the followings: The tumor is hemispherical with the ramp-like filling defect because part of the tumor is located in one side wall with smooth surface and clear boundary, this can easily be mistaken as leiomyoma. As the cancer cells infiltrate surrounding tissue in varying degrees, the dynamic observation of X-ray barium meal examination shows lack of obvious "acute angle" sign with local stiffness and peristalsis limited. If there is no obvious mucosa bulging to the esophagus lumen, x-ray diagnosis is more difficult. CT scan can determine the relationship between the esophageal wall and its surrounding tissue, but the CT scan examination can't be used in the qualitative diagnosis of the tumor.

Long-term prognosis of early esophageal cancer surgery is fine, but these patients' 5-year survival rate after surgery is not high, probably due to the delay in diagnosis and tumor biological behavior. Ohno have also reported that the esophageal submucosal cancer has poor prognosis.

Esophageal mucosa with no significant changing in esophageal cancer is easy to

misdiagnosis and missed diagnosis. No pathology in this group has been preoperative taken. Through intraoperative frozen sections or postoperative paraffin sections, we can obtain a pathological diagnosis. Vigilance is the key to prevent misdiagnosis and missed diagnosis, especially the patients who are more than 40 years old from esophageal cancer-prone areas, as well as the patients whose esophageal barium meal and CT scan are positive. They shouldn't easily be let go. Gastroscopy or fiber -esophagoscopy should be repeated more than one time if the result is not satisfied. When taking a pathological specimen, the biopsy forceps should take deeper than ordinary, trying to get to the esophageal submucosa. EUS contributes to the identification of esophageal leiomyoma or submucosal cancer (May et al. 2004). Patients with positive findings of esophageal barium meal or CT examinations should be persuaded to take surgery. To some patients who refuse surgery, we should establish a strict follow-up study. In other 10 patients (this 8 cases not included), the surface of the esophageal mucosa was normal at first, but after months of observation, the esophageal mucosa grew into the typical esophageal cancer.

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Corresponding Author:

Dr. Song Zhao

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Department of Thoracic surgery
The First Affiliated Hospital of Zhengzhou University
Zhengzhou, Henan 450052, China
E-mail: zhaosong@zzu.edu.cn

References

1. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics 2002. *CA Cancer J Clin* 2005; 55(2): 74-108.
2. Tachibana M, Kinugasa S, Dhar DK. Prognostic factors after extended esophagectomy for squamous cell carcinoma of the thoracic esophagus. *J Surg Oncol* 1999; 72(2):88-93.
3. Ando N, Ozawa S, Kitagawa Y, Shinozawa Y, Kitajima M. Improvement in the results of surgical treatment of advanced squamous esophageal carcinoma during 15 consecutive years. *Ann Surgery* 2000; 232(2):225-32.
4. Tachibana M, Kinugasa S, Dhar DK. Prognostic factors in T1 and T2 squamous cell carcinoma of the thoracic esophagus. *Arch Surg* 1999; 134(1):50-4.
5. Ohno S, Mori M, Tsutsui S, Matsuura H, Kuwano H, Soejima K, Sugimachi K: Growth Pattern and Prognosis of Submucosal Carcinoma of the Esophagus. *Cancer* 1991; 68(2):335-40.
6. May A, Günter E, Roth F, Gossner L, Stolte M, Vieth M, Ell C. Accuracy of staging in early oesophageal cancer using high resolution endoscopy and high resolution endosonography comparative, a prospective, and blinded trial. *Gut* 2004; 53(5): 634-40.