

Primary Squamous Cell Carcinoma of the Liver Initially Presenting with Pseudoachalasia

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Pseudoachalasia secondary to primary squamous cell carcinoma (SCC) of the liver is extremely rare and has not been reported until now. Here, we report a unique case of primary SCC of the liver initially presenting with progressive dysphagia along with short periods of significant weight loss. A 58-year-old man initially presented with progressive dysphagia along with significant weight loss over brief periods of time. The radiographic and manometric findings were consistent with achalasia. Subsequent esophagogastroduodenoscopy revealed a moderately dilated esophagus without evidence of neoplasm or organic obstruction. However, firm resistance was encountered while traversing the esophagogastric junction (EGJ), although no mucosal lesion was identified. Due to the clinical suspicion of the presence of a malignant tumor, endoscopic ultrasonography (EUS) and computed tomography scans of the chest and abdomen were obtained. A huge hepatic mass with irregular margins extending to the EGJ was found. EUS-guided fine-needle aspiration was performed, and the mass was diagnosed as a primary SCC of the liver by immunohistochemical staining. (*Gut Liver* 2012;6:275-279)

Key Words: Esophageal achalasia; Squamous cell carcinoma; Liver

INTRODUCTION

Pseudoachalasia secondary to primary squamous cell carcinoma (SCC) of the liver is extremely rare¹⁻³ and has not been reported until now. In this report, we describe a unique case of primary SCC of the liver initially presenting with progressive dysphagia along with short periods of significant weight loss.

Esophageal manometric and radiographic findings showed features of achalasia.

CASE REPORT

A 58-year-old man was referred to our hospital for further evaluation and management of progressive dysphasia for 3 months. He complained of postprandial vomiting and weight loss of 20 kg during the last 3 months. The patient's past medical history was unremarkable, and physical examination revealed an adequate state of health. Laboratory studies, including tumor markers, were normal except for increased white blood cell count of 13,510 cells/ μ L (normal 4,000 to 11,000 cells/ μ L), elevated alkaline phosphatase of 562 U/L (95 to 280 U/L), and a slightly high C-reactive protein of 6.16 mg/dL (0 to 0.5 mg/dL).

A barium swallow study revealed a smooth narrowing of the distal esophagus with a marked dilation of the proximal segment (Fig. 1). Esophageal manometry demonstrated a lack of primary peristalsis, increased resting lower esophageal sphincter (LES) pressure (89.4 mm Hg) and incomplete relaxation of the LES during wet swallows (53% relaxation), suggesting a diagnosis of achalasia (Fig. 2). Subsequent esophagogastroduodenoscopy (EGD) showed a moderately dilated esophagus without evidence of neoplasm or organic obstruction (Fig. 3A and B). However, firm resistance was encountered while traversing the esophagogastric junction (EGJ), although no mucosal lesion was identified. With clinical suspicion of the presence of a malignant tumor, we proceeded to perform endoscopic ultrasonography (EUS) and contrast-enhanced computed tomography (CT) scans of the chest and abdomen.

EUS revealed an approximately 7 cm hypoechoic, heteroge-

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Received on September 18, 2010. Revised on October 29, 2010. Accepted on November 11, 2010.

pISSN 1976-2283 eISSN 2005-1212 <http://dx.doi.org/10.5009/gnl.2012.6.2.275>

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neous mass with irregular margins around the EGJ (Fig. 3C). In addition, the main mass was mainly located outside the esophagus and it invaded into the muscle layer, not to submucosal layer. This suggests that the mass was originated outside the esophagus, not from the esophagus. Thoraco-abdominal CT scans showed a massive tumor at the left lobe of the liver in size to 9 cm in largest diameter, extending to the EGJ, but no features of underlying liver cirrhosis or pulmonary lesions (Fig. 4A and B). US-guided biopsies were performed of the mass at the left lobe of the liver, but the tissues obtained were deemed unsatisfactory for diagnosis due to necrosis and limited sampling of viable tumor cells. Therefore, we conducted a EUS-guided fine needle aspiration (FNA) biopsy on the peripheral non-necrotic area. Six needle passes were made with a 22-gauge needle (Echotip; Wilson-Cook, Winston-Salem, NC, USA), and the histopathological diagnosis was poorly differentiated SCC (Fig. 5A). Immunohistochemical staining was positive for p63 and cytokeratin (CK) 19, but negative for thyroid transcription factor-1 (TTF-1),



Fig. 1. Barium esophagography displays a markedly dilated esophagus tapering to a smoothly narrowed gastroesophageal junction.

indicating primary SCC of the liver (Fig. 5B-D). We performed a systemic evaluation to identify the primary tumor origin with an ENT survey and positron emission tomography-CT (PET-CT) scans (Fig. 4C), but did not detect any other abnormalities. The patient was diagnosed as pseudoachalasia secondary to primary SCC of the liver.

We recommended concurrent platinum-based chemotherapy and radiotherapy due to the inoperable state of the tumor, but the patient refused all treatments, including palliation with esophageal stents and died four months later.

DISCUSSION

Primary SCC of the liver is a rare malignant neoplasm, and right upper quadrant abdominal pain is a prominent symptom in previously reported cases.¹⁻³ In contrast, our patient presented

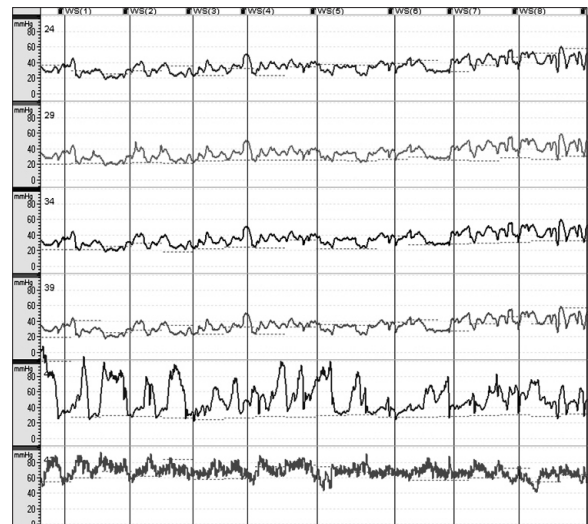


Fig. 2. The esophageal manometry findings are consistent with achalasia: a lack of primary peristalsis, increased resting lower esophageal sphincter (LES) pressure (89.4 mm Hg) and incomplete relaxation of the LES during wet swallows (53% relaxation).

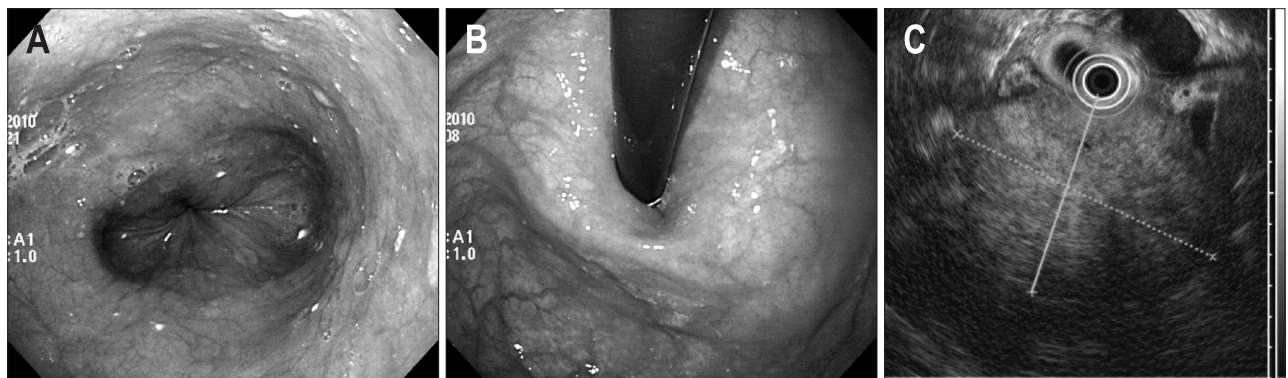


Fig. 3. (A) Esophagogastroduodenoscopy reveals a moderately dilated esophagus and tight esophagogastric junction (EGJ). (B) The U-turn view reveals no evidence of neoplasm at the cardia. (C) Endoscopic ultrasonography displays a large hypoechoic, inhomogeneous mass with irregular margins around the EGJ.



Fig. 4. (A, B) Abdominal computed tomography (CT) scans demonstrate a large tumor adjacent to the esophagogastric junction at the left lobe of the liver. (C) Positron emission tomography-CT scans display a mass at the left lobe of the liver with peripheral rim-shaped fluoro deoxyglucose uptake.

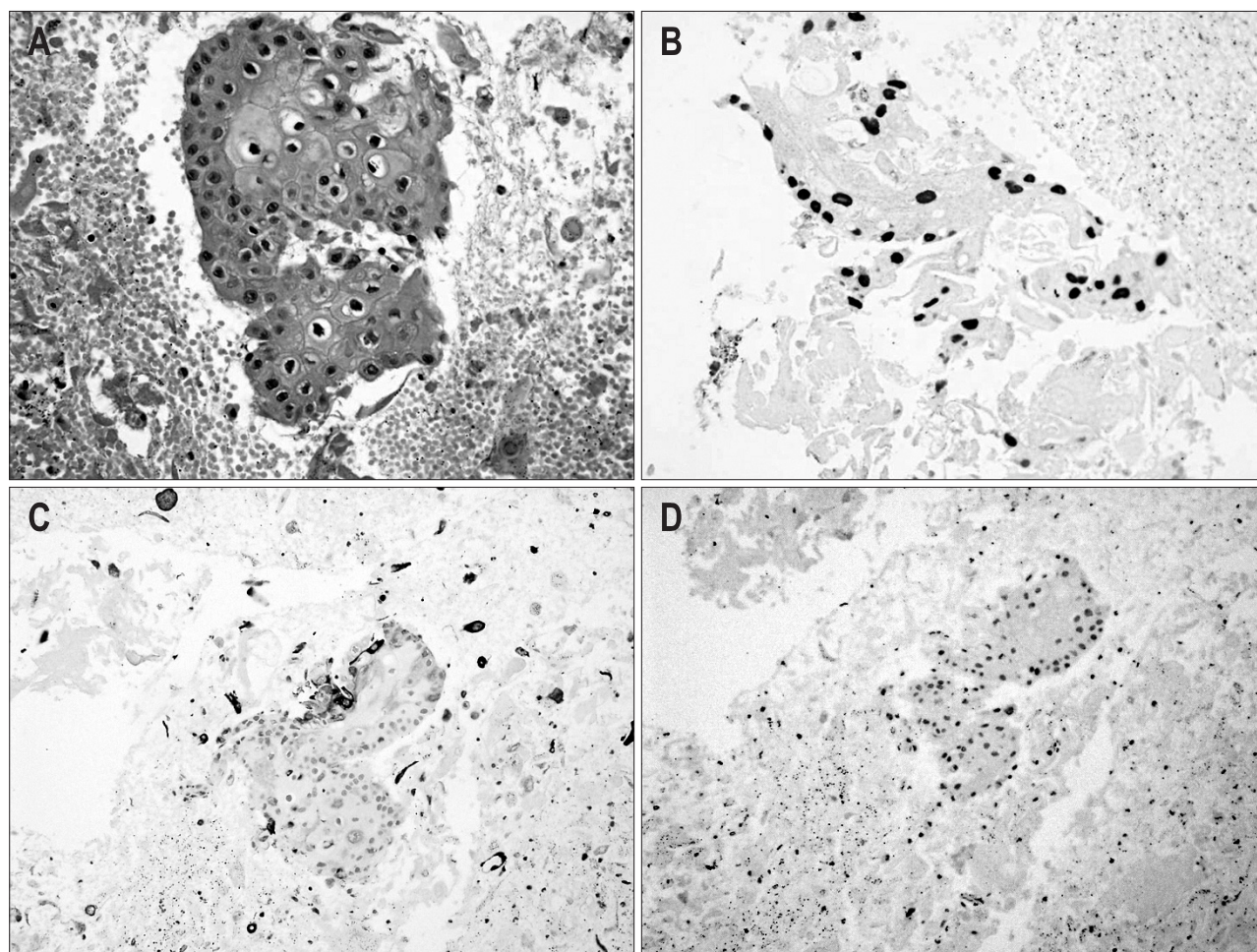


Fig. 5. (A) Clusters of atypical epithelial cells in the necrotic background, which are consistent with poorly differentiated squamous cell carcinoma (H&E stain, $\times 400$). (B) Positive p63 staining ($\times 400$). (C) Positive CK19 staining ($\times 200$). (D) Negative TTF-1 staining ($\times 200$).

with progressive dysphagia and postprandial vomiting, as well as manometric and radiographic features of achalasia. To our knowledge, this case of primary SCC of the liver initially presenting as pseudoachalasia is the first to be described in the literature.

Malignant pseudoachalasia accounts for 4% of all cases of achalasia.⁴ Whereas adenocarcinoma of the gastric cardia accounts for most cases, other malignant tumors such as lymphoma, mesothelioma, hepatoma, cholangiocarcinoma, renal cell carcinoma and carcinoma of the esophagus, lung, pancreas, prostate, breast, colon, and duodenum have been reported.⁵ Such malignant tumors usually produce achalasia as the result of one of three mechanisms.^{6,7} First, the tumor mass may encircle or compress the distal esophagus, thereby producing a constricting segment. Second, malignant cells may infiltrate the esophageal myenteric plexus and impair postganglionic innervation of the LES. Third, paraneoplastic visceral neuropathy of the myenteric plexus without neoplastic infiltration of the EGJ may produce clinical features of achalasia. The pseudoachalasia observed in this case was likely a result of tumor bulk compressing the distal esophagus with neoplastic infiltration of the esophageal myenteric plexus.

Pseudoachalasia associated with malignancy has clinical, radiographic, and manometric features that are often indistinguishable from primary achalasia. Moreover, due to the rarity of the disease, many patients with pseudoachalasia are initially diagnosed as primary achalasia. Unfortunately, if not promptly recognized, pseudoachalasia may be inappropriately treated with pneumatic dilation of the LES, which is both ineffective and dangerous,⁸ and may delay proper treatment of the underlying malignancy. Thus, all patients with suspected achalasia should undergo EGD to exclude a diagnosis of tumor at the cardia or EGJ. Although submucosal or extramural tumors will inevitably be missed by normal endoscopic examination, encountering excessive resistance while traversing the EGJ should strongly suggest a diagnosis of pseudoachalasia. In the present case, this fact was a significant key facilitating an accurate diagnosis.

In addition, certain historical features can help raise suspicion of a malignant tumor. A short duration of symptoms (less than 1 year), presentation later in life (more than 55 years of age), and significant weight loss (more than 15 lbs) are more typical of malignancy than of primary achalasia.⁹ All of these criteria were met in our patient. However, these criteria have poor predictive value, so early exploratory surgery is not recommended without radiologic or endoscopic evidence of tumors.¹⁰

Pseudoachalasia may be better confirmed by EUS, which provides more definitive imaging of the extrinsic lesion and enables identification of subepithelial tumor infiltration through biopsy or cytologic brushing.¹¹ CT scans and magnetic resonance imaging may also be useful for distinguishing the two disorders. CT findings that might favor a diagnosis of pseudoachalasia versus primary achalasia include a more marked or asymmetric thick-

ening of the esophagus and the presence of a mass.¹²

Our patient underwent further evaluation with EUS and CT scans, revealing a mass at the left lobe of the liver. Unexpectedly, EUS-FNA biopsy of the mass was positive for SCC. The positive staining of CK19 confirmed the bile ductular ontogeny of the neoplastic cells. Because TTF-1, an indicator of lung or thyroid origin, was negative, we were able to rule out metastasis of lung or thyroid cancer to the liver. Endoscopy, ENT examination, thoraco-abdominal CT scans, and PET-CT scans supported that the liver was the primary origin of the tumor.

In summary, it is important to differentiate primary achalasia from secondary achalasia. Diagnosis requires clinical suspicion in addition to routine radiographs, esophageal manometry and endoscopy. These should be followed by EUS or CT scans. Primary SCC of the liver is a very rare disease, and requires careful systemic evaluation and immunohistochemical examination.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGEMENTS

This report was supported by a grant from the National R&D Program for Cancer Control, Ministry for Health, Welfare and Family affairs, Republic of Korea (0920050).

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