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CASE REPORT

Diffuse xanthoma in early esophageal cancer: A case report

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Author contributions: Yang XY was the patient's attending physician and was responsible for collecting the medical history, performing magnifying endoscopy, reviewing the literature, and drafting the manuscript; Fu KI analyzed and interpreted the endoscopic findings and contributed to manuscript drafting; Chen YP performed the endoscopic submucosal dissection for the patient; Chen ZW was the pathologist who gave the pathological results; Ding J reviewed the literature and contributed to revising the manuscript; all authors issued the final approval for the version to be submitted.

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Abstract

BACKGROUND

Gastrointestinal xanthomas are asymptomatic and infrequent non-neoplastic lesions that commonly occur in the stomach with *Helicobacter pylori*-associated gastritis and rarely in the esophagus. To date, there have been no reports of esophageal xanthoma combined with esophageal cancer. Herein, we present the first case in the literature of a diffuse xanthoma complicated with early esophageal cancer. Moreover, this combination makes the endoscopic diagnosis difficult if it is not in mind.

CASE SUMMARY

A 68-year-old man visited our department with a 2-mo history of epigastric discomfort. He underwent surgery for gastric cancer 6 years ago. Esophagogastroduodenoscopy showed a semi-circumferential irregular yellowish-colored and granular lesion in the esophagus (30-35 cm from the incisors). Using magnifying endoscopy with narrow band imaging, aggregated minute and yellowish-colored spots with tortuous microvessels on the surface were observed, and background coloration was clearly seen in the lesion. As endoscopic biopsy suggested a histologically high-grade dysplasia; the lesion was completely resected *en bloc* by endoscopic submucosal dissection (ESD). The resected specimen was confirmed to be a squamous cell carcinoma *in situ* with extensive foamy cells in the superficial mucosal layer. Immunohistochemically, the observed foamy cells were strongly positive for CD68, which is characteristic of xanthoma. The clinical course was favorable, and no recurrence was observed 2 years and 7 mo after ESD.

CONCLUSION

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Diffuse xanthoma concurrent with early esophageal cancer is extremely rare. The characteristic endoscopic features may assist endoscopists in diagnosing similar lesions.

Key Words: Esophageal xanthoma; Early esophageal cancer; Magnifying endoscopy; Endoscopic submucosal dissection; Case report

Core Tip: Esophageal xanthomas are uncommon, non-neoplastic lesions characterized by the accumulation of foamy histiocytes. Herein, we present the first case of early esophageal cancer covered by xanthomas, diffusely and superficially treated by endoscopic submucosal dissection. Knowing these characteristic endoscopic features can help endoscopists reach a correct diagnosis for appropriate treatment.

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INTRODUCTION

Xanthomas are considered to be asymptomatic, non-neoplastic lesions that can be found anywhere along the gastrointestinal tract, commonly in the stomach and colon, and rarely in the esophagus. Endoscopically, they are small (1-2 mm in size), single or multiple, yellow, orange, or white well-demarcated sessile macules with irregular outlines that rarely exceed 5 mm[1,2]. Diffuse xanthoma complicated by early esophageal cancer has never been reported in the literature. We herein present the first case treated by endoscopic submucosal dissection (ESD).

CASE PRESENTATION

Chief complaints

A 68-year-old man was admitted with a 2-mo history of epigastric discomfort.

History of present illness

The patient presented with a complaint of intermittent, dull, and non-radiating epigastric pain. No associated nausea, vomiting, melena, or loss of body mass was observed.

History of past illness

The patient underwent distal gastrectomy for gastric cancer 6 years ago. Histological analysis revealed a moderately poorly differentiated adenocarcinoma, staged at pT4aN2M0 IIIB. The patient recovered well after adjuvant chemotherapy, and he was followed regularly. No evidence of local recurrence or distant metastasis was identified 6 years after surgery. His history included hypertension and type 2 diabetes mellitus controlled with medications for more than 10 years.

Personal and family history

The patient reported consuming alcohol daily and smoking one pack of cigarettes per day for 42 years until he was 60 years old. His family history was negative for cancers.

Physical examination

The patient's temperature was 36.5 °C, heart rate was 63 bpm, respiratory rate was 18 breaths per minute, and blood pressure was 141/93 mmHg. The physical examination was unremarkable.

Laboratory examinations

The laboratory work-up showed that the levels of the tumor markers CA19-9, CA-125, carcinoembryonic antigen, squamous cell carcinoma antigen, and alpha-fetoprotein were in the normal range. Other biochemistry test results were also within normal limits.

Imaging examinations

Abdominal computed tomography revealed postoperative changes. Chest computed tomography and cardiac ultrasound were normal. No nodal involvement or distant metastasis was identified.

Further diagnostic work-up

Esophagogastroduodenoscopy showed a semi-circumferential, irregular, yellowish-colored and granular lesion in the esophagus (30-35 cm from the incisors) (Figure 1A). Magnifying endoscopy with narrow band imaging (NBI) revealed aggregated minute yellowish spots with tortuous microvessels inside (Figure 1B). Moreover, type B1 intrapapillary capillary loops (IPCLs) and intervascular background coloration were observed around the yellow spots (Figure 1C). Lugo's iodine staining (1%) demonstrated a well-demarcated, irregular, unstained lesion (Figure 1D). As endoscopic biopsy suggested a high-grade dysplasia with the accumulation of foamy macrophages histologically, the lesion was diagnosed as an early esophageal cancer with esophageal xanthomas.

FINAL DIAGNOSIS

The final preoperative diagnosis was diffuse esophageal xanthoma complicated with early esophageal cancer.

TREATMENT

The lesion was completely resected *en bloc* by ESD (Figure 2). Oral prednisolone was administered at a dose of 30 mg/d on the third day after ESD. The dose was then gradually tapered in decrements of 5 mg/d every 2 wk for 1 mo followed by decrements of 5 mg/d every week for the next 4 wk. Steroids were discontinued after 8 wk.

OUTCOME AND FOLLOW-UP

Histologically, the resected specimen was confirmed to be a squamous cell carcinoma *in situ* in which extensive foam cells were seen in the superficial mucosal layer (Figure 3). Immunohistochemical staining showed that the lesion was positive for P53 and negative for P16 (Figure 4A and B). The Ki-67 index was 90% (Figure 4C). The observed foamy cells were strongly positive for CD68, identical to a histiocytic cell origin, which is characteristic of xanthoma (Figure 4D). Postoperatively, the patient recovered well and was discharged from the hospital on day 5. There were no complaints of dysphagia following ESD. On follow-up endoscopy, which was scheduled at 3, 6, 12 and 24 mo after ESD, there was no postprocedural esophageal stricture, and neither recurrent nor metachronous lesions were found (Figure 5).

DISCUSSION

Gastrointestinal xanthomas are asymptomatic and infrequent non-neoplastic lesions characterized by the accumulation of foamy cells in the lamina propria[3]. They occur more frequently in the stomach with *Helicobacter pylori*-associated gastritis, and are rarely seen in the intestine or esophagus. The endoscopic findings of esophageal xanthomas have been reported as yellowish granular spots, yellowish elevated lesions, yellow-white colored plaques, or yellow verruciform lesions, measuring from 2 to 20 mm (usually ≤ 5 mm)[4-8]. Diffuse and extensive esophageal xanthoma in a patient is extremely rare. Gastrointestinal xanthoma is considered benign without clinical

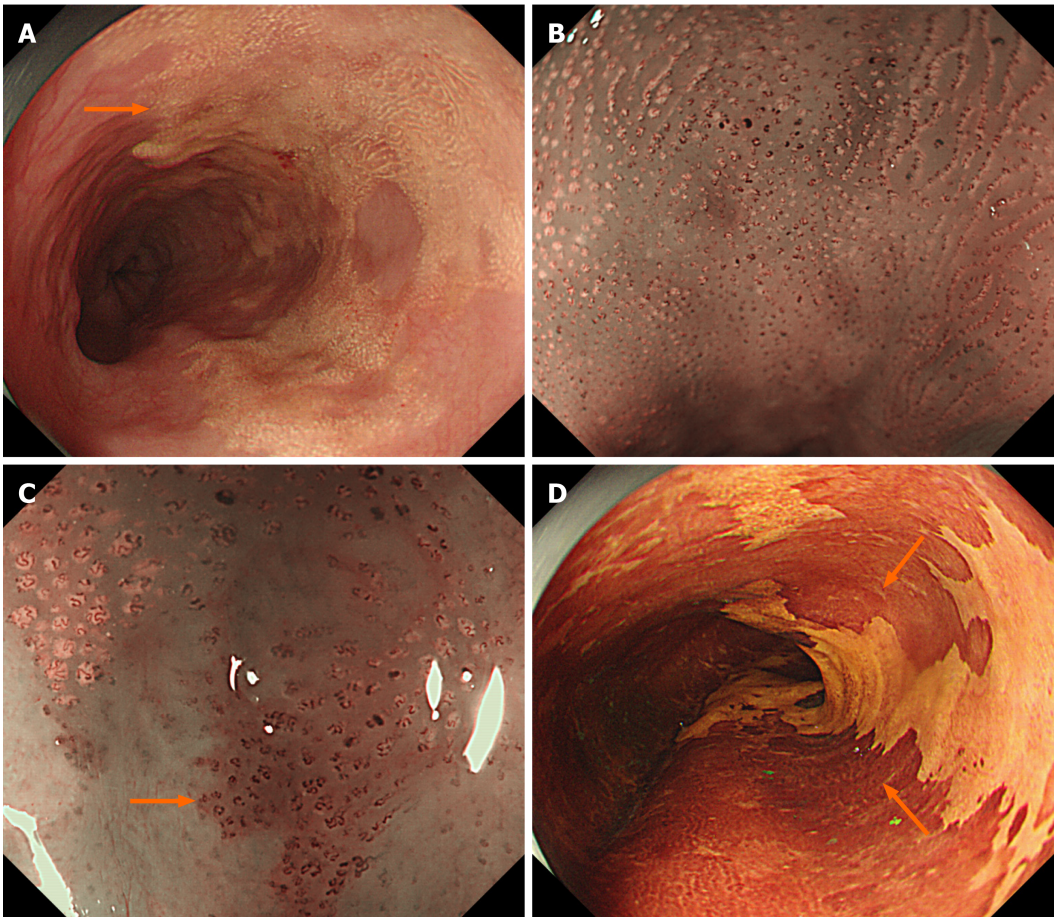

Figure 1 Endoscopic illustrations (GIF-H260Z, Olympus). A: White light endoscopy showed a semi-circumferential, irregular, yellowish-colored, and granular lesion localized in the middle and lower esophagus (orange arrow); B: Narrow band imaging endoscopy revealed aggregation of minute yellowish spots with tortuous microvessels inside; C: Type B1 intrapapillary capillary loops were identified by magnifying endoscopy in the region around the yellow spots, and the lesion was positive for background coloration (orange arrow); D: Lugol's iodine staining revealed a well-demarcated unstained lesion (orange arrow).

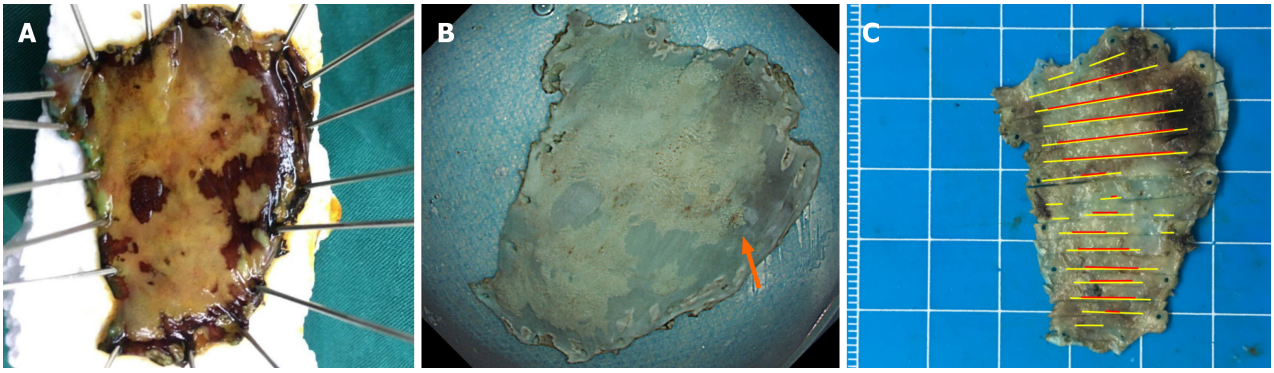

Figure 2 Macroscopic findings. A: Lugol's iodine staining of the specimen revealed that the tumor was removed *en bloc* by endoscopic submucosal dissection; B: Diffuse yellowish-colored lesion was recognized in this fixed specimen (orange arrow); C: The size of the specimen is 45 × 33 mm. The yellow line indicates the esophageal xanthoma. The red line demonstrates squamous cell carcinoma in the superficial mucosal layer.

significance. However, it can be missed unless proven by a negative biopsy[2]. Therefore, endoscopic biopsy is recommended for such yellowish elevated lesions to distinguish ectopic sebaceous glands, carcinoid tumors, granular cell tumors, malignant lymphomas, or papillomas[1,3,9,10]. Histologically, the accumulation of foamy histiocytes of xanthoma could be a clue for differential diagnosis. Positive immunohistochemical staining for CD68, which indicates a histiocytic origin, is another characteristic finding of xanthoma[1].

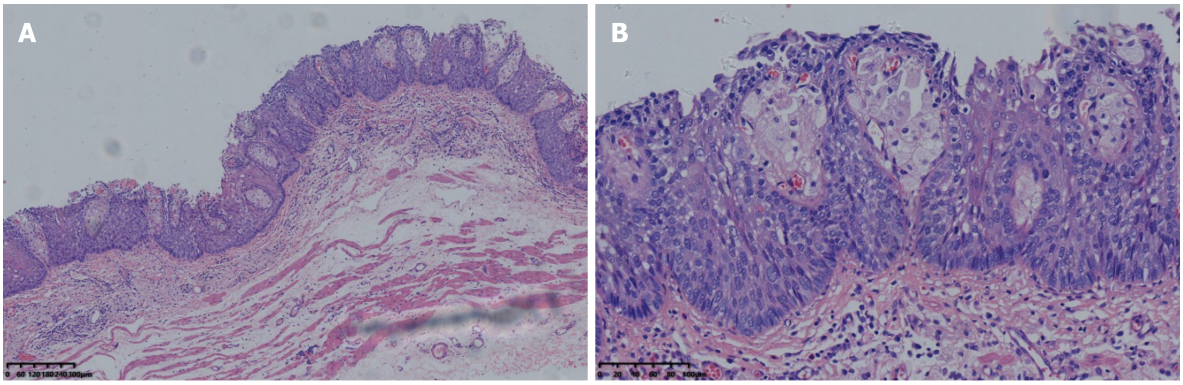

Figure 3 Histopathological findings. Hematoxylin and eosin staining of the lesion showed squamous cell carcinoma *in situ* in which extensive foam cells were seen in the superficial mucosal layer. A: Magnification × 5; B: Magnification × 20.

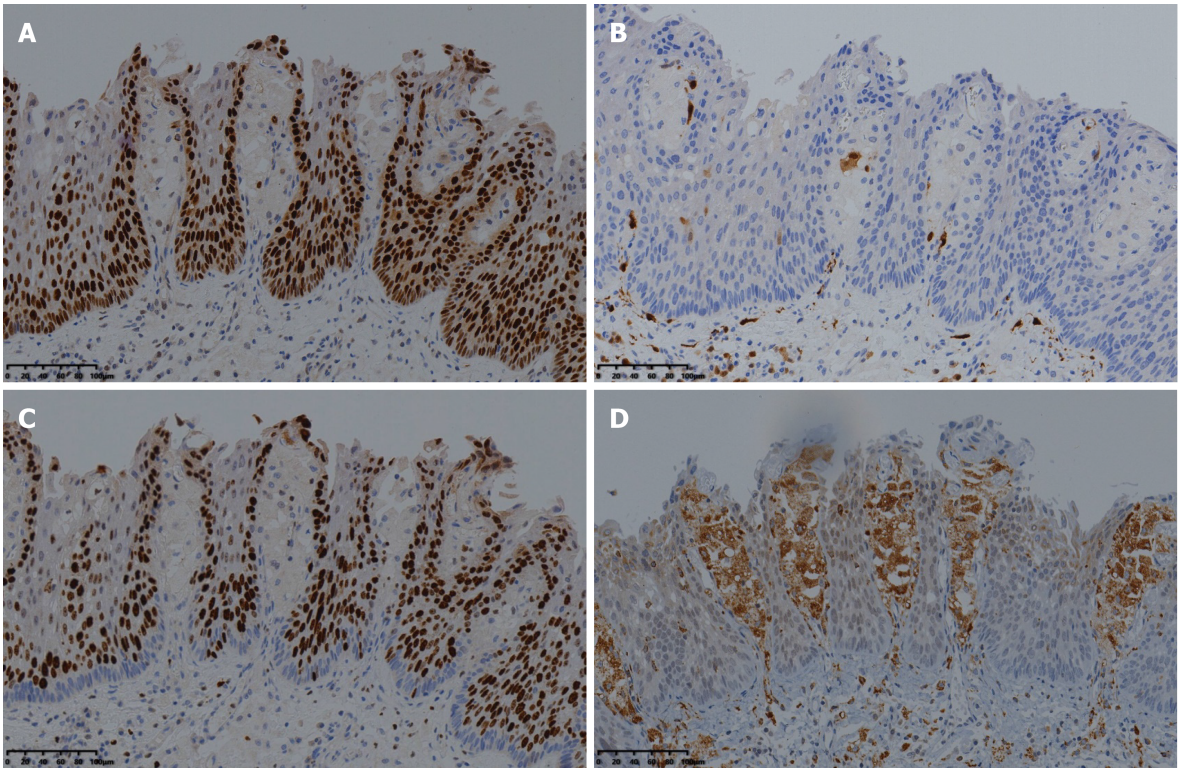

Figure 4 Immunohistochemical findings. A and B: Immunohistochemical staining showed that the regions of squamous cell carcinoma were positive for P53 and negative for P16 (× 20); C: The Ki-67 index was 90% (× 20); D: The observed foam cells were strongly positive for CD68 (× 20).

Although the etiology of esophageal xanthoma remains unknown, it was reported to be derived from focal mucosal damage, in which lipids from damaged cell membranes are captured by interstitial histiocytes[11]. This may explain why they occur less frequently in the esophagus than in the stomach because the esophageal mucosa can better tolerate mucosal injury[12]. Xanthoma may also be associated with conditions such as history of radiotherapy or chemotherapy, infection, and biliary reflux[3,4,10]. To date, no apparent relationship between esophageal xanthoma and hyperlipidemia has been reported[13]. To the best of our knowledge, there have been no reports of esophageal xanthoma combined with esophageal malignancy. A history of subtotal gastrectomy and adjuvant chemotherapy may be related to the occurrence of diffuse xanthoma of the esophagus in our patient. Furthermore, the patient's long-term history of smoking together with heavy alcohol consumption could be a risk factor for concurrent esophageal cancer.

Changes in IPCLs, seen in magnifying NBI with the endoscopic classification of the Japan Esophageal Society, have been demonstrated to be simple and useful for differentiating whether identified lesions are neoplastic, and the prediction of the depth of

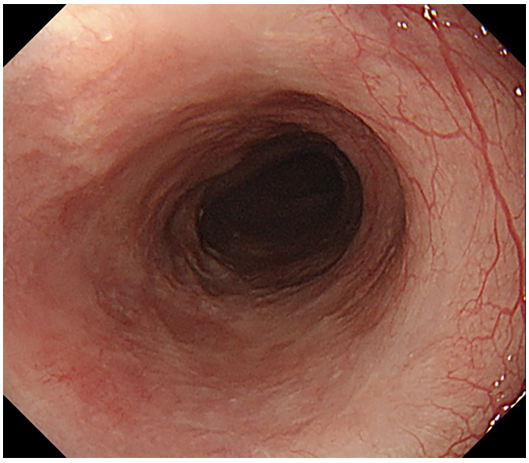

Figure 5 White light endoscopy showed no stricture and local recurrence 24 mo after endoscopic submucosal dissection.

invasion of superficial esophageal squamous cell carcinoma (SESCC) was also available[14]. Type A, lacking severe irregularity, corresponds to non-cancerous lesions; type B exhibits severe irregularity, identical to neoplastic lesions. Type B IPCLs were sub-classified into B1, B2, and B3 for T1a-EP or T1a-LPM, T1a-MM or T1b-SM1, and T1b-SM2 tumors, respectively[14]. In previous reports, magnifying endoscopy revealed esophageal xanthoma lesions as areas with aggregated minute yellowish spots with tortuous micro-vessels inside[15,16]. In addition to these reported characteristics, type B1 IPCLs and intervascular background coloration were also observed in our case. Intervascular background coloration has been reported to be useful for predicting the histology of high-grade intraepithelial neoplasia and invasive SESCC[17,18]. Type B1 tumors consist of abnormal IPCLs with a conserved loop-like formation, which is considered to correspond to T1a-EP or T1a-LPM[14]. These endoscopic findings correspond well with the histological findings in this case. As mentioned above, despite the fact that esophageal xanthomas are usually considered to be uncommon non-neoplastic lesions, determination of these lesions is imperative since they might be concurrent with malignancy. In addition, the characteristic endoscopic findings of our case may assist endoscopists in diagnosing similar lesions.

CONCLUSION

We report the first case of diffuse xanthoma complicated with early esophageal cancer. The characteristic endoscopic findings of xanthomas and esophageal cancer seen in image-enhanced endoscopy can help endoscopists to reach the correct diagnosis for appropriate treatment if this rare combination of disease is kept in mind.

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