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CASE REPORT

Sporadic Minute Pharyngeal Xanthomas Detected Incidentally During Esophagogastroduodenoscopy: A Case Series

Kenta Hamada[1,2] · Yoji Takeuchi[1] · Chiaki Kubo[3] · Yasuhiko Tomita[3] · Masayasu Omori[1,2] · Noriya Uedo[1] · Ryu Ishihara[1] · Yasushi Yamasaki[1,2] · Sachiko Yamamoto[1] · Tomofumi Akasaka[1] · Noboru Hanaoka[1] · Koji Higashino[1] · Hiroyuki Okada[2] · Hiroyasu Iishi[1]

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Abstract
Pharyngeal xanthomas are considered rare, and no reports have described their endoscopic appearance under magnifying or image-enhanced endoscopy. We report three cases of asymptomatic sporadic pharyngeal xanthoma that were detected incidentally during routine esophagogastroduodenoscopy. All the patients were men and had a solitary lesion of about 1 mm in size. Two of the lesions were located in the oropharynx, while one was in the hypopharynx. Non-magnifying endoscopy showed yellowish lesions, and magnifying endoscopy showed an aggregation of minute yellowish nodules with tortuous microvessels on their surface. Histopathological examination revealed foam cells filling the intraepithelial papillae. The foam cells were strongly immunopositive for cluster of differentiation (CD) 68. Immunohistochemical staining for CD34 showed intrapapillary capillaries around the foam cells. This characteristic magnifying endoscopic appearance corresponded to the histopathological findings of pharyngeal xanthomas. The present cases reveal the relationship between the endoscopic appearance and histopathological findings of pharyngeal xanthomas.

Keywords Pharynx · Xanthelasma · Xanthoma · Pharyngeal xanthelasma · Pharyngeal xanthoma

Introduction

Xanthomas are non-neoplastic lesions that result from the accumulation of foamy histiocytes. They are characteristically found in the oral cavity and genital skin [1], although several reports have also described pharyngeal xanthomas, which are considered rarer [2]. In fact, most pharyngeal xanthomas occur in the context of the systemic disease xanthoma disseminatum [3–7]. No previous studies have used either magnifying endoscopy or image-enhanced endoscopy to describe the endoscopic appearance of pharyngeal xanthomas. Herein, we report three cases of asymptomatic sporadic pharyngeal xanthoma that were incidentally detected during routine esophagogastroduodenoscopy.

Case Report

Between October 2016 and February 2017, three pharyngeal xanthomas in three patients were histopathologically diagnosed at Osaka International Cancer Institute. Written informed consent to perform esophagogastroduodenoscopy was obtained from all patients. The protocol of this case series study was approved by the local ethics committee of Osaka International Cancer Institute.

The patient and lesion characteristics are shown in Table 1. All of the lesions were incidentally detected during routine esophagogastroduodenoscopy. All patients were men and had a single lesion; their median age was 77 years (range 65–79 years) and they all had current or past drinking and smoking habits. Two of the patients had past histories of head and neck cancer; two had gastric cancer and one had esophageal cancer. Only one patient had hyperlipidemia.

✉ Yoji Takeuchi
takeuti-yo@mc.pref.osaka.jp

1 Department of Gastrointestinal Oncology, Osaka International Cancer Institute, 3-1-69, Otemae, Chuo-ku, Osaka 541-8567, Japan

2 Department of Gastroenterology and Hepatology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

3 Department of Pathology, Osaka International Cancer Institute, Osaka, Japan

Table 1 Patient and lesion characteristics

Patient no.	Sex	Age (years)	Co-morbidities	Past history (treatment)	Drinking	Smoking	Lesion no.	Location	Size (mm)
1	Male	69	Hyperlipidemia	Oral cancer (OP)	Current	Current	Solitary	Oropharynx	1
2	Male	77	Hypertension Gout	Hypopharyngeal cancer (ESD) Esophageal cancers (ESD) Gastric cancer (OP)	Former	Former	Solitary	Oropharynx	1
3	Male	75	Hypertension CKD	Gastric cancers (ESD, OP)	Former	Former	Solitary	Hypopharynx	1

CKD chronic kidney disease, *OP* operation, *ESD* endoscopic submucosal dissection

Two of the lesions were located in the oropharynx, while one was in the hypopharynx; all were around 1 mm in size. In one case, non-magnifying endoscopy showed an aggregation of minute yellowish dots (Fig. 1a), while the other two cases presented solitary yellowish lesions (Figs. 2a, 3a). In all cases, magnifying endoscopy showed an aggregation of minute yellowish nodules with tortuous microvessels on their surface (Figs. 1b, 2b, 3b). Magnifying narrow-band imaging showed the nodules and microvessels more clearly (Figs. 1c, 2c, 3c).

Histopathological examination revealed foam cells filling the intraepithelial papillae (Fig. 1d). The foam cells were strongly immunopositive for cluster of differentiation (CD) 68 (Fig. 1e). Immunohistochemical staining for CD34 showed intrapapillary capillaries around the foam cells (Fig. 1f).

Discussion

Pharyngeal xanthomas are considered rare and, to our best knowledge, the present case series is the first report to describe the lesions' endoscopic appearance. In the present study, non-magnifying endoscopy visualized the pharyngeal xanthomas as aggregations of minute yellowish dots or as solitary yellowish lesions. Magnifying endoscopy revealed aggregations of minute yellowish nodules with tortuous microvessels on their surface. The pharyngeal xanthomas

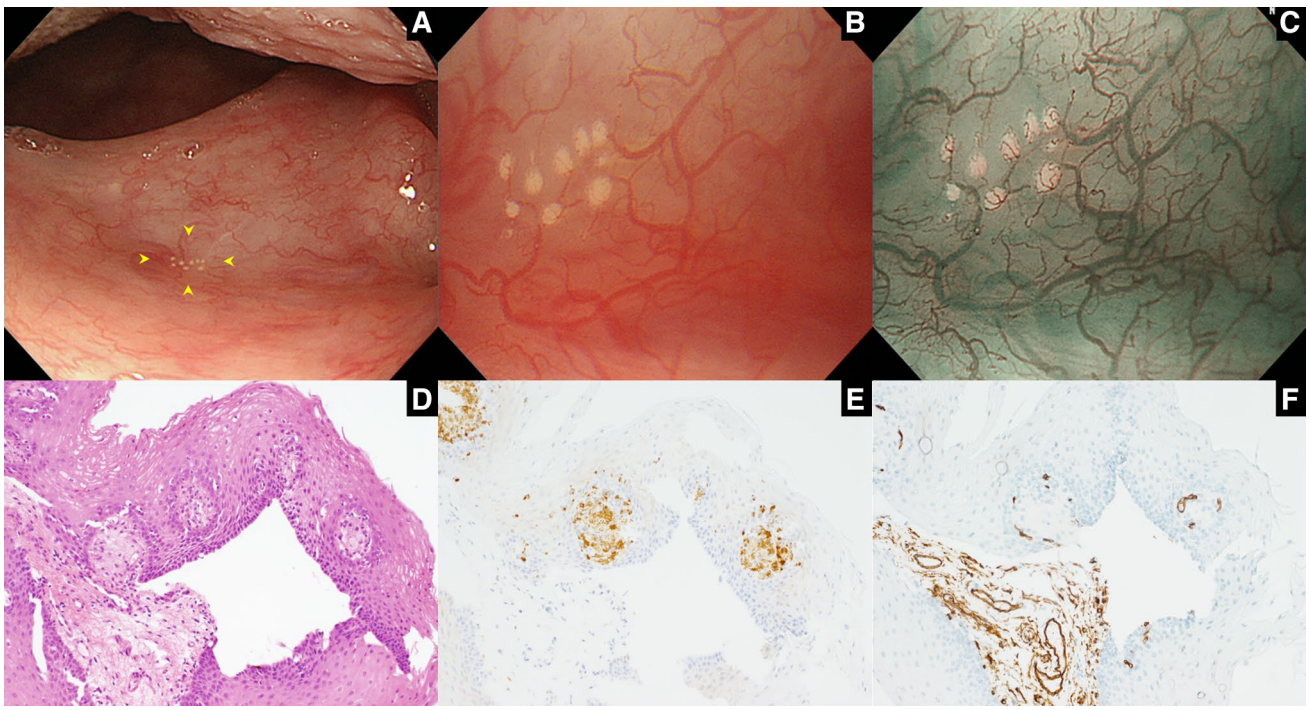

Fig. 1 **a** Endoscopic image showing a 1-mm lesion as an aggregation of minute yellowish dots on the ceiling of the oropharynx (Case 1). **b** Magnifying white-light image showing an aggregation of minute yellowish nodules with tortuous microvessels on their surface. **c** Magnifying narrow-band image showing the nodules and microvessels more clearly. **d** Histopathological examination showing foam cells filling the intraepithelial papillae. **e** Foam cells strongly immunopositive for cluster of differentiation (CD) 68. **f** Immunohistochemical staining for CD34 showing intrapapillary capillaries around the foam cells

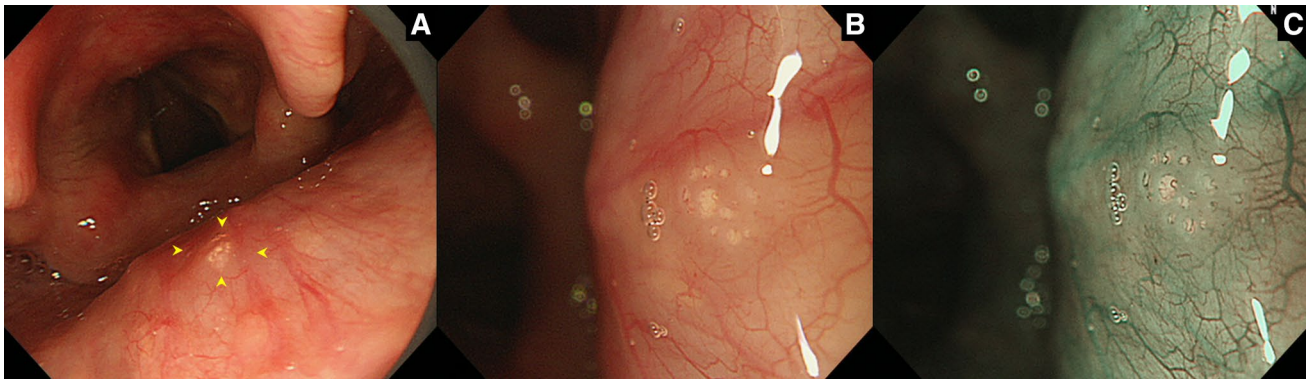

Fig. 2 **a** Endoscopic image showing a 1-mm yellowish lesion on the posterior wall of the oropharynx (Case 2). **b** Magnifying white-light image showing an aggregation of minute yellowish nodules with tortuous microvessels on their surface. **c** Magnifying narrow-band image showing the nodules and microvessels more clearly

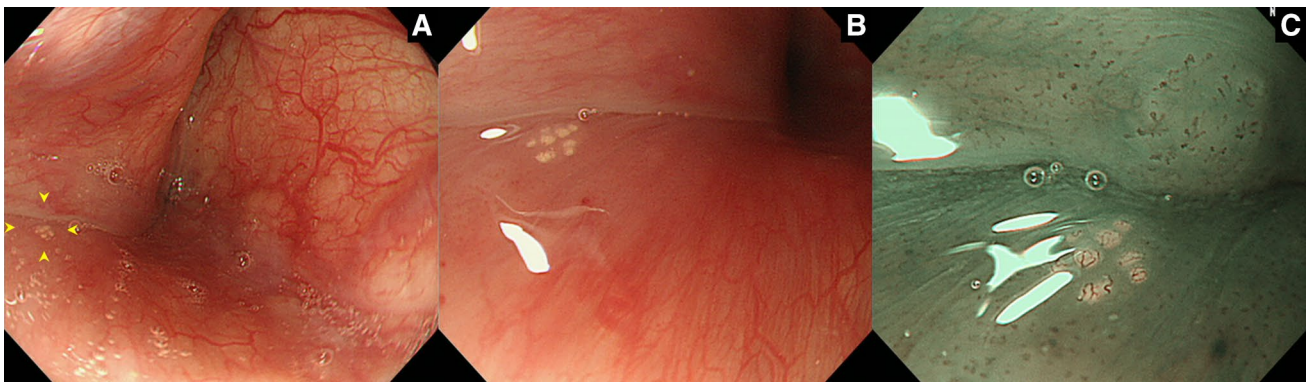

Fig. 3 **a** Endoscopy image showing a 1-mm yellowish lesion on the posterior wall of the right pyriform sinus in the hypopharynx (Case 3). **b** Magnifying white-light image showing an aggregation of minute yellowish nodules. **c** Magnifying narrow-band image showing the nodules with tortuous microvessels on their surface

in the present study were minute. However, the findings, especially those of magnifying endoscopy, have not been reported previously. Furthermore, the magnifying endoscopic findings corresponded to histopathological findings of pharyngeal xanthoma. Because foam cells filled the intraepithelial papillae, the pharyngeal xanthomas were observed as aggregations of minute yellowish nodules. Relatedly, as shown by immunohistochemical staining for CD34, tortuous microvessels occurred on the surface of the nodules, because there were intrapapillary capillaries around the foam cells.

The etiology and clinical significance of pharyngeal xanthomas remain unknown. Most pharyngeal xanthomas occur in the context of the systemic disease xanthoma disseminatum, which is a rare normolipemic mucocutaneous xanthomatosis that results from the proliferation of non-x histiocytes [6]. In several cases, laryngo-pharyngeal involvement of xanthoma disseminatum caused dyspnea [5–7]. In the present study, all patients had a minute solitary lesion in the pharynx and no lesions on the skin. One case of sporadic xanthomatosis with epiglottic and basilingual involvement and dyslipidemia has been reported [2]. The lesion was a protrusion of more than 3 cm that caused oropharyngeal foreign body sensation and dysphagia. In the present study, only one patient among the three had dyslipidemia, and there was no apparent relationship between the pharyngeal xanthomas and dyslipidemia. All three of the patients had long histories of both drinking and smoking, and two of them had past histories of head and neck cancer. Two had gastric cancer and one had esophageal cancer. Alcohol consumption and tobacco smoking over a long period can contribute to pharyngeal xanthoma development, as can malignant disease. However, the results of the present study may be strongly biased in this regard, because this was a retrospective study performed at a single cancer center. Indeed, in our hospital, almost all patients have past or present histories of cancer, or are strongly suspected of some cancers. Consequently, most of our patients have some risk factors for cancer, such as drinking or smoking. To date, no reports

have indicated a relationship between pharyngeal xanthomas and drinking or smoking. Esophageal xanthomas following radiotherapy to the lesion area have been reported [8, 9]. In the present study, however, none of the patients had past histories of radiotherapy to the head and neck region. Oral xanthomas are frequently found on the masticatory mucosa, where localized trauma is common [10]. Similarly, pharyngeal xanthomas may result from localized trauma caused by swallowing of tough foods. If so, pharyngeal xanthomas may be more common than the literature would suggest. In the present study, the second two lesions were detected only a short time after the first, indicating that endoscopists may miss many pharyngeal xanthomas during endoscopy because they are not familiar with the lesions' endoscopic appearance. It is not clear whether the minute pharyngeal xanthomas detected in the present study will develop into larger symptomatic lesions like those described in a previous report [2]. Nonetheless, the present study described the endoscopic findings of pharyngeal xanthomas. As a result, future endoscopists may recognize these lesions more readily and thus be able to elucidate the etiology, clinical significance, and natural history of pharyngeal xanthomas.

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Compliance with Ethical Standards

Conflict of interest The authors have no conflicts of interest to declare for this article.

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