INTRODUCTION

Xanthoma is an uncommon nonneoplastic lesion resulting from the accumulation of histiocytes. It predominantly shows cutaneous manifestations associated with dyslipidemia. However, xanthoma of the esophagus is extremely rare. To the best of our knowledge, only 14 cases have been reported thus far. The clinical significance of this lesion has not been established. However, this lesion should be distinguished grossly from ectopic sebaceous glands and small subepithelial tumors such as carcinoid and granular cell tumor. Moreover, signet ring cell carcinoma, which contains round cells with abundant cytoplasm and has similar histologic features to xanthoma, should be distinguished microscopically.

Key Words: Xanthomatosis; Esophagus; Histiocytes; Endoscopy

CASE REPORT

Xanthoma of the Esophagus
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Xanthoma is an uncommon nonneoplastic lesion resulting from the accumulation of foamy histiocytes. It predominantly shows cutaneous manifestations associated with dyslipidemia. However, xanthoma of the esophagus is extremely rare. To the best of our knowledge, only 14 cases have been reported thus far. The clinical significance of this lesion has not been established. However, this lesion should be distinguished grossly from ectopic sebaceous glands and small subepithelial tumors such as carcinoid and granular cell tumor. Moreover, signet ring cell carcinoma, which contains round cells with abundant cytoplasm and has similar histologic features to xanthoma, should be distinguished microscopically.

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INTRODUCTION

Xanthoma is an uncommon nonneoplastic lesion resulting from the accumulation of foamy histiocytes. It predominantly shows cutaneous manifestations associated with dyslipidemia. Verruciform xanthoma (VX), which has almost similar histologic features, is also a rare lesion usually found on the oral mucosa or the genital area. It is presumably associated with the inflammatory response to mucosal damage. However, xanthoma and VX of the esophagus are extremely rare. Since the first report by Remmele and Engelsing2 only 13 cases of esophageal xanthoma have been reported,1-9 and since the report by Herrera-Goepfert et al.10 only four cases of VX of the esophagus have been reported.10-13 The etiologies of both lesions are not understood. The authors recently encountered a new case of esophageal xanthoma. Besides its rarity, the confusing descriptions of these two lesions have made distinguishing between them difficult. We describe herein a new case, including a review of all reported cases of xanthoma and VX of the esophagus.

CASE REPORT

A 70-year-old man with an unremarkable medical history was hospitalized with a complaint of epigastric pain. Physical examination revealed epigastric tenderness; however, other examination findings were normal. No abnormal findings were detected on laboratory and radiologic examinations. Serum total cholesterol, triglyceride, high density lipoprotein cholesterol, and low density lipoprotein cholesterol levels were 151, 215, 33, and 102 mg/dL, respectively. Endoscopic examination was performed to find the cause of the epigastric pain. Multiple shallow gastric ulcers and a duodenal ulcer were detected and suspected to be the cause of the pain. Aspirin medication was the suspected cause of the multiple ulcers. Besides the ulcers, in the upper esophagus 20 cm from the incisors, a 3-mm yellowish granular elevated mucosal lesion was found and a biopsy was performed (Fig. 1). Microscopically, large round cells were aggregated in the lamina propria immediately beneath the squamous epithelium. The cells had small nuclei that were centrally or eccentrically located. The cytoplasm was sparse and contained vacuoles (Fig. 2). The lesion was diagnosed histologically as xanthoma of the esophagus.

DISCUSSION

Xanthoma and VX are usually considered different diseases.
| Case | Authors                           | Age/Sex | Site     | No.   | Size, mm | Endoscopic findings        | Other conditions                                      |
|------|-----------------------------------|---------|----------|-------|----------|----------------------------|-------------------------------------------------------|
| 1    | Remmele et al. (1984)²            | 54/M    | Upper    | Solitary | 10       | Yellow spot                | Gastrectomy                                           |
| 2    | Stolte et al. (1985)³             | 45/M    | Middle   | Three  | Thumb nail | Yellow flat elevation     | Hyperlipidemia, diabetes mellitus                     |
| 3    | Vimala et al. (2000)⁴            | 37/F    | Lower    | Multiple | 2–5      | Yellowish nodular          | Gastric xanthoma                                      |
| 4    | Hirokawa et al. (2003)⁵           | 52/F    | Lower    | Solitary | 2        | Yellowish granular         | Duodenal ulcer                                        |
| 5    | Hirokawa et al. (2003)⁵           | 67/M    | Lower    | Solitary | 2        | Yellow spots               | Hepatocellular carcinoma, hypertension, choledolithiasis |
| 6    | Herrera-Goepfert et al. (2003)⁸   | 61/M    | Middle   | Solitary | 5        | Verruciform                | Non-Hodgkin lymphoma of testis                        |
| 7    | Gencosmanoglu et al. (2004)⁵      | Not specified | Not specified | Multiple | Less than 5 mm | Yellow-white colored plaques | Not specified                                          |
| 8    | Gencosmanoglu et al. (2004)⁵      | Not specified | Not specified | Solitary | Less than 5 mm | Yellow-white colored plaques | Not specified                                          |
| 9    | Cho et al. (2008)⁶                | 49/M    | Lower    | Solitary | 3        | Yellowish elevated granular lesion | Atrophic gastritis                                   |
| 10   | Arima (2008)⁷                     | 74/M    | Middle   | Solitary | 4        | Yellowish white patch      | Not specified                                          |
| 11   | Arima (2008)⁷                     | 74/M    | Upper    | Solitary | 2        | Whitish protruding lesion  | Not specified                                          |
| 12   | Licci et al. (2010)⁸             | 49/M    | Upper    | Solitary | 3        | Verruciform                | Not specified                                          |
| 13   | Becheanu et al. (2011)⁹          | 62/M    | Lower    | Solitary | 3        | Yellowish elevated granular lesion | Atrophic gastritis                                   |
| 14   | Becheanu et al. (2011)⁹          | 56/F    | Lower    | Solitary | 4        | Yellowish elevated lesion  | Biermer anemia, HCV, antral hyperplastic polyp with focal adenocarcinoma, atrophic gastritis |
| 15   | Min et al. (2012)¹²              | 74/F    | Middle   | Solitary | 3        | Verruciform                | Atrophic gastritis, hyperlipidemia, dementia          |
| 16   | Salamanca et al. (2012)¹³         | 70/M    | Upper    | Solitary | 20       | Verruciform                | Hypertension, HCV, hemochromatosis, glottis cancer, hepatocellular carcinoma, tracheal cancer, radiation therapy, chemotheraphy |
| 17   | Park et al. (2013)⁹              | 67/M    | Lower    | Solitary | 2        | White-yellowish elevated lesion | Ileoceleal lymphoma                                   |
| 18   | Present study                     | 70/M    | Upper    | Solitary | 3        | Yellowish granular elevated lesion | Gastric and duodenal ulcer                           |

M, male; F, female; HCV, hepatitis C virus.
Xanthoma of Esophagus

The etiologies are different, as xanthoma is caused by hyperlipidemia and VX arises presumably as a result of an inflammatory response to continuous mucosal damage. However, the etiologies of the two lesions arising in the esophagus are not understood. The characteristics of all reported cases of xanthoma and VX of the esophagus are summarized in Table 1.

Fourteen cases of xanthoma and four cases of VX of the esophagus have been reported. However, some reports loosely stratified VX into esophageal xanthoma, whereas others have excluded it. In terms of clinical data, both diseases were found predominantly in men than in women: 9 versus 3 in xanthoma and 3 versus 1 in VX. The median age was 59 years (range, 37 to 74) in xanthoma and 65.5 years (range, 49 to 74) in VX. The predominant location was the lower esophagus for xanthoma (lower, 7; middle, 2; upper, 3), whereas VX was not reported in the lower esophagus (upper, 2; middle, 2). The median size was not different: 3 mm (range, 2 to 10) for xanthoma and 4 mm (range, 3 to 20) for VX.

The associated medical conditions were diverse; however, two patients with malignant tumors were included in each group: hepatocellular carcinoma and ileocecal lymphoma in xanthoma, and gastric cancer and multifocal cancer (cancer of the glottis, liver, and trachea) in VX, although there was no definite association.

VX is characterized by its histologic features, including papillomatosis, acanthosis, and hyperparakeratosis. Also, the external morphology is verrucoid. Nevertheless, findings of large round foam cells in the lamina propria under the squamous epithelium are the same as those in xanthoma. It is difficult to differentiate between the two lesions on the basis of gross examination when they arise on the esophagus. Exophytic and verrucoid features seen in VX of the skin were not observed in the esophagus because most of the reported cases were small in size.

Considering that xanthoma and VX are nonneoplastic lesions, differentiating between them could be a waste of effort. However, these lesions have to be grossly distinguished from ectopic sebaceous glands and small subepithelial tumors such as carcinoid and granular cell tumor because most of the reported esophageal xanthomas are yellowish or white mucosal elevated lesions. In terms of microscopic findings, signet ring cell carcinoma, which contains round cells with abundant cytoplasm, should be distinguished. While signet ring cell carcinoma has an eccentrically located nucleus because of the intracellularly abundant mucin, xanthoma has a centrally located and small nucleus. Accumulation of foamy histiocytes of xanthoma could be a clue for the differential diagnosis. Positive immunohistochemical staining for CD68, which indicates a histiocytic origin, is another characteristic finding of xanthoma. Moreover, esophageal cancer and ectopic sebaceous glands do not commonly stain with Lugol’s solution; thus, endoscopists need to be aware of these lesions for the differential diagnosis.

With more case reports of esophageal xanthoma and VX of the esophagus, the characteristics of both lesions will be more clearly elucidated.

Conflicts of Interest

The authors have no financial conflicts of interest.

REFERENCES

1. Gencosmanoglu R, Sen-Oran E, K urtkaya-Y apıcıer O, Tozun N. Xan thelasmas of the upper gastrointestinal tract. J Gastroenterol 2004;39: 215-219.
2. Remmele W, Engelsing B. Lipid island of the esophagus. Case report. Endoscopy 1984;16:240-241.
3. Stolte M, Seifert E. Lipid islands in the esophagus. Leber Magen Darm 1985;15:137-139.
4. Vimala R, Ananthalakshmi V, Murthy M, Shankar TR, Jayanthi V. Xanthelasma of esophagus and stomach. Indian J Gastroenterol 2000;19:135.
5. Hirokawa M, Takenaka R, Takahashi A, et al. Esophageal xanthoma: report of two cases and a review of the literature. J Gastroenterol Hepatol 2003;18:1105-1108.
6. Cho DS, Park HK, Park SK, et al. An esophageal xanthoma diagnosed by upper gastrointestinal endoscopy. Korean J Med 2008;75(Suppl 3):S784-S786.
7. Arima M. Esophageal xanthoma: report of two cases. Stomach Intest 2008;43:317-320.
8. Becheanu G, Dumbrava M, Arbanas T, Diculescu M, Hoyeau-Idrissi N, Flejou JF. Esophageal xanthoma: report of two new cases and review of the literature. J Gastrointestin Liver Dis 2011;20:431-433.
9. Park HS, Jang KY, Moon WS. Incidental esophageal xanthoma in a patient with ileocecal lymphoma. Dig Endosc 2013;25:92-93.
10. Herrera-Goepfert R, Lizano-Soberón M, García-Perales M. Verruciform xanthoma of the esophagus. Hum Pathol 2003;34:814-815.
11. Licci S, Campo SM, Ventura P. Verruciform xanthoma of the esophagus: an uncommon entity in an unusual site. Endoscopy 2010;42 Suppl 2:E330.
12. Min KW, Koh JS, Lee KG, Kim HC, Jang KS, Paik SS. Verruciform xanthoma arising in the mid esophagus. Dig Endosc 2012;24:387.
13. Salamanca J, Alemany I, Sosa G, Pinedo F, Hernando S, Martín-Acosta P. Esophageal verruciform xanthoma following radiotherapy. Gastroenterol Hepatol 2012;35:317-320.
14. Kim YS, Jin SY, Shim CS. Esophageal ectopic sebaceous glands. Clin Gastroenterol Hepatol 2007;5:A23.