Case Report

Esophageal adenocarcinoma with white opaque substance observed by magnifying endoscopy with narrow band imaging

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White opaque substance (WOS) is observed in the gastric neoplasia of 0-IIa type using magnifying endoscopy with narrow band imaging (NBI-ME). Colonic and duodenal neoplasms with WOS have also been reported. Immunohistochemical examination with adipophilin reveals WOS in gastric neoplasms as lipid droplets, and WOS is specific for neoplasm with intestinal or gastrointestinal phenotype. We herein report a case of adenocarcinoma of the esophagogastric junction with WOS. A male patient in his sixties was found by esophagogastroduodenoscopy to have an esophageal elevated lesion. NBI-ME showed whitish deposits that looked similar to WOS in gastric neoplasms. The patient underwent endoscopic submucosal dissection and the lesion was resected in a single piece. This tumor had diffuse positivity for adipophilin and gastrointestinal phenotype.

Key words: adenocarcinoma, esophageal cancer, magnifying endoscopy, narrow band imaging (NBI), white opaque substance (WOS)

INTRODUCTION

WHITE OP AQUE SUBSTANCE (WOS) was first reported by Yao et al. in 2008 as a finding of elevated-type gastric adenoma or adenocarcinoma using magnifying endoscopy with narrow band imaging (NBI-ME). WOS is a white deposit that sometimes interferes with visualization of the subepithelial microvascular pattern in gastric neoplasia.1 It has been pathologically confirmed that WOS observed by NBI-ME represents the accumulation of lipid droplets using oil red O staining and adipophilin immunostaining.23 Furthermore, it has been reported to be found in colonic and duodenal neoplasms but not in other gastrointestinal neoplasms.4 Here, we report a case of adenocarcinoma of the esophagogastric junction (EGJ) in which we observed WOS using NBI-ME. To our knowledge, this is the first report describing a WOS-positive esophageal neoplasm.

CASE REPORT

MALE IN his sixties was referred for examination for the cause of epigastralgia. Endoscopic examination showed an elevated lesion in the lower esophagus. He had medical histories of hypertension and chronic renal failure on hemodialysis because of nephrosclerosis. He had never smoked and drank socially. He was negative for anti-Helicobacter pylori IgG antibody.

Conventional white light imaging showed a smooth, flat, elevated lesion of 20 mm in diameter, without ulceration and redness at the adjacent oral side of the squamocolumnar junction (SCJ) in the posterior wall (Fig. 1A). NBI-ME showed irregular microsurface structures with small and high-density pits. In one part, the lesion revealed an irregular microvascular pattern. In the other part, whitish deposits were observed that were similar to WOS in gastric neoplasms (Fig. 1B). The oral margin of the lesion was covered with squamous epithelium, suggesting subepithelial invasion. Histology of the specimen obtained by endoscopic forceps biopsy revealed well-differentiated adenocarcinoma. Based on the findings described above, he was clinically diagnosed with adenocarcinoma arising...
from EGJ and it was estimated that invasion depth was within the mucosa. The patient underwent ESD and the lesion was resected in a single piece without major complications.

Histology revealed atypical glandular epithelium proliferating widely in the lamina propria mucosae. In the oral margin of the lesion, atypical epithelium invaded below the squamous epithelium (Fig. 2A,B). In the center of the lesion, tumor invaded beyond the mucosa adjacent to the muscularis mucosae (Fig. 2C,D). D2/40 immunohistochemistry showed there was no lymphovascular involvement. Histopathologically, short segmental Barrett’s epithelium was observed, but it had no contact with the lesion. Immunohistochemical staining revealed that the lesion was focally positive for mucin (MUC) 2, CD10 and MUC6 and negative for MUC5AC. The lesion also had diffuse positivity for caudal-related homeobox transcription factor (CDX) 2 (Fig. 3). In addition, immunohistochemical staining of adipophilin revealed that lipid droplets accumulated in the neoplastic epithelium. Adipophilin was detected in almost all the neoplastic cells in marginal crypt epithelium, whereas this was not observed in the non-neoplastic epithelium (Fig. 4). The final diagnosis was well to moderately differentiated adenocarcinoma of the gastroesophageal junction E, 20 mm, 0-IIa, tub1 >tub2, pT1a-MM, ly0, v0, pHM0, pVM0 (Japanese Classification of Esophageal Cancer, the 10th Edition).
Figure 3  Immunohistochemical examination. (A) MUC2, magnification, ×100. (B) MUC5AC, magnification, ×100. (C) MUC6, magnification, ×100. (D) CD10, magnification, ×200. (E) CDX2. Lesion had focal positivity for MUC2, MUC6 and CD10 but negative staining for MUC5AC. The lesion also had diffuse positivity for CDX2, magnification, ×100.

Figure 4  Immunohistochemical examination of adipophilin. Adipophilin was detected in approximately all of the neoplastic cells.
DISCUSSION

Recently, NBI-ME has been reported to be clinically useful for differentiation of gastric cancerous and non-cancerous lesions. One of the most important findings of cancerous lesions is considered to be the presence of irregularity of the microvascular architecture. However, when NBI-ME is applied in clinical practice, a white substance in the superficial area of the neoplasia sometimes interrupts visualization of the precise microvascular morphology. Yao et al. first reported this substance and named it WOS and they also reported that WOS not only interferes with visualization of the epithelial microvascular architecture but is also useful for discriminating gastric adenoma from carcinoma according to the presence or absence of irregular shapes and the distribution of WOS.

WOS has been pathologically confirmed to be intramucosal accumulation of lipid detected using oil red O staining of the endoscopic biopsy specimen. Oil red O staining enables direct visualization of lipid droplets; however, it has a limitation in that it can only be applied to fresh frozen samples but not to paraffin-embedded sections because the lipid is removed during the process of paraffin fixing. Recently, adipophilin has been recognized as a novel marker of lipid accumulation and it can be applied even to paraffin-embedded section. It is an adipose differentiation-related protein located on the surface of lipid droplets. It was reported that immunohistochemistry of adipophilin of gastric neoplasia was well correlated with WOS observed by NBI-ME. To the best of our knowledge, this is the first report describing a WOS-positive esophageal neoplasm, and we confirmed the phenomenon that lipid accumulation may occur in neoplasms arising from the esophagus.

Two mechanisms of accumulation of lipid droplets are suggested: lipid absorption and lipid production. First, an electron microscopy study using a lipid-staining method has already revealed that the epithelium of the gastric intestinal metaplasia has an ability to absorb lipid droplets similar to the normal small intestinal epithelium. This finding suggests that even gastric epithelium can obtain an intestinal phenotype to absorb lipids. Absorbed lipid droplets are retained within the epithelium, and are drained into the lymphatics within the lamina propria after forming chylomicrons in the normal small intestine. In the neoplasm, the accumulation of lipid droplets might be caused by its impaired lymphatic clearance as a result of structural abnormality. Second, the expression process of adipophilin can be enhanced. The expression of adipophilin is suspected to be induced during the process of carcinogenesis because it is known to be regulated by hypoxia inducible factor (HIF) and the peroxisome proliferator-activated receptor (PPAR) family, both of which are closely involved in carcinogenesis.

A previous report demonstrated that WOS is present in either gastrointestinal-type or intestinal-type gastric neoplasia, but absent in gastric-type neoplasia. In our case, the tumor cells were positive for MUC2, MUC6, CD10, and CDX2 and were considered to have gastrointestinal phenotype. Although the detailed mechanism of lipid droplet accumulation in the esophageal neoplastic epithelium is unknown, the fact that our case expressed gastrointestinal phenotype as well as gastric neoplasm suggests that lipid could accumulate in adenocarcinoma, if the tumor has, at least partly, intestinal phenotype irrespective of the organ where the tumor arises. It would be a useful optical predictor for the mucin-expressing phenotype of the tumor.

There are four possible origins of adenocarcinomas of the esophagus; Barrett’s esophagus (epithelium), esophageal glands proper, ectopic gastric mucosa, and esophageal cardiac glands. In our case, a short segmental Barrett’s epithelium was present in the specimen, but it had no contact with the tumor. Tumors arising from esophageal glands proper usually grow in the submucosa and those from ectopic gastric mucosa were reported to localize only in the upper or cervical esophagus; therefore, these are unlikely as the origins for our case. The tumor mainly grew in the lamina propria mucosae, and the cardiac glands of the esophagus in a non-cancerous squamous epithelium on the anal side of the tumor had dysplastic changes. Thus, we considered the possible origin of this tumor was esophageal cardiac glands.

In summary, we present the first case of esophageal adenocarcinoma with WOS, which seems to arise from esophageal cardiac glands. WOS might be a clue to understanding carcinogenesis and pathophysiology of intestinal-type adenocarcinoma of the digestive system.

CONFLICT OF INTERESTS

Authors declare no conflict of interests for this article.

REFERENCES


SUPPORTING INFORMATION

ADDITIONAL SUPPORTING INFORMATION may be found in the online version of this article at the publisher’s web-site:

Figure S1 Loupe view of the deeper cut examination. Invasion depth and vertical margin are confirmed by hematoxylin-eosin stain.

Figure S2 Loupe view of the immunohistochemical examination of desmin. Muscularis mucosae were confirmed to be maintained in the specimen by immunohistochemical examination of desmin.