Case Report

White opaque substance in superficial esophageal squamous cell carcinoma: report of a case

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Abstract: White opaque substance (WOS) observed in the gastric neoplasia by magnifying endoscopy with narrow band imaging (NBI-ME) has been reported to be useful for differentiation of gastric cancerous and non-cancerous lesions. Using oil red O staining and adipophilin immunostaining reveals WOS in gastric neoplasms as lipid droplets, and WOS is specific for neoplasm with intestinal or gastrointestinal phenotype. We here in report a case of superficial esophageal squamous cell carcinoma with WOS. A male patient in his seventies was found by esophagogastroduodenoscopy to have two superficial esophageal lesions and two superficial gastric lesions. NBI-ME observed WOS in both gastric lesions and in one esophageal lesion. The patient underwent endoscopic submucosal dissection and all the lesions were resected en bloc successfully. All four lesions had diffuse positivity for adipophilin on immunostaining. This is the first case reported that WOS was observed in esophageal squamous cell carcinoma.

Keywords: Squamous cell carcinoma, esophageal cancer, white opaque substance (WOS), magnifying endoscopy, narrow band imaging (NBI)

Introduction

Magnifying endoscopy with narrow band imaging (NBI-ME) has enabled visualization of mucosal microvascular and microsurface patterns. Yao et al. have identified the microvascular and microsurface patterns that are typical for early gastric cancers [1-3]. Recently, NBI-ME is also an excellent modality for identifying the boundary delineation of early gastric cancers [4-6]. Meanwhile, white opaque substance (WOS), first reported by Yao et al., is one of the peculiar findings of NBI-ME, it is a white substance in the superficial area of the gastric neoplasia and sometimes interrupts visualization of the precise microvascular morphology, which results in difficulties in discrimination of gastric cancerous and non-cancerous lesions. WOS does not just 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 regular shapes and distribution of WOS [7]. WOS has been pathologically confirmed to be intramucosal accumulation of lipid detected using oil red O staining of the endoscopic biopsy specimen [8]. 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 as the lipid is removed during the process of paraffin fixing. Recently, adipophilin has been used as a novel marker of lipid accumulation which can be applied even to paraffin embedded section. It is an adipose differentiation related protein located on the surface of lipid droplets [9]. It was reported that immunohistochemistry of adipophilin of gastric neoplasia was well correlated with WOS observed by NBI-ME [10]. WOS has been reported to be found in neoplasms located in colorectum, duodenum and esophagogastric junction, where are all covered by columnar epithelium, histologically [11-13]. We herein report a case of superficial esophageal squamous cell carcinoma in which WOS was observed by NBI-ME.

Case presentation

A 77-year-old Chinese man visited our department because of epigastralgia. His medical his-
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Histology revealed intramucosal well differentiated squamous cell carcinomas (m2) in both esophageal ESD resected specimens (Figure 3A). No lymphovascular involvement was detected on immunostaining of D2/40. Oil red O staining and immunohistochemical staining of adipophilin of the biopsy specimen of the distal lesion shown lipid droplets scattered in the cytoplasm of squamous carcinoma cells (Figure 4). Immunohistochemical staining of adipophilin of the ESD resected specimens revealed that lipid droplets accumulated in both esophageal neoplastic epithelium. Adipophilin was intensely detected in almost all the neoplastic cells in both esophageal lesions, of which the morphology was diffuse and has no polarized structure compared with gastric lesion. In the non-neoplastic squamous epithelium adipophilin was weakly expressed (Figure 3B, 3C). The morphology and density of adipophilin was similar in both lesions. The final diagnosis was well differentiated squamous cell carcinoma of the esophagus, 6×6 mm (28 cm from the incisor teeth)/17×4 mm (31 cm from the incisor teeth), 0-IIb, pT1a-LPM, ly0, v0, pHM0, pVM0 (according to the Japanese...
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Figure 2. (A) A slightly elevated lesion (IIa) of 15 mm in major diameter at 31 cm from the incisor teeth. (B, C) WOS was observed by NBI-ME and the morphology was irregular reticular/speckled pattern. IPCLs were not distinct. (B) showed the centre of the lesion, (C) showed the margin of the lesion.

Figure 3. A. Early well differentiated squamous cell carcinoma with microinvasion (basal cell type, M2) with HE staining. B, C. Adipophilin was expressed in the squamous carcinoma cells with cytoplasmic staining and no polarization.

Figure 4. A, B. Oil red O staining of the biopsy specimen of the lesion at 31 cm from the incisor teeth showed lipid droplets scattered in the cytoplasm of squamous carcinoma cells. C, D. In this lesion adipophilin was expressed in the squamous carcinoma cells with cytoplasmic staining and no polarization.

Classification of Esophageal Cancer, the 10th Edition, revised version). Both gastric lesions were histologically diagnosed as intramucosal well differentiated tubular adenocarcinoma (m). No lymphovascular involvement was found. Adipophilin staining revealed that lipid droplets
In this case adipophilin was detected in esophageal squamous carcinoma and pericarcinious tissue, but the degree of adipophilin’s expression was different, which was intense in cancer tissue and weak in pericarcinious normal tissue, so we can detect WOS only in cancerous area by endoscopy. There are two possible reasons about this phenomenon: one is WOS is a sign of neoplasm not only in stomach but also in esophagus; the other is WOS is only a sign of deficiency of lipid metabolism of esophageal squamous cells and has no relationship with esophageal neoplasm, it is accidentally appeared in this WOS-positive gastric cancer patient. We prefer the former because we never detect WOS in patients with normal esophagus or benign esophageal disease. We can speculate that the intense expression of WOS is a sign of neoplasia and the weak expression of WOS is a sign of malignant potential to neoplasia. It is well established that tumor microenvironment plays an important role in cancer development and progression, so the pericarcinious normal tissue expressing WOS weakly would be the soil of neoplasia. WOS may be a key sign of cancerous and precancerous lesion of esophageal squamous epithelium. In this case the endoscopic morphology of WOS is irregular reticular/speckled pattern which is similar to gastric lesion, but morphology of adipophilin expression in squamous cancer cells is diffuse and has no polarized structure compared with gastric lesion. Hence, we can speculate that the mechanism of accumulation of lipid droplets is different in esophagus and stomach. The present findings may provide novel insights into the molecular mechanism of esophageal squamous cell carcinoma development and progression and into the development of new anticancer therapeutics. We need to conduct further studies to clarify the molecular mechanism of WOS in squamous cell carcinoma.

In summary, we present the first case of esophageal squamous cell carcinoma with WOS, which arises from esophageal squamous epithelial. Because WOS can interrupt visualization of the precise microvascular morphology of the esophageal lesion, rather than assessing the IPCLs, the emergence of WOS could be an alternative new optical sign for discriminating cancerous from non-cancerous lesion in esophagus using NBI-ME.
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Disclosure of conflict of interest

None.

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