

Benign glycogenic acanthosis lesions of the esophagus

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Background/aims: Glycogenic acanthosis is described as benign thickening of the esophageal squamous epithelium of unknown etiology. Although its etiology is unknown, it has been reported that glycogenic acanthosis may be related to gastroesophageal reflux and hiatal hernia. The aim of the present study was to review the patients who were diagnosed with glycogenic acanthosis on upper gastrointestinal endoscopy and to determine whether there is any association between glycogenic acanthosis and gastroesophageal reflux and hiatal hernia. **Material and Methods:** A total of 504 patients who underwent upper gastrointestinal endoscopy for evaluation of non-ulcer dyspepsia were reviewed retrospectively. **Results:** Glycogenic acanthosis was detected in 143 (28.3%) of those 504 patients. Of the 143 patients, 82 (57.3%) were male and 61 (42.7%) were female. Patients with glycogenic acanthosis were aged 20-83 years. Gastroesophageal reflux was detected in 50 (34.9%) cases with glycogenic acanthosis, while hiatal hernia was detected in 30 (20.9%) cases. Gastroesophageal reflux was detected in 102 (28.2%) control subjects, while hiatal hernia was detected in 50 (13.8%). Hiatal hernia was significantly higher in glycogenic acanthosis patients than in controls subjects ($p<0.05$). Glycogenic acanthosis patients had higher gastroesophageal reflux than seen in controls subjects, but the difference between groups was not statistically significant ($p>0.05$). **Conclusions:** Our results suggest that glycogenic acanthosis is primarily an age-related disease. We demonstrated that glycogenic acanthosis may be associated with gastroesophageal reflux and hiatal hernia. Further studies are necessary to confirm these findings.

Key words: Esophagus, gastroesophageal reflux, hiatal hernia, glycogenic acanthosis

Özofagusun benign glikojen akantozis lezyonları

Amaç: Glikojen akantozis, etiyolojisi bilinmeyen nedenlerden dolayı özofagusun skuamoz epitelinin benign kalınlaşması olarak bilinmektedir. Etiyolojisi bilinmemesine rağmen gastroözofageal reflü ve hiatal herni ile ilişkili olabileceği rapor edilmiştir. Bu çalışmamızda üst gastrointestinal endoskopisi yapılan ve glikojen akantozis tanısı konulan hastaların gastroözofageal reflü ve hiatal herni ile ilişkisi retrospektif olarak araştırıldı. **Yöntem:** Non ülser dispepsi nedeniyle üst gastrointestinal endoskopisi yapılan 504 hasta retrospektif olarak incelendi. **Bulgular:** 504 hastanın 143 (%28.3)'ünde glikojen akantozis tespit edildi. Glikojen akantozis tanısı konulan 143 hastanın 82 (%57.3)'si erkek, 61 (%42.7)'i bayan idi. Glikojen akantozisli hastaların yaş aralığı 20 ile 83 arasındaydı. Bu hastaların 7'si 20 ile 29 yaş aralığında, 12'si 30 ile 39 yaş aralığında, 40'ı 40 ile 49 yaş aralığında, 35'i 50 ile 59 yaş aralığında, 49 hasta ise 60 yaşın üzerinde idi. Glikojen akantozisli vakaların 50 (%34.9)'ünde gastroözofageal reflü tespit edildi. Vakaların 30 (%20.9)'unda ise hiatal herni tespit edildi. Kontrol grubunda ise 102 (28.2%) kişide gastroözofageal reflü tespit edildi. Ayrıca kontrol grubunda hiatal herni 50 (13.8%) kişide tespit edildi. Glikojen akantozisli vakalarda hiatal herni sayısı kontrol grubuna göre anlamlı derecede yüksekti ($p<0.05$). Glikojen akantozisli vakalarda gastroözofageal reflü sayısı kontrol grubuna göre yüksekti, ancak istatistiksel olarak anlamlı değildi ($p>0.05$). **Sonuç:** Bu çalışmamızda glikojen akantozisin primer olarak ileri bir yaş hastalığı olduğu görüldü. Ayrıca glikojen akantozisin gastroözofageal reflü ve hiatal herni ile ilişkili olabileceği gösterildi.

Anahtar kelimeler: Özofagus, gastroözofageal reflü, hiatal herni, glikojen akantozis

INTRODUCTION

Endoscopy is a valuable imaging modality for the evaluation of the esophagus. When a benign tumor of the esophagus is suspected, the clinical evaluation begins with radiological studies, and the diagnosis is confirmed with esophagoscopy and biopsy. Benign tumors of the esophagus can be classified as mucosal or submucosal in origin. The most common mucosal lesions include squamous papillomas, adenomas arising in Barrett's mucosa, inflammatory esophagogastric polyps, and glycogenic acanthosis (1).

Glycogenic acanthosis of the esophagus is a common benign entity that is often seen in the elderly and is characterized by multifocal plaques of hyperplastic squamous epithelium with abundant intracellular glycogen deposits (2). On gastroscopy, glycogenic acanthosis is most commonly observed as numerous uniformly sized, usually less than 3 mm, subtle, round elevations involving the entire esophageal surface. If performed carefully, endoscopy will almost always confirm these findings (3). Although this condition is commonly seen on endoscopy (4,5) and autopsy (6), its precise clinical and pathological significance is unknown. It has been reported as an incidental finding in 3.5% of gastroscopies (7). Glycogenic acanthosis is observed in up to 30% of patients undergoing double-contrast radiography (3). Because the nodules of glycogenic acanthosis appear in the fifth to sixth decades of life and become more numerous and larger with increasing age, the condition is thought to be an age-related, degenerative process (2). Recently, Suoglu *et al.* [8] reported that glycogenic acanthosis may be observed in children with celiac disease.

Although the etiology and pathogenesis of glycogenic acanthosis are unknown, it has been reported that glycogenic acanthosis may be related to gastroesophageal reflux (GER) and hiatal hernia (2,7). The aim of the present retrospective study was to review the patients who were diagnosed with glycogenic acanthosis on upper gastrointestinal endoscopy and to determine whether there is any association between glycogenic acanthosis and GER and hiatal hernia.

MATERIALS AND METHODS

A total of 504 patients who underwent upper gastrointestinal endoscopy for evaluation of non-ulcer dyspepsia were reviewed retrospectively.

The indications for endoscopic examination and the patient's medical chart were reviewed for symptoms suggestive of esophageal disease, including dysphagia, heartburn, and epigastric or chest pain. The patient's age and gender were also recorded.

The diagnosis of glycogenic acanthosis was based on the typical endoscopy findings described as numerous uniformly sized, usually <3 mm, 1–4 mm in diameter, subtle, whitish, round elevations involving the entire esophageal surface.

The GER diagnosis was based on endoscopic imaging. GER was diagnosed with endoscopic signs of edema, erythema, friability, granularity, and red streaks.

Endoscopy was performed using a conventional endoscopic system (Olympus, Japan).

The study protocol was carried out in accordance with the Helsinki Declaration as revised in 2000. All participants were informed about the study protocol, and written consent was obtained from each subject.

Statistical Analysis

The results are expressed as the mean±standard deviation. Nonparametric continuous variables were compared using the Mann–Whitney U test. Parametric variables were compared using the Student's-t test. The chi-square test was used for comparison between the groups of parameters such as sex, GER and hiatal hernia. Differences were regarded as significant at $p < 0.05$. Data were analyzed using the SPSS® for Windows statistical software package (Version 11.0).

RESULTS

The study group consisted of two groups: glycogenic acanthosis ($n=143$) and controls ($n=361$).

Glycogenic acanthosis was detected in 143 (28.3%) of 504 patients undergoing upper gastrointestinal endoscopy. Of the 143 glycogenic acanthosis patients, 82 (57.3%) were male and 61 (42.7%) were female. The mean age of these 143 patients was 52 ± 13 years. GER was detected in 50 (34.9%) and hiatal hernia in 30 (20.9%) of these cases.

The patients with glycogenic acanthosis were aged 20–83 years. Seven patients were aged 20–29, 12 patients 30–39, 40 patients 40–49, 35 patients 50–59, and 49 patients >60 years. None of the glycogenic acanthosis patients had polyposis in the upper gastrointestinal tract, which is a sign of Cowden disease.

Of the 361 controls subjects, 186 (51.6%) were male and 175 (48.4%) were female. The mean age was 52 ± 15 years. GER was detected in 102 (28.2%) and hiatal hernia in 50 (13.8%) of the 361 control subjects.

Hiatal hernia was significantly higher in the glycogenic acanthosis patients than in control subjects ($p < 0.05$). In addition, the glycogenic acanthosis patients had higher GER than the control subjects, but this difference was not statistically significant ($p > 0.05$).

DISCUSSION

We analyzed the study group with respect to gender distribution, age range, mean age, and the distribution of the 143 glycogenic acanthosis patients in a general upper endoscopy population. In our study, 49 patients with glycogenic acanthosis were older than 50 years.

The incidence of glycogenic acanthosis seems to increase with age (2) without gender predilection. Our results revealed that the nodules of glycogenic acanthosis appear in the fifth to sixth decades of life. Thus, our findings were similar with those in the literature (2). The overall incidence in the general population is difficult to determine. The endoscopic series (4,5,9) have ranged from 5%-15%, while autopsy series (6,10) have ranged from 15%-100%.

Glycogenic acanthosis are small discrete elevations in the esophageal mucosa. They have a whiter color than the surrounding mucosa, due to a high content of glycogen. Biopsies of the lesions show hypertrophied stratified squamous mucosa with glycogen deposition in the submucosa (2). Glycogenic acanthosis of the esophagus has been adequately documented on endoscopy (5,8,9) and autopsy (6). On esophagoscopy or on autopsy specimens, these lesions appear as slightly raised grey-white plaques that are usually 2–10 mm in diameter. They cause a finely nodular or cobblestone mucosal pattern that is demonstrable on double-contrast views of a well-distended esophagus (2).

Clinically, glycogenic acanthosis has no relevance, and does not progress to esophageal cancer or to esophageal stricture. It was originally thought to be associated with GER disease (GERD), but the association is not entirely clear (2). In addition, Vadva et al. (7) reported that glycogenic acanthosis may be related to GER. In that study, they observed glycogenic acanthosis in 35 (3.5%) of 2,328

patients. Furthermore, in this study, although antireflux therapy improved symptoms in all patients, it failed to eradicate the lesions of glycogenic acanthosis. In addition, Stern et al. (5) observed glycogenic acanthosis in 24 of 160 patients. In that study, they observed no correlation between glycogenic acanthosis and any other disease affecting the gastrointestinal tract, including reflux esophagitis. In our study, GER was detected in 50 (34.9%) of the endoscopically suspected glycogenic acanthosis cases and hiatal hernia was detected in 30 (20.9%) of these cases. Thus, our findings were similar to those in the literature (2,4). Recently, it has been suggested that glycogenic acanthosis is associated with celiac disease (8).

Jaskiewicz et al. (11) found an association between *Campylobacter pylori* colonization and microscopic evidence of esophagitis and esophageal glycogenic acanthosis. However, some studies showed a negative correlation between *Helicobacter pylori* and GERD with esophagitis (12,13). Jaskiewicz et al. (14) reported that esophagitis and glycogenic acanthosis were related to smoking and alcohol intake. Although it has been not been correlated with any other disease that affects reflux esophagitis (15), recent evidence suggested an association with GERD (16). Nevertheless, confirmatory studies are still required.

Despite the name, there is no association between glycogenic acanthosis and abnormalities of glucose metabolism, such as diabetes, or between glycogenic acanthosis and skin disorders, such as acanthosis nigricans (17).

The radiographic findings can be confused with the finely nodular mucosa observed in reflux esophagitis and the plaques observed in Candida esophagitis. Glycogenic acanthosis, however, can be distinguished usually from reflux esophagitis and Candida esophagitis based on several characteristics. Unless there is a coexisting disease, patients with glycogenic acanthosis are usually asymptomatic, while patients with reflux esophagitis are usually symptomatic (17).

Endoscopy should be used only when the appearance is atypical and/or the clinical suspicion of esophageal disease is high. This common benign condition must be differentiated from lesions of similar appearance, but with more important prognostic significance. In addition, as glycogenic acanthosis does not have any clinical significance, there is no need for biopsy or therapy.

In conclusion, our findings suggest that glycogenic acanthosis is primarily an age-related disease, which has also been reported in childhood. In addition, we demonstrated that glycogenic acanthosis may be associated with GER and hiatal hernia.

Further studies are necessary to confirm these findings.

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