

A 60-year-old male with no other past medical history presented with symptoms of gastroesophageal reflux disease. He underwent an upper GI endoscopy. A 2 mm white plaque was identified in the middle third of the esophagus, which was biopsied (Figures 1-6). The remainder of the endoscopy was unremarkable.



Figure 1; H&E, 40x

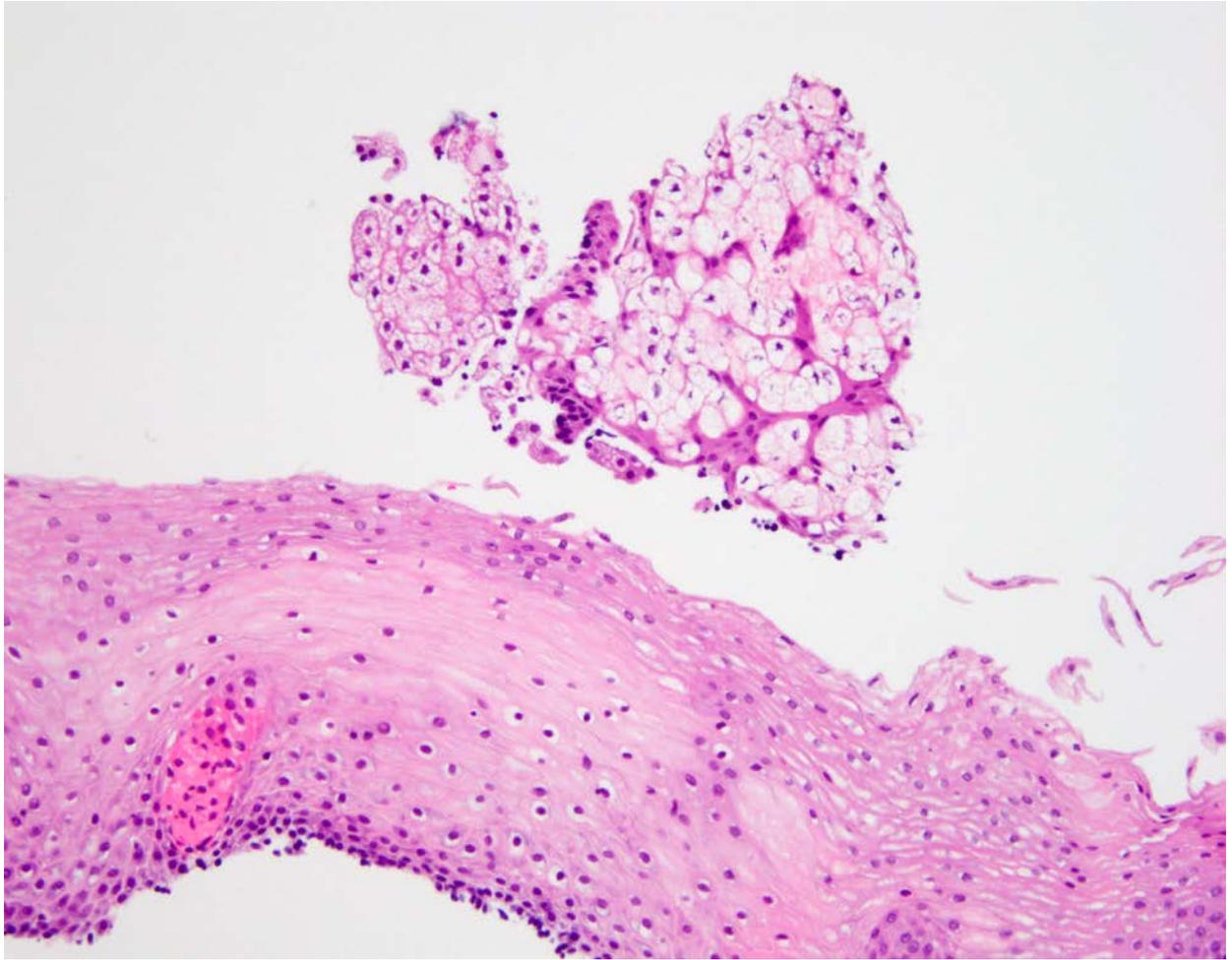


Figure 2; H&E, 100x

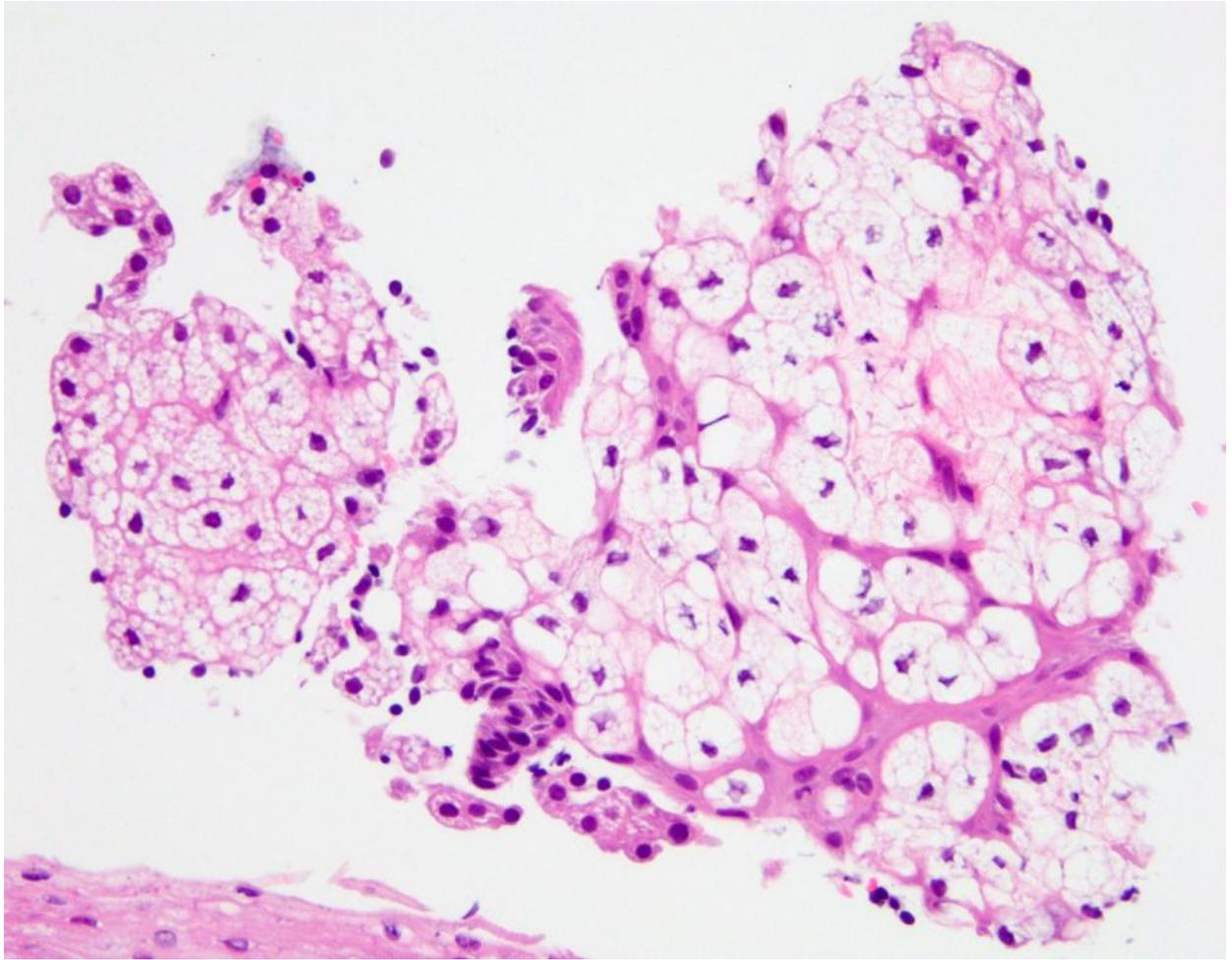


Figure 3; H&E, 200x

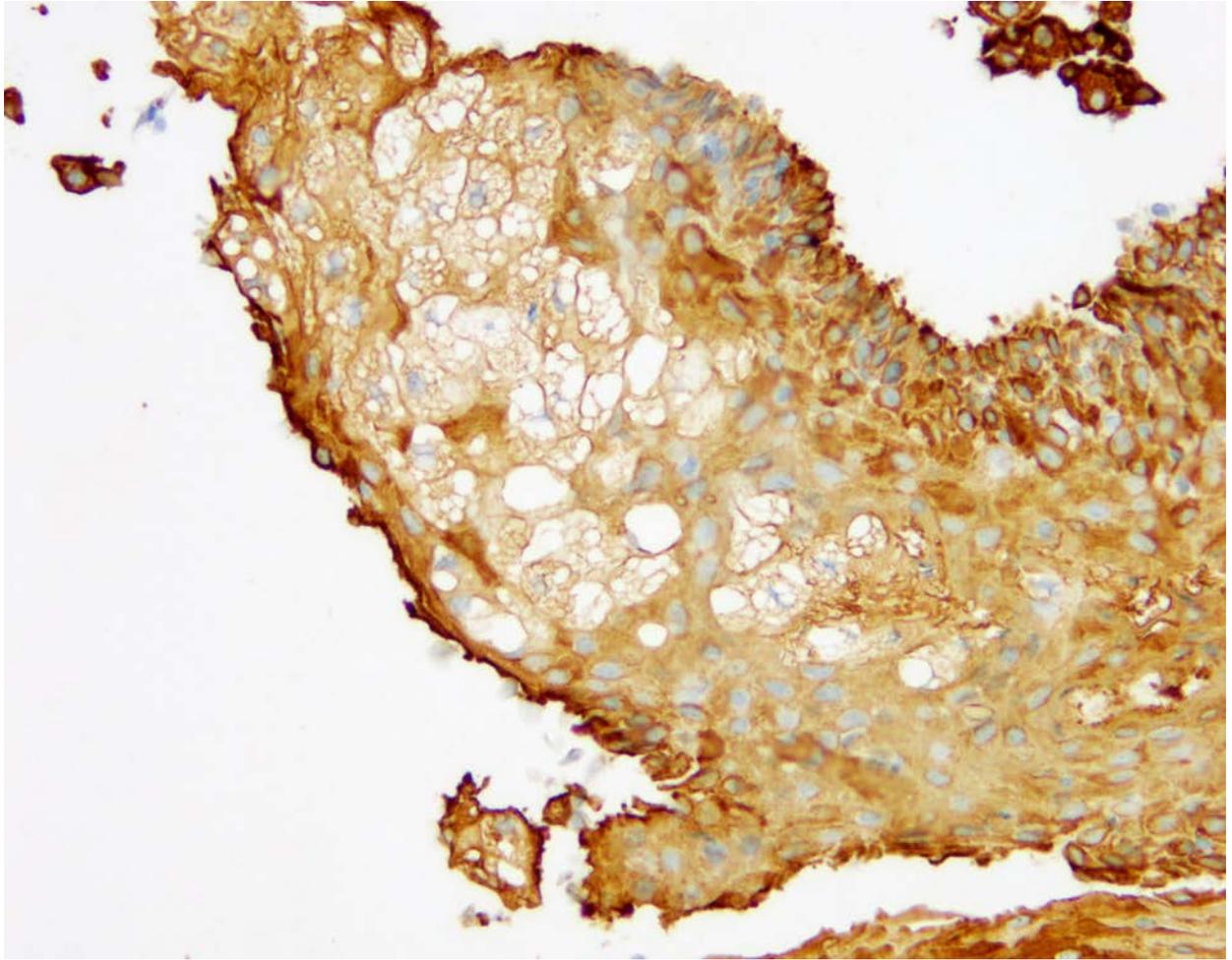


Figure 4; Cytokeratin cocktail (AE1/3 & CAM5.2) stain, 200x

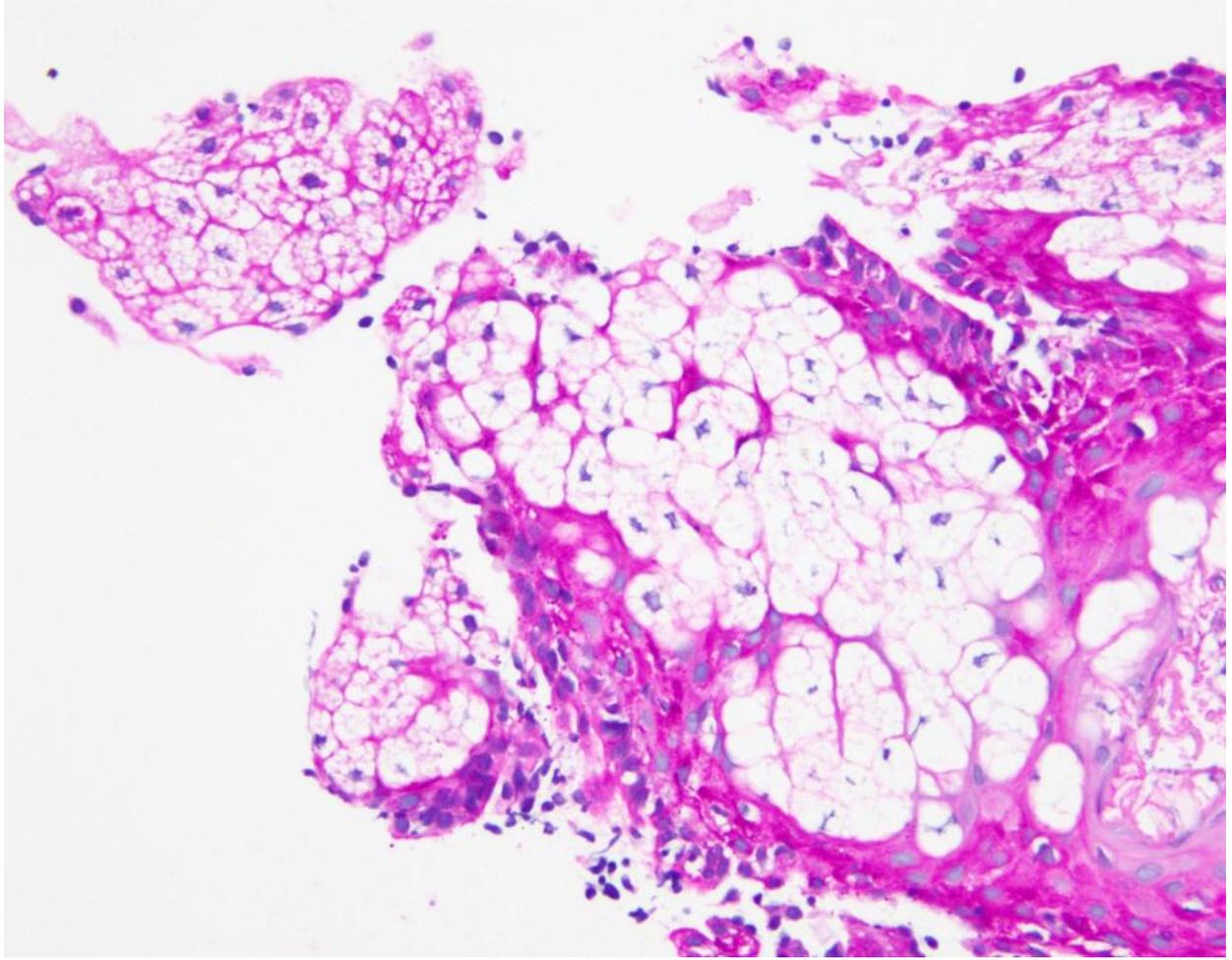


Figure 5; PAS stain, 200x

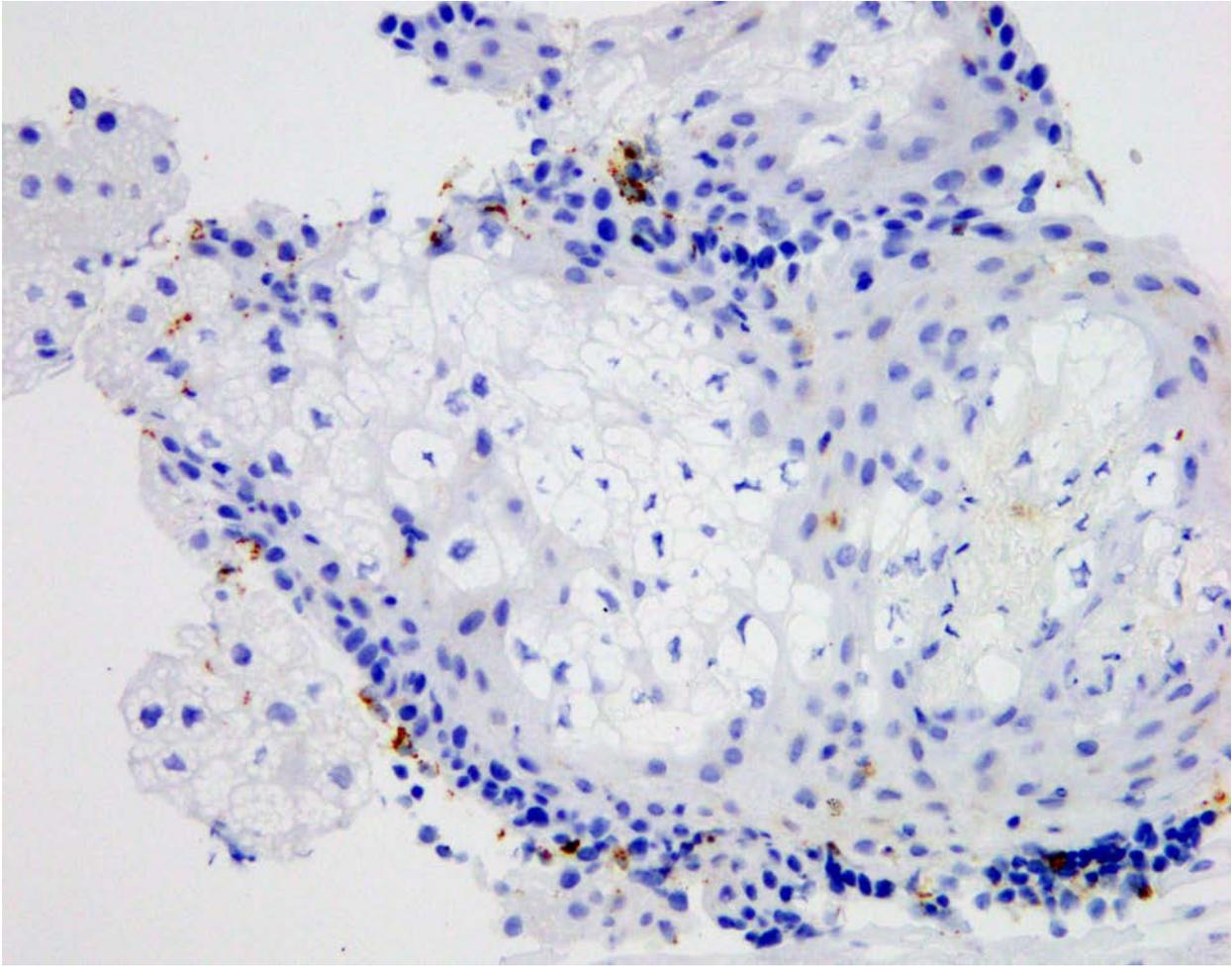


Figure 6; CD68 stain, 200x

Question: Based on the morphology and special stains, what is the diagnosis?

- A. Glycogenic acanthosis
- B. Granular cell tumor
- C. Lipoma
- D. Paget disease
- E. Sebaceous gland heterotopia

Answer: E. Sebaceous gland heterotopia

The biopsies show a focus of large polygonal cells with small nuclei and abundant clear microvesicular vacuolated cytoplasm, present within a fragment of squamous epithelium. They are arranged in a lobular configuration. The adjacent squamous epithelium is otherwise unremarkable, without inflammation in this case. Immunohistochemical and special stains show that the cells are positive for cytokeratins and negative for CD68 and PAS. The findings are diagnostic of sebaceous gland heterotopia of the esophagus.

Sebaceous gland heterotopia is an uncommon finding in the esophagus, with an incidence of <0.005% based on endoscopy studies (1). An older study found it as an incidental finding in 4 out of 200 autopsies (2). Characteristically, sebaceous gland heterotopia is seen as lobules of sebaceous glands within the esophageal squamous mucosa that can be surrounded by mononuclear inflammation. They may communicate with the surface epithelium *via* a squamous-lined duct. No associated hair follicle is seen. Sebaceous gland heterotopia is a benign entity, without potential for malignant transformation. No syndromic link has been postulated either. Although the histogenesis of heterotopic sebaceous glands in the esophagus is unclear, it is hypothesized that they are a metaplastic process rather than a congenital anomaly, due to the endodermal origin of the esophagus and the ectodermal origin of sebaceous glands (3).

No specific symptoms are associated with sebaceous gland heterotopia (4). Most cases are discovered incidentally during endoscopy, appearing as yellowish plaques. The endoscopic differential diagnosis includes xanthomas, glycogenic acanthosis, candidiasis, and papillomas. One study showed a mean age of affected patients of 55 years (range: 39-69 years), with a slight male predominance (5). The number of heterotopic sebaceous glands varied from single to more than 100 and ranged in size from 1-20 mm, with the majority smaller than 5 mm (6).

Glycogenic acanthosis can present endoscopically similarly to sebaceous gland heterotopia, as an incidental white plaque. However, on histology, glycogenic acanthosis displays glycogen accumulation in the squamous cells themselves, which stains with PAS (in contrast to our case).

Lipomas along the gastrointestinal tract most commonly occur in the large and small intestine, only very rarely occurring in the esophagus. About 90% of these lesions are located in the submucosa (7). In contrast, heterotopic sebaceous glands are located within the squamous epithelium. Lipomas show a uniform population of benign-appearing adipocytes, whereas sebaceous cells display microvesicular vacuolated cytoplasm.

Paget disease of the esophagus is an extremely rare entity, with only a handful of reported cases. It is characterized by infiltrative malignant glandular cells in the squamous mucosa, present as single cells or in small clusters.

Granular cell tumors of the esophagus are most commonly submucosal and consist of sheets of cells with amphophilic granular cytoplasm and small nuclei. The vast majority of cases are benign. In contrast to heterotopic sebaceous glands, the cells stain with PAS and immunohistochemically for S100.

References

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