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CASE REPORT

Esophageal squamous cell papilloma in a child with cystic fibrosis: A rare incidental endoscopic finding

Kistik fibrozis tanılı bir çocuk hastada saptanan özofageal skuamoz hücreli papillom: Nadir ve insidental bir endoskopik bulgu

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Esophageal squamous cell papilloma is an uncommon epithelial lesion of the esophagus. Epidemiological data regarding esophageal squamous cell papilloma in children is scarce and consists of few case reports. Although the etiology of esophageal squamous cell papilloma remains unclear, chemical/mechanical irritation induced hyper-regenerative response of esophageal mucosa and human papillomavirus infection have been suggested as most probable causes. A case of a 14-year-old girl with cystic fibrosis and chronic dyspepsia had a 0.5 x 0.5 cm sessile, multilobulated, whitish and verrucous polypoid mass close to the lower esophageal sphincter removed. Histologically, a benign squamous papilloma was confirmed. Her dyspeptic symptoms suggestive for gastroesophageal reflux resolved after papilloma removal and anti-acid treatment. Esophageal squamous cell papilloma is an incidental finding at upper endoscopy. Gastroesophageal reflux disease may be responsible for distally localized papillomas. Due to its rarity in childhood, there are not any well-established management and surveillance guidelines. Esophageal squamous cell papilloma should be removed, when possible, because of the ambiguity about its malignant potential.

Key words: Squamous papilloma, esophagus, gastroesophageal reflux, cystic fibrosis, esophagogastroduodenoscopy, dyspepsia

Özofageal skuamoz hücreli papillom, özofagusun nadir görülen bir epitel lezyonudur. Çocuklarda özofageal skuamoz hücreli papillom ile ilgili epidemiyolojik veriler kısıtlıdır ve birkaç vaka raporundan oluşmaktadır. Özofageal skuamoz hücreli papillomun etiyolojisi belirsizliğini korusa da, özofagus mukozasının kimyasal/mekanik tahrişe bağlı gösterdiği hiper-rejeneratif yanıt ve human papillomavirus enfeksiyonu en olası nedenler olarak öne sürülmüştür. Kistik fibrozisli ve kronik dispepsisi olan 14 yaşında bir kız çocuğunda alt özofagus sfinkterine yakın lokalizasyonda 0.5 x 0.5 cm boyutlarında, sesil, multilobüle, beyazımsı ve verrüköz polipoid lezyon çıkarıldı. Histolojik olarak lezyonun benign skuamoz papillom olduğu gösterildi. Hastanın gastroözofageal reflü düşündüren dispeptik semptomları, lezyonun çıkarılması ve anti-asit tedavi sonrası düzeldi. Özofageal skuamoz hücreli papillom, üst endoskopide insidental olarak saptanan bir bulgudur. Distal özofageal yerleşimli papillomlardan gastroözofageal reflü hastalığı sorumlu olabilir. Çocuklukta nadir görülmesi nedeniyle, yönetimi ve takibiyle ilgili rehber önerileri yoktur. Malignite potansiyeli konusundaki belirsizlik nedeniyle mümkün olduğunda çıkarılmalıdırlar.

Anahtar kelimeler: Skuamoz papillom, özofagus, gastroözofageal reflü, kistik fibrozis, özofagogastroduodenoskopi, dispepsi

INTRODUCTION

Esophageal squamous cell papilloma (ESCP) is an uncommon epithelial lesion of the esophagus that was first described in 1959 by Adler (1). ESCPs are incidental lesions found at upper endoscopy or at autopsy and extremely rare in children. Although the etiology of ESCP is still a debate, chronic mucosal inflammation, and human papilloma virus (HPV) have been suggested to be responsible (2). Here, we report a case of a cystic fibrosis patient with chronic dyspepsia whose upper endoscopy revealed an ESCP.

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CASE REPORT

The patient was a 14-year-old girl with the diagnosis of cystic fibrosis. She was suffering from recurrent abdominal pain and had symptoms suggestive for gastroesophageal reflux. Her physical examination was normal. Routine etiologic evaluation for chronic dyspepsia including laboratory and imaging tests were inconclusive. Upper gastrointestinal system endoscopy revealed mild duodenogastric bile reflux, antral hyperemia and a 0.5 x 0.5 cm sessile, multilobulated, whitish and verrucous polypoid mass close to the lower esophageal sphincter (Figure 1). In addition to the removal of the polypoid lesion by cold forceps, routine tissue sampling from other parts of the upper gastrointestinal tract (one biopsy from each part; distal esophagus, corpus, antrum, duodenal bulb and second portion of the duodenum) was performed as suggested by current guidelines. No specific pathological finding was observed in mucosal specimens from esophagus, stomach, and duodenum. *Helicobacter pylori* was negative in gastric and duodenal specimens. Histopathological evaluation of polypectomy material was consistent with squamous papilloma (Figure 2A). Papilloma was composed of non-keratinizing squamous epithelium and no koilocytic or dysplastic change was observed. HPV infection was not detected in the papilloma. Surrounding esophageal mucosa was histologically normal with no inflammatory cell infiltration (Figure 2B). There was also no pathologic eosinophilia in the esophageal, gastric, and duodenal mucosa. Peripheral blood did not show eosinophilia at the time of procedure and the patient never had eosinophilia during her follow-up. Recommendations regarding dietary modification and body positioning were given to the patient and proton pump inhibitor therapy was started. Her symptoms were resolved on the follow up without any additional intervention. Informed consent was obtained from her parents.

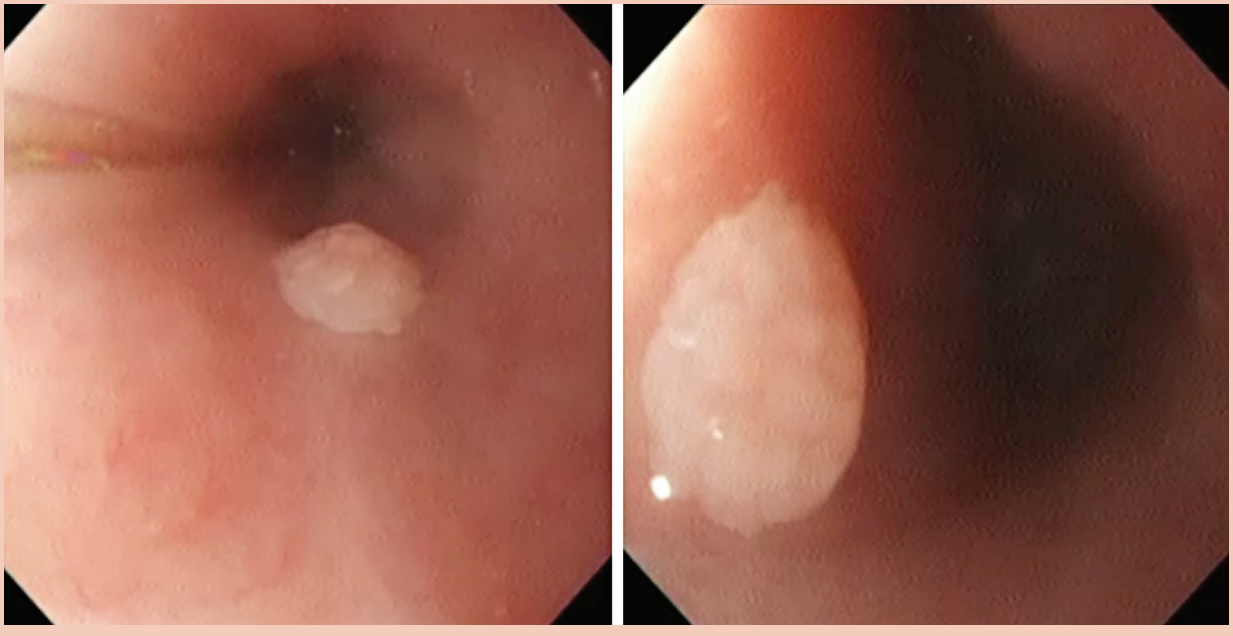

Figure 1. Endoscopic view of squamous papilloma in the distal esophagus of the patient.

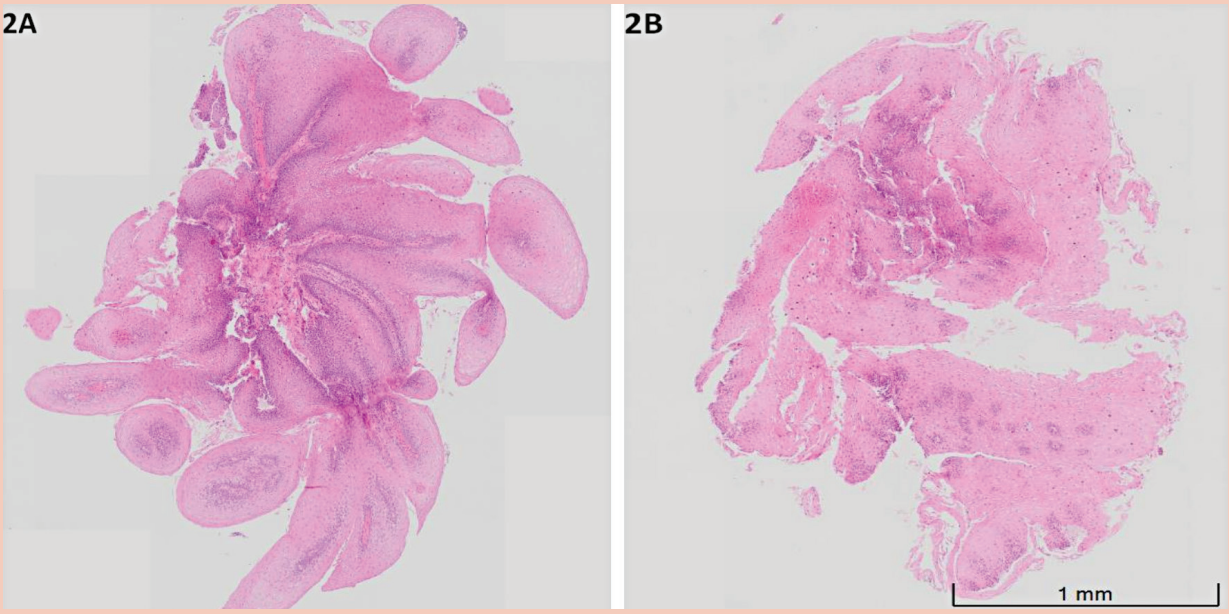

Figure 2. Histopathologic findings of esophageal biopsies. **2A.** Papillary projections lined by squamous epithelium with a fibrovascular core (hematoxylin and eosin, 4x). **2B.** Normal esophageal mucosa surrounding the papilloma (hematoxylin and eosin, 4x).

DISCUSSION

The estimated prevalence of ESCP in adult population was reported to be less than 1% in different series (3). However, epidemiological data regarding ESCP in children is scarce and mainly consists of case reports. The largest case series of ESCP in the pediatric population provided an estimated prevalence of 0.08% through a 15-year study period which approximates to 0.17% in the last 5 years of the study period indicating an increasing prevalence in time (4). The etiology of ESCP remains unclear. Chemical/mechanical irritation induced hyper-regenerative response of esophageal mucosa and HPV infection were held responsible for ESCP (5). Direct mucosal trauma (nasogastric tubes, bougienage for benign stricture, placement of a self-expanding metal stent, variceal sclerotherapy, and chronic food impaction), alcohol consumption, cigarette smoking, previous gastroesophageal surgery, hiatal hernia, and especially gastroesophageal reflux disease (GERD) have been reported to be associated with ESCP in various studies (6). The role of HPV infection in the pathogenesis of ESCP is controversial (7). HPV prevalence in esophageal papillomatous tissue was reported to be 0% - 87% in different studies (8). In the largest pediatric case series, among 12,459 children who required an upper endoscopy only 10 cases were identified with ESCP. None of the cases were tested positive for HPV and the authors concluded that reflex testing for HPV may not be beneficial nor cost effective in children (4). Among possible etiologies, GERD was the most likely cause of squamous papilloma in our patient as she had no risk factors for direct mucosal trauma, no exposure to alcohol or cigarette smoke, no history of abdominal surgery or anatomical anomaly and no histologic finding suggestive for HPV infection. She also had typical symptoms highly suggestive for GERD including heartburn and epigastric pain. In focal dermal hypoplasia, a genetic disorder known to be associated with the formati-

on of squamous papillomas, the esophageal papillomas are hypothesized to be related to the high frequency of severe gastroesophageal reflux starting in infancy (9). A potential association between esophageal papillomas and eosinophilic esophagitis has been recently reported in a pediatric case with focal dermal hypoplasia (10). The patient we present here had a single papilloma in the distal esophagus and did not have eosinophilic esophagitis and dermal hypoplasia. *H. pylori* infection was also suggested as a potential underlying etiology in one study reporting a 10-year-old child with ESCP (11). However, there has been no further evidence indicating an association between *H. pylori* gastritis and ESCP in the pediatric and adult literature. Although her symptomatology was suggestive for a possible *H. pylori* gastritis, our patient's biopsy specimens were negative for *H. pylori*.

There is no pathognomonic finding for ESCP at endoscopic evaluation. However, ESCP usually appears as a well delineated, round, sessile, verrucous-looking lesion, whitish or pinkish in color, with a soft consistency and a smooth or slightly rough surface (5). Although ESCPs are usually solitary and small (2 – 6 mm in diameter), there are reports of giant esophageal papillomas (up to 5 cm) or esophageal papillomatosis (12,13). The localization of the lesion seems to be associated with underlying etiology. While distal esophageal papillomas are likely to be associated with acid reflux, HPV is detected in a variable percentage of mid- and upper esophageal papillomas and in cases of esophageal papillomatosis (2). Lower third of the esophagus has been reported to be the main site for esophageal papilloma localization (6). However, higher prevalence in the middle esophagus was also reported from different centers in Europe and Asia (6,14,15). The results of the largest adult case series from Turkey also pointed the middle esophagus as the most frequent location of ESCPs indicating that there was no relationship between ESCP and GERD (16). However, localization of our patient's papilloma close to the lower esophageal sphincter is another factor pointing a possible role of GERD in etiology. Differential diagnosis of ESCP include glycogenic acanthosis, verrucous border of squamous cell carcinoma, verrucous carcinoma, fibrovascular polyp, inflammatory fibroid polyp, leiomyoma, granular cell tumor, squamous cell carcinoma and malignant melanoma most of which are also very rare clinical conditions in children.

ESCPs are most often asymptomatic and usually diagnosed incidentally at esophagogastroduodenoscopy performed for non-specific symptoms. However, mechanical obstruction due to giant or multiple papillomas can be seen and patients may present with dysphagia in early childhood (17). We cannot directly relate our patient's symptom resolution to ESCP removal as she also received acid suppressive treatment for GERD and duodenogastric bile reflux. Although it is widely accepted as a benign condition, there have been anecdotal reports suggesting an association between ESCP and squamous cell cancer in adults (18). More intensive evaluation of patients with large or multiple squamous papillomas has been proposed as lesions may have malignant potential (19). There has not been any report regarding malignant transformation of ESCP in the pediatric literature.

To the best of our knowledge, this is the first report in pediatric and adult literature regarding ESCP in a cystic fibrosis patient. GERD is a common manifestation in pediatric cystic fibrosis patients with a reported prevalence of 27-81% (20). The relationship between squamous cell lesions and GERD in cystic fibrosis has not been reported in children. However, higher prevalence of GERD in cystic fibrosis patients might be related with development of ESCP in this patient population. The distal localization of the lesion, the absence of other significant mechanical/chemical irritants, negative histologic findings for HPV infection, and higher

prevalence of GER in cystic fibrosis patients than normal population leave GER as the most probable cause for ESCP in our patient. Endoscopic appearance and histology of the adjacent esophageal mucosa were normal in our patient. However, neither normal macroscopic appearance nor the absence of histological abnormalities can sufficiently rule out the presence of GERD in children. It would be optimal if we could perform a pH-impedance testing to evaluate the presence and nature (acidic or alkaline) of gastroesophageal reflux in our patient however, a trial of proton pump inhibitors in the presence of typical symptoms like heartburn and epigastric pain for a definite duration (4 to 8 weeks), as we practiced in our patient, is also a suggested diagnostic test for GERD in children (21). The relief of patient's symptoms with anti-acid treatment and lifestyle modification is suggestive for GERD in our patient.

In conclusion, ESCP is an incidental finding at upper endoscopy. GERD may be responsible for distally localized papillomas. Due to its rarity in childhood, there are not any well-established management and surveillance guidelines. ESCP should be removed, when possible, because of the ambiguity about its malignant potential although no malignancies associated with ESCP was reported in children to date to the best of our knowledge. As upper endoscopy in children is a relatively invasive procedure, awareness of this lesion by the endoscopist is critical for the decision of removal at the time of endoscopy and for avoiding further unnecessary intervention.

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Informed consent: *Written informed consent was obtained from the patient's parents for publication of this case report.*

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